EMBRYOLAB ACADEMY

NEWSLETTER

QUARTERLY EDITION ABOUT THE NEWS AND ACTIVITIES OF EMBRYOLAB ACADEMY

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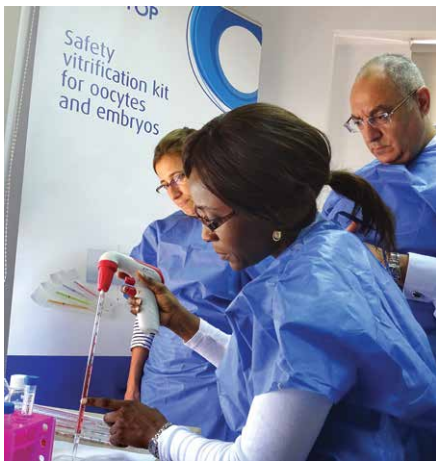

Embryolab Academy: blazing the trail internationally

Embryolab Academy has been setting down a rather impressive track record, both in Greece and abroad since 2013. In 2017 it held two educational seminars on the subject of preimplantation genetic diagnosis in St. Petersburg, Russia, and as an invitee visited India.

Preimplantation genetic diagnosis is a new, very dynamic area of activity in assisted reproduction. There have been a number of significant scientific advances recorded in this field, both at the technical and a diagnostic level. As far as concerns the technical, a global shift has taken place from day 3 biopsy to day 5 biopsy (blastocyst).

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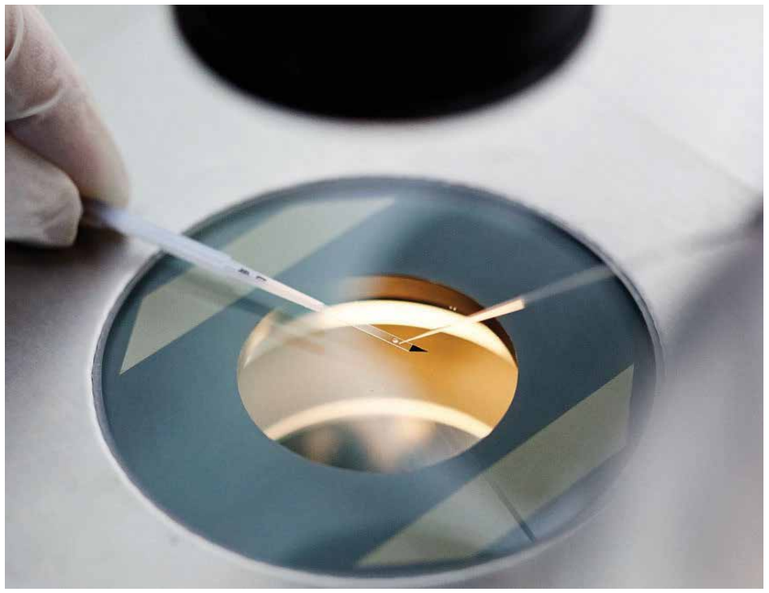

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Embryolab Academy: blazing the trail internationally

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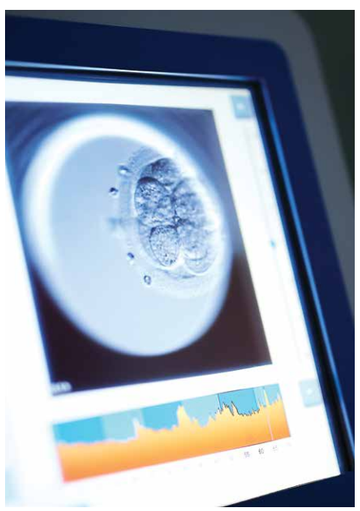
The new data indicate that a biopsy at the blastocyst stage is not only less harmful for the embryo but also provides greater assurance in the result. These data led to a more systematic application of day 5 biopsy on a global level and to the gradual withdrawal of the day 3 biopsy method, which until recent times had been applied in approximately 83% of all cases. This shift has created the need for young scientists to be trained in the blastocyst biopsy technique. And indeed this is where the Embryolab Academy has risen to the challenge in 2017, following an invitation to train scientists from throughout Russia. The Academy, true to its vision to train and promote communication among scientists, undertook to train around 35 scientists from the length and breadth of Russia.

A further important event in our Academy's calendar for 2017 was the Academy's participation at the annual FEMM Conference in Mumbai, India, where it was invited to speak about the application of quality systems and effective risk management in assisted reproduction laboratories, as well as about the effectiveness of preimplantation genetic diagnosis. Indian scientists were greatly interested in the Academy's activities, establishing the pursuit of a new common course aiming to educate and to promote knowledge.

To date, the Academy has visited many destinations around the world. This year it has completed 4 years of activities, remaining true to its initial purpose, to assemble scientists from around the world and to train them in the new Assisted Reproduction methods.



Low fertility requires a personalised approach

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Over recent years, significant progress has been made at countering low fertility. As a result, increasing numbers of couples are systematically seeking out the options available so as to achieve pregnancy and a healthy child. Nevertheless, concerns are often expressed by such questions as, 'Do I need this specialised test?' 'Will I benefit from having this new treatment?' and so on.

It is a fact that reproductive medicine has in large measure utilised the results of clinical research, and applies ever more innovations in everyday clinical practice. However, it is not certain that each new discovery and each breakthrough in treatment will be of benefit to all couples facing low fertility problems. What is important is that for each couple indicative diagnostic tests are performed and that individualized treatment and methods to overcome low fertility are implemented. This approach, known as 'personalised reproductive medicine', enjoys the benefits of modern medical research, adapted to each individual case. Thus, we are gradually moving away from the older approach of 'one size fits all'.

To be more specific, we can now adapt the ovarian stimulus protocol for IVF based on the Anti-Mullerian Hormone (AMH), an ovarian reserve index, which is easily measured and helps us to tailor the protocol and treatment dosage to be used. Thus, IVF protocols have been tailored for the individual, resulting in a higher pregnancy rate, while at the same time keeping the hyperstimulation syndrome (OHSS) rates very low.

Another instance of personalised medicine to counter low fertility is the application of time-lapse technology, which allows for embryologists to best monitor embryos throughout culture duration in the laboratory. Older women who have a history of failed attempts through IVF will benefit most from this technology, as will those couples with serious male-factor low fertility.

Preimplantation genetic diagnosis is another relatively recent laboratory technique available, providing important diagnostic data regarding the chromosomal structure of embryos. Though not frequently used for younger couples, due to the reduced likelihood of chromosome abnormalities, it is an important tool for treating older women. These women will benefit enormously from embryo transfer, following IVF, of an embryo with normal chromosomes. Thus, in this way, miscarriages are limited, as well as the concomitant reduction in stress, which might otherwise have resulted.

Hysteroscopy, in conjunction with endometrial biopsy can provide useful data when there are signs of polyps, fibroids or implantation problems, such as chronic inflammation of the endometrium. Once again, a careful evaluation of patient history and previous IVF attempts at will permit the use of the most suitable option.

Since practitioners in reproductive medicine aim to achieve yet higher pregnancy rates, it becomes increasingly important that they can fulfil this objective with the least number of operations and at the lowest possible cost. Personalised reproductive medicine represents very much the new chapter in the history of assisted reproduction, and it is certain that couples with fertility difficulties have significantly benefitted.

"Over recent years significant progress has been made in countering low fertility. As a result, an increasing number of couples are systematically seeking out the options available so as to achieve pregnancy anda healthy child.

Duly marked
For a... marker

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Stelios sounded upset on the other end of the phone: 'They said that maybe I was 'daft' but I'm not!!!' He had just received the results of the karyotype, the genetic test we had asked him to do. I clutched at the phone and quickly sat down to stop myself falling down in shock. I asked him to send me the results by email. I endeavored to calm him down, arranging a meeting for the next day at the Unit. Once again, I felt my hand freeze on the door handle as I opened it. The look on the couple's faces seemed to be saying, 'how could this have happened to us'... How does one's finger pause over the last number to take one last deep breath before calling to explain, even 'apologise' regarding the risk the embryo has of producing problems... However much one might learn about chromosomes, genetic material, its markers, the analysis and decoding of it, you have still much to learn about people's eyes, their anxious hand-wringing, the pursed lips, and your effort to manage your own emotions when the explanations are upsetting, tough, inadequate...

Fortunately the email arrived promptly and things started to become clearer. A small added piece of genetic material had been located, a marker in the chromosomes. In human cells the DNA is arranged in string-like structures, the chromosomes forming pairs. Normally we have 46 chromosomes and geneticists use the description of 46 for the karyotype, XX for women, XY for men. In the human karyotype with a certain addition, a 47th small piece appears, described as a chromosome marker (e.g.47, XY, +mar). This extra piece may derive from any one of the 24 chromosomes, which are described arithmetically 1-22 and as X or Y, those which determines the sex.

They may be described in different ways: sSMC (small supernumerary marker chromosome), ESAC (extra structurally abnormal chromosome), SRC (supernumerary ring chromosome), for the same thing: a chromosome marker, with certain characteristics which usually relate to its shape.

What is the impact of sSMC?

Such a marker may have different results. Most human carriers, around 70% grow up and develop naturally without health issues and are usually uncovered by chance in a karyotype check. Some however manifest problems in development, learning, behavior and perception which regularly are related to a syndrome. For example, when a marker includes material from the small arm of chromosome 12, or a specific area from 18 or 22 and 11. In general, today we cannot predict with certainty or precision the manifestation-phenotype for all chromosome markers detected, as new cases are being described internationally. Our data bases permit us to compare corresponding cases already described before we proceed.

What can a marker actually mean?

If one of the parents has the same marker and he or she is in good health, it is highly probable that whichever of his/her children have this marker will be similarly healthy. That is the general rule, though there are numerous exceptions, and, regarding these, we need to know on each occasion the makeup of the genetic material the identified marker contains. Modern molecular techniques now allow for the complete analysis of such markers, revealing the presence of genetic material, whether significant or not so significant, for the development and functioning of the organism. This information is both vital and valuable. Only in this way can we compare each instance with corresponding ones that have been described, and then we can answer the question with greater assurance.

Finally, it is important to explore the probability of the phenomenon of uniparental disomy (UPD) appearing in the rest of the material. In this case, the two completely regular chromosomes which correspond to the marker have been inherited from the same parent (e.g., the mother) and only the small part of the marker from the other parent (e.g., the father). This phenomenon is found in 5-10% of people with sSMC and is particularly significant for chromosomes 6, 7, 11, 14, 15 and 16.

Can a marker va affect fertility?

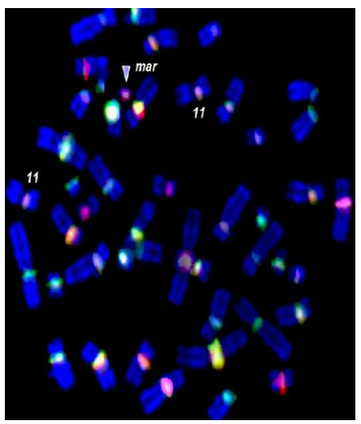
Generally, identifying sSMC justifies and is related with problems concerning fertility and multiple miscarriages, occurring three times more frequently in couples with low fertility. In a number of cases, the extra chromosome has been inherited by one of the parents, confirming the possibility that people with sSMC can in fact have children themselves. Some of their children may inherit the marker, while others will have the normal number of chromosomes, without the presence of a marker. In any case, the probability of inheriting the marker from the mother is almost double than that from the father-carrier, since the marker is usually 'lost' in the process of the sperm maturation.

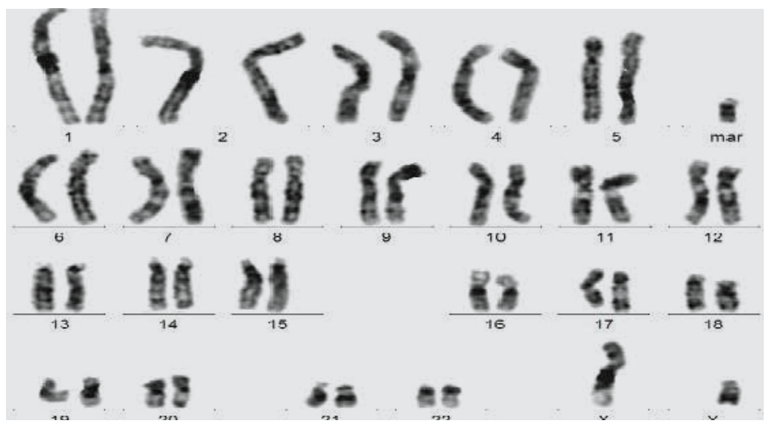
Furthermore, it has been observed that sSMC occurs more frequently in men with fertility problems than in women. This is usually observed as a decrease in the number of sperm (oligospermia), as well as problems in morphology and motility, that is oligoasthenoteratozoospermia (OAT). Men with OAT possess chromosome markers at a rate of 7% without us knowing the way in which the marker affects fertility each time, since only 30% of cases contain genetically significant information.

Fertility problems may be overcome by IVF treatment. For the risk regarding the phenotype which may appear in children, there is the choice of both the prenatal and the preimplantation test, particularly for cases where IVF is chosen due to low fertility.

Stelios joined us in our meeting with Maria and we discussed the issue. The small chromosome marker, despite the initial shock, eventually provided solutions to the problems he had with his sperm and illuminated paths that had once looked dark. It is true that in certain cases the small marker can be linked with developmental problems, but Stelios did not belong to this category, since he had inherited this from his healthy mother. Another instance where genetic analysis requires the services of the genetic advisor to ensure that it is more understood and useful.

Material used from:
http://ssmc-tl.com/sSMC.html
http://markerchromosomes.wg.am
www.rarechromo.org





Tubal factor infertility (TFI) as a low fertility factor

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According to the World Health Organisation, low fertility constitutes a health disorder requiring particular measures. Today in developed countries around 1 in 5 couples are subject to low fertility. Of these, in 25-30% of cases, low fertility is linked to women, another 25-30% is linked to men, while 20% of instances is linked to both partners, and finally around 15% describes no specific cause, meaning that these couples have unexplained low fertility.

The tubal (fallopian) element accounts for the second highest factor of low fertility in women. The fallopian tubes are two thin tubes of the female reproductive system, through which takes place fertilisation of the oocyte by spermatozoa followed by its transfer into the uterus, where the embryo develops. The dysfunction of the fallopian tubes is mainly attributed to inflammation from ascending infections of the reproductive organs or from surgical operations such as appendicitis and operations of the intestine. As a result of the above, symphysis is created, which produces stenosis and/or blocking of the fallopian tubes as well as damage to the epithelium or liquid collection as the consequence of endopelvic inflammation (hydrosalpinx, pyosalpinx). There are three factors which may affect the function of the fallopian tubes: mechanical, embryotoxicity and factors which influence functioning of the endometrium. The fallopian tube test is performed by the hysterosalpingography (HSG) or through diagnostic laparoscopy. Treating conditions of the fallopian tubes is personalized and performed non-invasively (medication) or surgically (laparoscopy).

IVF treatment is the method of choice to counter low fertility stemming from TFI. Though the most common cause of fallopian dysfunction is tube obstruction (mechanical factor), one would expect that with IVF treatment the effectiveness of this method would be greater compared with other causes of low fertility. In studies carried out comparing the results among couples of a similar age and body mass index who chose IVF because of TFI and others who had other factors such as male infertility factor, endometriosis, polycystic ovaries, anatomical complaints and ovulation disorders, it was found to have a similar effectiveness. The likely explanations as far as concerns the male infertility factor is the application of micro insemination which markedly increased the effectiveness of the method in recent years, and that were comparable with other causes of low fertilization. In cases of fallopian tube conditions apart from the mechanical causes, it would appear that the presence of symphyses affect the blood supply to the ovaries and consequently the quality of the oocytes and perhaps this explains the similar results compared with women who experience ovulation disorders or endometriosis. Finally, among women suffering from fallopian tube conditions, the production of inflammatory and toxic factors which harm the function of the endometrium seems to be the principal reason for the failure of implantation of the fertilized oocyte.

To sum up, it would appear that IVF has similar results on couples with different low fertility factors, and that more studies are needed to help us understand better the mechanisms which influence the result, which is the birth of a healthy child.

New data Regarding low male fertility

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'Each piece of knowledge which is added
Is an addition to human strength'
Horatio, 1st cent. B.C.

With the above words in mind, reference shall be made to new knowledge, which comes to be added to the old in the field of low male fertility, including the latest instructions regarding its diagnosis and treatment.

With the above words in mind, reference shall be made to new knowledge, which comes to be added to the old in the field of low male fertility, including the latest instructions regarding its diagnosis and treatment.

The precise diagnosis of the causes of low male fertility is very much the corner stone to devising a better, more effective and scientifically documented treatment. It is at first vital to get a detailed patient history, a clinical-andrological assessment, a semen analysis, while the usefulness of the Sperm DNA fragmentation assessment is questionable. Since there is a dual testicular function, that of spermatogenesis and androgen production, a detailed endocrinological assessment is very important. A genetic assessment is also essential in some instances, since certain genetic conditions are linked to low fertility. An ultrasound assessment of the male reproductive system is essential for men with oligospermia or azoospermia, as these are regarded as risk factors in the occurrence of neoplasms in the testicles and also for the manifestation of other pathological conditions in the anatomy of the male reproductive system.

The therapeutic approach towards the less fertile man must initially aim to limit or remove the exogenous factors which can influence the production, function and transfer of the sperm, the activation of the testicular function, the surgical treatment of anatomical problems and the surgical discovery of spermatozoa to be used in IVF.

Recent studies have presented the adverse environmental impact and the modern lifestyle has had on sperm count. Over a period of 38 years (1973-2011) a drop in male sperm count in the developed world to the tune of 52.4% (1.4% annually) was recorded. It has now been documented that the quality of sperm is damaged by smoking, alcohol consumption, various narcotics, obesity, high-energy diets, fried food, stress and most likely mobile phone use. Also, the consumption of large amounts of caffeine has been correlated to the increase in reproductive damage to sperm and cola consumption to the drop in the volume of sperm.

The significance of the man's age at reproduction should also be mentioned here, since according to recent data, mutations in reproductive cells increase with the increase in the father's age. In the past there was a correlation between a man over 45 years of age and the greater frequency of miscarriages and premature births with genetic syndromes and related abnormalities as well as to a higher incidence of childhood cancers. More recent data related the increase in the father's age with autism spectrum disorder together with behavioural disorders, such as attention deficit and hyperactivity. Consequently, not only should the woman but also the man make a timely decision on starting a family not only for social reasons but also on medical grounds.

Mild treatment in daily clinical practice

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'Bombs don't always win the war'

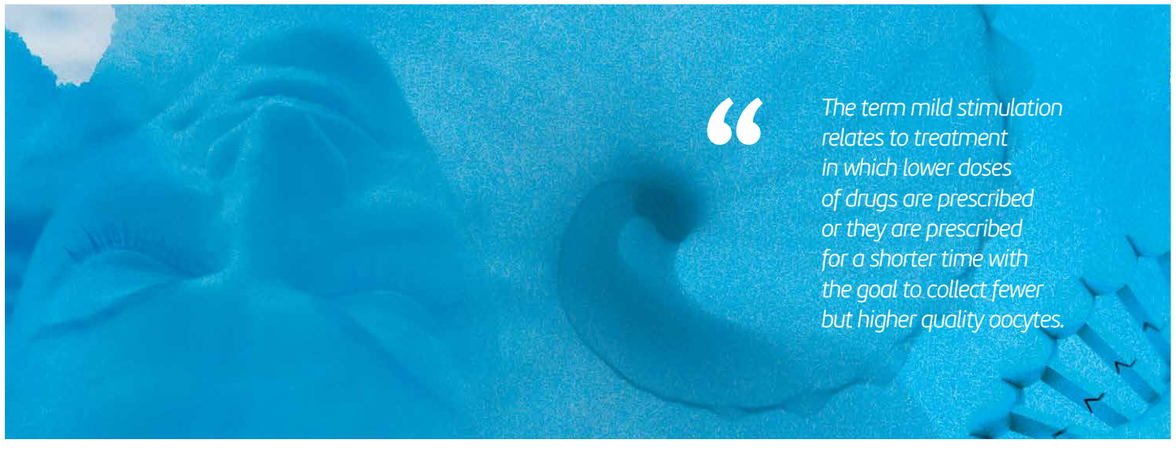
It has been almost forty years since the birth of Louise Brown, the first child born by in vitro fertilization (IVF), and despite the passage of time the basic principle of the therapy remains unchanged to this day. Globally, the essential effort is to find the ideal means of stimulating the ovaries in order to boost the number of oocytes, and by extension the embryos a couple has, in the belief that in this way the probabilities of success will rise. Such an approach of course has begged some questions. Is the goal of ovarian stimulation simply to create as many oocytes as possible? Is there any 'cost' to the body related to ovarian stimulation, and if, yes, what? Is it that by increasing the quantity of oocytes in one treatment the quality of the resulting embryo is affected? And finally, is there a way of tailoring the treatment for the individual patient?

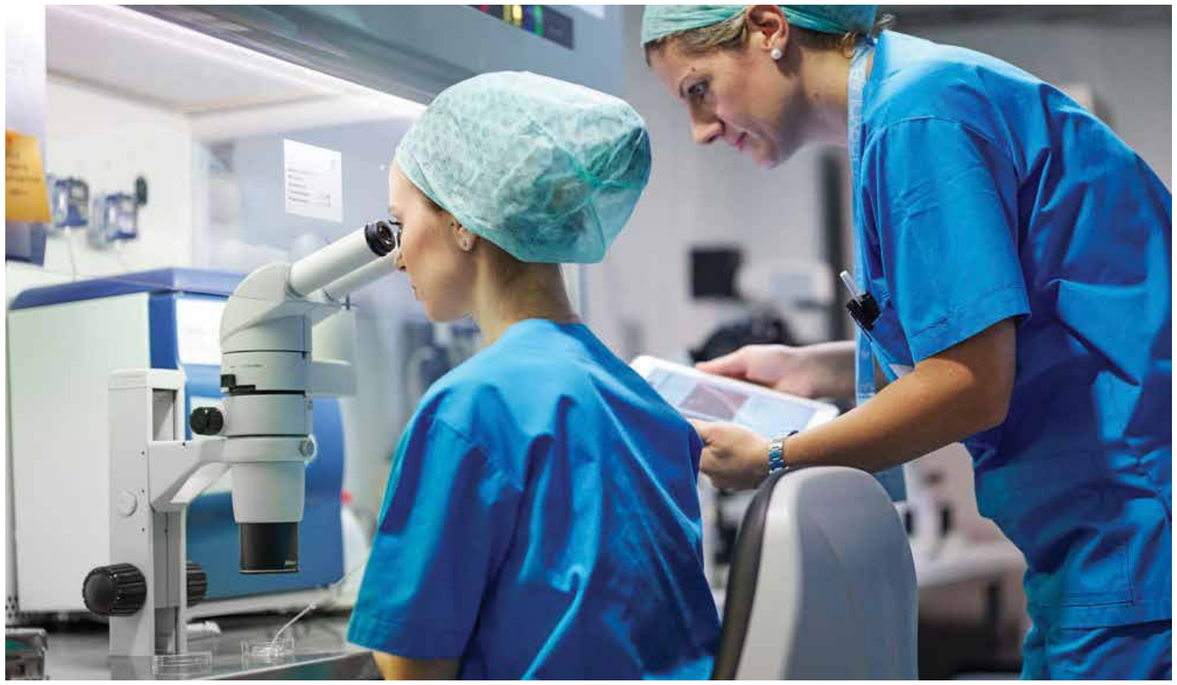
The continuing need for safe treatment has led to the revival of more mild and natural ways to stimulate ovaries. The term mild stimulation relates to treatment in which lower doses of drugs are prescribed or they are prescribed for a shorter time with the goal to collect fewer but higher quality oocytes. Mild ovarian stimulation has gained recognition as the safest, least expensive and most patient-friendly choice. There is certainly a tendency towards scepticism in the medical community - more down to doubts regarding its effectiveness.

The basic rationale behind mild treatment, is that, due to mild stimulation, only the healthiest ovarian follicles with the most able oocyte will develop. Indeed, there have been a greater number laboratory indications that mild treatment creates a more natural and friendly environment for oocytes to develop and later the embryo inside the uterus. It would seem in any case that by applying these methods both for patients with a good prognosis and for those with a low response, does not affect the success rate. What then are the advantages of mild ovarian stimulation?

The first and perhaps most important advantage is the better safety profile of this treatment. The Ovarian Hyperstimulation Syndrome and multiple gestations are the basic risks of IVF. To present, our data presents a significantly smaller occurrence of Ovarian Hyperstimulation Syndrome in women who underwent mild treatment. On the other hand, the eclectic embryo transfer is the most effective strategy to avoid multiple gestations. Indeed, better quality embryos and a milder endometrial environment deriving from mild ovarian stimulation could lead to a very successful course of treatment. The second advantage of mild treatment is the better perinatal profile of children born as well as its mother-friendly aspect. On the other hand it would also appear that women undergoing mild treatment have much less likelihood of giving birth prematurely and also their new-born's final weight is better. Further, mild treatment drastically reduces any psychological stress which arises and makes all the procedure more bearable and straightforward. By avoiding high drug intake, mild ovarian stimulation may also reduce the cost of any pharmaceutical treatment and thus allow the price of treatment to be within the grasp of couples even on lower incomes.

More and more IVF using mild ovarian stimulation is proven to be a safer, more bearable, woman-friendly and less expensive treatment. There are also growing evidence that it is just as effective as the conventional IVF treatments. It is thus imperative that we weigh up the merits of this treatment which might well greatly reduce the physical, emotional as well as financial impact on couples while at the same time producing an improved perinatal result, both for the mother and the child.





The significance of oocyte capture

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In recent years developments in technology accompanied by developments in medicine have brought about significant changes in a number of areas. One of these has been in IVF, which has been ever evolving at the laboratory as well as the medical level (new IVF protocol – introduction of new, more effective drugs).

The egg collection is done through oocyte retrieval procedure, which is one of the most important stages of IVF treatment. Each oocyte (egg) is important because it has the potential to produce an embryo which will result in a pregnancy.

The oocyte capture procedure is performed under mild sedation and entails certain stages requiring particular caution. The first step is rendering the vagina antiseptic, followed by egg collection, performed through a special needle which is fitted to the transvaginal ultrasound probe, which sucks up the contents of each ovarian follicle. The whole procedure requires care to avoid harming fibres adjacent to the ovary and to prevent any serious complications (intraventricular hemorrhage from accidental vessel injury – peritonitis resulting from a punctured intestine). Finally we should stress that oocyte capture is completed by the drawing in of all the ovarian follicles and diligent hemostasis in the vagina.

Oocyte capture and the significance of collecting every egg is vital for all women subject to IVF and the utmost possible safety in all stages of treatment should be assured.

40 years of Assisted Reproduction

As a part of European Fertility Week (6-12 of November), we are celebrating 40 years of assisted reproduction in an event arranged to inform the public in collaboration with the Association of Fertility Support, KYVELI, the Fertility Europe Organization, and the vital support of AHEPA. The general public as well as a large number of students attended the event.

In this event, IVF specialists and representatives of the Association, KYVELI gave a presentation on the various milestones in IVF, the clinical and lab practices, the efforts and everyday stories of couples in IVF, and provided advice and the choices available regarding fertility, low fertility, psychology and diet.

From 1978 until the present day more than 6,500,000 children around the world have been born thanks to the treatments and techniques of assisted reproduction.

Mrs Alexia Chatziparasidou, Sr. Clinical Embryologist and Director of Embryolab declared that, 'We are here to ensure the creation of a family as a basic right of every person. The science which we develop and the technology we apply offer solutions for couples and the dream of life becoming reality'.

'We are living in a new era in IVF, being equipped with new drug technology, the technology of recombinant DNA, micro- fertilization, cryobiology, genetics, and the list goes on... And also there is 'personalized reproductive medicine', which opens up a new chapter in the history of assisted reproduction, and it is certain that couples with fertility problems will benefit enormously' (Clinical Director of Embryolab and Assisted Reproduction Gynaecologist, Mr Nikos Christoforidis MD, MRCOG, DFFP).

The message of the event was strongly conveyed and deserves to reach all those couples trying to have a child:
We support fertility and choose good practices!
With positive thinking, scientific excellence and real care... the dream IS realised!

Visit #40 reasons
www.kiveli.gr
www.embryolab.eu

Informative Event Meet the experts

The one-day conference 'Meet the Experts' took place in the august surroundings of the library of Royal Society of Chemistry in Piccadilly, London, and was very well attended by the British public.

On Sunday June 4th 2017, the International Department of Embryolab in collaboration with the IVF Babble journal held the event, 'Meet the Experts', aiming to inform the British public on subjects related to IVF.

Many distinguished speakers and specialists on IVF treatments were present, UK couples who had their therapy at Embryolab, as well as people interested, attended.

The event began by an opening address from the IVF Babble and the clinical director of Embryolab, Dr. Nikos Christoforidis who underlined the importance of personalized treatment and achieving success at each attempt. Experts and consultants in IVF, as well as Embryolab IVF Coordinators expressed their views in various speeches. Dr. Michalis Kyriakidis, Head of the Clinic's International Department presented the choices in IVF which can transform a treatment into a pleasant experience. Mrs Louise Brown the first ever human to be born through IVF treatment, honoured the event, as well as eminent speakers on the subjects of diet and psychological preparation before and during treatment.

Educational seminars in Saint Petersburg

For the second consecutive time, Embryolab Academy successfully held its educational seminars in Saint Petersburg, Russia between 14 and 17 of October 2017. Scientist from the length and breadth of Russia were in attendance (Siberia, Caucasus, the Urals, Lake Baikal) to be updated on the latest advances in Preimplantation Genetic Diagnosis.

There was detailed discussion on:
- the latest data on this rapidly evolving method
- the anticipated success rate
- the groups in the population expected to benefit the most from Preimplantation Genetic Diagnosis
- the concerns arising from the application of the advanced genetic analysis method.

The seminars were completed by a training workshop for participants on the designing and application of the biopsy technique on blastocysts (5th day embryos). This technique is now sprinting ahead of other available techniques applied until recently, as it appears to be safer for the embryos.
Mrs Alexia Chatziparasidou, MSc, Sr. Clinical Embryologist and Director of Embryolab, remarked on the successful event thus: 'Our Academy has now completed 4 years of continuous activity and presence on the global stage. It is faithfully serving its initial goal, that of bringing scientists together from across the world to train them in new IVF methods'.

Fertility Enhancement Management and More

Between 17 and 19 November 2017 the prestigious 'Fertility Enhancement Management and More' FEMM Conference was held in Mumbai, India with Embryolab Academy making a strong showing there through its presentations and workshops. The conference's theme and aim was the optimization of fertility management and enhancement.

Mrs A. Chatziparasidou, Sr. Clinical Embryologist and Director of Embryolab, held a workshop on 'Risk management in the Assisted Reproduction Lab' with physicians, embryologists and executives from India's Assisted Reproduction Units. The following topics were also presented: 'Organisation of a modern fertility unit. New cultivation systems and quality control' and 'Preimplantation Genetic Diagnosis today'. Dr Ch. Pappas, MD, M.Sc., Ph.D., BSCCP., spoke on the subjects of 'Preimplantation Genetic Diagnosis and Aneuploidy' and 'Pregnancy and birth rates in women with Tubal Factor Infertility (TFI)'.

This year, the conference presented the subject of fertility management within a broad framework of research and scientific interest, while also covering specialized issues on assisted reproduction in all its fields of application. On Thursday 17 November live events and video workshops were presented. As a part of the conference summit on 18-19 November, leading scientists from around the world and from all over India gave speeches and participated in clinics, group discussions and interactive workshops.

All in all, the conference was a resounding success, having assembled hundreds of distinguished scientists from India and elsewhere around the world to present, attend and discuss all the latest currents in gynaecology and assisted reproduction. Emphasis was placed on the new ambitious program of the Federation of Obstetric and Gynaecological Societies of India (FOGSI), called 'She Matters'. This program aims to reduce the incidence in India of maternal and infant mortality during childbirth. In India today more than 100 women each day die in childbirth.

For Embryolab Academy it has indeed been a great honor and the source of much satisfaction to be supported by so many initiatives with a global reach. Embryolab's scientific team, now on the global stage, is making its mark among the world's top scientists on the latest developments in assisted reproduction worldwide!

MEDICAL BREAKTHROUGHS MAY COME OUT OF THE LAB. BUT THEY BEGIN IN THE HEART.

For more than a century, a very special passion has driven the people of MSD. Our goal is to develop medicines, vaccines, and animal health innovations that will improve the lives of millions. Still, we know there is much more to be done. And we're doing it, with a long-standing commitment to research and development. We're just as committed to expanding access to healthcare and working with others who share our passion to create a healthier world. Together, we'll meet that challenge. With all our heart.

MSD *Be well*

125 YEARS SINCE 1891