

A Basic Guide from Aster IVF to hand-hold our patients when She plans her Fertility Treatment

A woman's inability to conceive after 12 months of regular unprotected sexual intercourse is the definition of infertility. Couples anxious to conceive start having questions or consider consulting a doctor after 6 months and this is true for a couple with advanced age of female partner say >35 years.

Women who face this issue are often found wallowing in a vicious cycle of guilt and blame, draining them off from the strength that they need as a couple - whatever the cause may be. Motivation to find answers to their problems encourages them to explore available and reliable treatment protocols and options.

If the couple has been trying to conceive for 12 months or more (6 months if you are 35 years and over), we encourage them to seek advice from a fertility specialist at the earliest.

How to Start Fertility Treatment

The steps to be taken in preparation for fertility treatment are listed below so you know what to expect when you visit us for the first time:

1. Initial Fertility Specialist Appointment

The first step is to organize an appointment with an Aster IVF Fertility Specialist who will review your medical history, organize initial investigations and discuss treatment options with you.

Investigations

Depending on the level of testing performed by your referring Gynecologist/Obstetrician, your Fertility Specialist may order further tests for evaluation including:

For Wife:

- Rubella immunity (German Measles)
- HIV Status
- Hepatitis B and C
- Pap Smear (within last 2 years)
- Baseline Hormonal Profile – Day 2/3 FSH, LH, Prolactin, TSH and AMH
- Base line Pelvic Ultrasound

For Husband:

- HIV Status
- Hepatitis B and C
- VDRL
- Semen analysis and culture at specialist Andrology Laboratory (within 6 months)

A follow up appointment will be fixed to review the results of these tests and explain in detail your recommended treatment plan.

New Patient Initial Appointments

Commencing Investigations

At your initial appointment with a Specialist, your medical history and any preliminary tests that have been carried out with your referring Gynecologist/Physician will be reviewed. Further investigations may or may not be necessary. Your specialist will recommend a treatment plan based on the outcomes of these tests if they are sufficient enough for your future treatment.

Infertility is a shared concern, but most often it is forgotten and concentration will be completely focused on the female partner only even the problem may reside with the male partner, so it is always mandatory that both partners attend this appointment together and undergo routine screening blood tests and investigations together. For male partner, the first line of investigation is a semen analysis. For female partner, the first step is to assess her fertility through a blood test on the first or second day of her periods, (although further investigations may be necessary to evaluate the tubes, ovaries and uterus).

The cause of infertility may be attributed to "female factors" such as tubal disease, ovulatory dysfunctions, or endometriosis, in approximately 40% of cases and to sperm problems, so called male factor in another 40% of cases. Or it can be "unexplained" in 15-20% of cases. In about 33% of couples with infertility, there will be more than one problem present or multiple problems in both partners.

Investigations for Male Partner

The semen analysis is the most important test in the evaluation of the male. The test gives an accurate measurement of the number of sperm (stated in millions per ml), the motility (swimming capacity) of the sperm cells, the morphology (the size and shape of the sperm cells), the volume and consistency of the ejaculate. The examination should be performed on a fresh specimen within two hours of collection in a sterile container. It is obtained by masturbation and the entire ejaculate should be collected. We prefer to rely on a semen analysis done in a specialist andrology laboratory according to the WHO guidelines. This is very important because the decision for specific treatment will be decided based on the semen parameters and will in turn decide the success of your treatment.

It is important for IVF purposes to have the percentage of normal morphology (shape) accurately assessed by an experienced andrology scientist who is specialized in sperm analysis. It is desirable wherever possible for these tests to be performed at Aster IVF Andrology Laboratory, where more extensive testing of semen for sperm antibodies or for penetration defects and sperm preparation along with the assessment of total motile count (number of total sperm with swimming capacity) may also be performed which is needed for the further evaluation of semen and this extensive testing is not usually not performed

in the ordinary laboratories.

Whenever abnormalities are found on semen analysis, repeat tests are often required to assess the type and degree of the problem found, and if it is a persistent feature.

Diagnosis of causes of male factor infertility may require blood tests for the hormones like FSH, LH and testosterone, which play a role in the development and maturation of sperm, and a referral to an Andrologist/Urologist (a specialist in Male reproductive disorders) may be made if certain male problems are found. A Karyotype (chromosome analysis) and other tests like assessment of Y chromosome microdeletions may be ordered if the sperm count is very low or zero. Also evaluation of the hormonal profile including the thyroid function & serum prolactin also may be required whenever the sperm counts are very low or completely absent.

Investigations for Female Partner

Initial Investigations

The first step in investigating a woman's fertility is to establish whether or not she is ovulating (producing an egg) every month regularly. This can be determined through a variety of tests including blood tests, ultrasounds and urine testing kits, but blood tests are more commonly used because of ease of performing the tests & reliability of blood tests. Ultrasound scanning can be used to check the condition of the endometrium (the lining of the womb) and help diagnose any polyps and fibroids (growth inside & outside the uterus). Vaginal ultrasound scan is very reliable in assessing the abnormalities of the ovaries as well as conditions like functional Ovarian Cysts (fluid collection inside the ovary), endometriotic cysts and hydrosalpinx (dilated damaged tube with fluid secondary to pelvic infections). To a certain degree ultrasound can also tell us about the adhesions inside the pelvis.

Diagnosis of Normal Reproductive Physiology

The single most important hormone to be assessed is the Serum AMH (Anti-Mullerian Hormone) which gives us an indication of the Ovarian reserve and helps in planning the correct dose of fertility medications. We also assess two hormones which are produced from the pituitary gland and are responsible for the development of eggs within the ovary: Follicle Stimulating Hormone (FSH) and Luteinizing Hormone (LH). The cells in the follicle (growing egg within the ovary) also produce estrogen and progesterone hormones. The rise and fall of these hormones depend on the stage of a woman's cycle.

Also, a transvaginal ultrasound scan can be used to visualize the follicles within the ovary and measure their size. This way, the stage of follicle development can be assessed. Serial ultrasound monitoring of growing follicles and its rupture with disappearance of follicle and collection of fluid inside the tummy can also predict ovulation.

Depending on the each patient's individual circumstances, other investigations that may be recommended to assess the fertility status include:

Sonosalpingogram (SSG) and Hysterosalpingogram(HSG)

This is a non-invasive test, which gives some valuable information about the anatomy of the uterine cavity and the patency of the tubes. This involves an ultrasound with the concurrent speculum examination, and insertion of a tiny tube into the cervix to pass dye through the uterine cavity and tubes.

A similar technique using X-ray technology may also be used to assess the uterus & tubes. It is called an Hysterosalpingogram (HSG). These techniques are often performed as alternative to a Laparoscopy and Hysteroscopy which are invasive and costly investigation. This also will tell us about the anatomy of uterus and tubes with patency of tubes.

IVF Counseling Sessions:

As part of the preparation for IVF treatment, we believe that prior to the first cycle, every couple should have an interactive session to understand and discuss the various aspects of her fertility treatment with one of the Aster IVF Fertility physicians. Most specialists and couples find these sessions useful and informative. The Fertility Physicians will also discuss treatment protocols, complications, adverse effects if any and also outcome of the treatment. The admin staff will clarify your doubts regarding the cost of the treatment.

Panoramic View of Infertility Treatment

After the initial evaluation, your fertility specialist will recommend, based on your medical history and results of initial testing, a treatment plan to that will provide the best outcome to suit your individual problems. Keeping in mind the mission and vision of Aster IVF, we aim to optimize our results with the least invasive and least costly option first, before moving onto more advanced treatments such as IVF or ICSI. But certain other couples who have tried all other simple conventional methods with no success; we may suggest IVF or ICSI as the first line of treatment.

Treatment Options

Ovulation Induction

Clomiphene citrate (Clomid) or Letrozole (Femara) and hormone preparations of follicle stimulating hormone (FSH) may be used to encourage the development of one or more follicles and thus more than one egg, during the woman's cycle. This process is known as Ovulation Induction if the woman is not ovulating or irregularly ovulating, or super-ovulation or ovarian hyperstimulation if she is already ovulating without treatment. Clomiphene or Letrozole tablets may be used in conjunction with timed intercourse, or artificial insemination, to ensure that the sperm are introduced at the right time inside the female genital tract. The cycle is monitored more closely than a natural cycle with vaginal ultrasounds and/or urine tests to check follicle development and observe hormone levels. Human chorionic gonadotropin, known as hCG is the hormone may be used in injection form to trigger the process of ovulation.

Intra-Uterine Insemination (IUI-AIH)

IUI treatment involves inserting the male partner's concentrated semen through the neck of the womb and into the uterus close to the time of ovulation. This procedure can be performed during a natural cycle or with fertility medications. Usually an injection of hCG is given when follicle development has reached a certain stage. The partner's fresh semen sample is usually prepared by scientists to separate sperm from the semen, wash and suspend it in a salt solution. This preparation is then injected directly into the uterine cavity (intra-uterine insemination - IUI).

Artificial insemination may be recommended by your doctor in cases of unexplained infertility, hostile cervical mucus, minor sperm abnormalities, coital difficulty and male sexual disorders.

Advanced Assisted Fertility Treatments

INVITRO FERTILIZATION (IVF)

For many couples Assisted Reproductive Technology (ART) is the treatment option that offers the best opportunity of achieving a pregnancy. With In Vitro Fertilization (IVF) the eggs are fertilized by the sperm in the laboratory instead of fertilization happening inside the woman's fallopian tubes. The process was initially developed to overcome blocked or damaged tubes or absent tubes due surgery, where fertilization will not occur due to the hindrance between the egg and sperm. As of now IVF/ICSI is a common form of treatment used to overcome other factors affecting fertility, including sperm problems, endometriosis, and unexplained infertility.

IVF treatment involves the collection of eggs from the woman, sperm from the man, placing the egg with the sperm in a culture dish in a controlled environment in the laboratory which mimics the tubal and uterine environment, to create an embryo outside the body. The resulting embryo is then placed back into the woman's uterus by a simple procedure called the embryo transfer. Embryo transfer is routinely not done under anesthesia.

If more embryos are available, the remaining or surplus embryos can be stored by freezing for transfer in the forthcoming cycles if lady fails to conceive in the fresh cycle. Replacing thawed embryos in subsequent cycles, therefore, is a much less demanding treatment. Advantage of the cycles are it will not have injections for ovarian stimulation and hence totally devoid of risk of OHSS. But in UAE, according to the federal law freezing of embryos are banned. So here we have the facility for freezing the eggs and later ICSI can be performed and can be transferred into the uterus without the risk of OHSS.

At Aster IVF it is our aim to offer a service, which optimizes the outcome of treatment with reduction of disruption to our patients' lives including the stress level during, before and after the treatment. To achieve these goals, we have adopted a minimal monitoring approach to treatment that is minimally invasive to the woman and leads to the least disruption in a couple's life during a stressful time of treatment till pregnancy test.

INTRACYTOPLASMIC SPERM INJECTION (ICSI)

Conventional IVF involves placing the egg from the female partner together with many thousands of sperm prepared from a semen sample provided by the male partner, and allowing the process of fertilization to take place over a number of hours in the culture dish kept in the incubator, which maintains the body temperature all the time. However, for many couples this technique will be unlikely to result in fertilization, rather can result in total fertilization failure either because the number of sperm available is insufficient or because there is reason to believe that the sperm will be unable to penetrate the egg. In such cases the technique of Intra Cytoplasmic Sperm Injection (ICSI) is usually the answer with which a man with completely absent sperm in the ejaculate also can father a normal pregnancy.

Together with IVF, ICSI is one of the most common technique used in Assisted Reproductive Technology, and many thousands of babies have been born worldwide - since it was introduced routinely into clinical practice. It involves the direct injection of a single sperm into each egg using very fine micromanipulation equipment, which contains fine glass injection pipettes. Given that the human egg is one tenth of a millimeter in diameter, this is a very delicate procedure performed by highly skilled embryologists. The technique can also be used along with sperm (TESA/PESA) which has been obtained surgically from the male reproductive tract (from vas deferens or epididymis or testes) when sperm are not present in the semen.

STEP BY STEP APPROACH FOR IVF TREATMENT

Step 1: Specialist Appointment At your consultation with your fertility specialist, your medical history will be reviewed, any initial tests ordered, and advice regarding further management will be provided. Based on the results of the initial investigations, a final treatment plan will be recommended for you and it will be the best option for your fertility problem. If your doctor has advised you for IVF, the following points narrates the main steps involved in a typical IVF treatment.

Step 1: New patient information session with a nurse Attend a new patient information session with an IVF nurse who will explain your treatment cycle. During this session injections techniques will be taught and usual medications used during different treatments will be discussed.

Step 2: New Patient Appointment Session with the Administrator During the appointment with the Administrator, patients will be explained about the costs structure associated with your treatment and answer any questions that may arise.

Step 3: Monitoring of IVF cycle Throughout treatment we monitor how you are responding to medication with blood tests and ultrasound scans, to measure the endometrial thickness, size and number of follicles on both ovaries. Based on this we will determine when you are ready for egg collection.

Step 4: Final Trigger for Complete Maturation of Eggs Once you have the optimum number and size of developed follicles you are ready for the final trigger injection which allows complete maturation of eggs inside the follicle. The nurses advise you two days

before your egg collection of the exact time that you are required to administer the trigger injection. This is usually 35 hours before egg collection. This injection most often you may have to come back to the clinic and take. Because if not administered properly the chance of your pregnancy completely loses due to non-availability of mature eggs.

Step 5: Vaginal Egg Collection The vaginal egg collection is undertaken in the morning on a day surgery under a short general anesthesia and takes around 20 to 30 minutes. You will be at the hospital for around 4 hours and will need someone to drive or escort you home afterwards and please don't plan to work that day because you can have minimal lower abdominal pain and hang over of sedative medication. The procedure is performed using a transvaginal ultrasound probe guide through which a fine needle passes through the vaginal wall into the ovary and draws the fluid from the follicle which contains the egg. The tube containing the follicular fluid is then immediately passed to the IVF laboratory and checked to ascertain whether it contains an egg.

On the morning of your egg collection your husband will need to provide a fresh semen (sperm) sample (unless using frozen sperm) so we can inseminate/microinject your eggs after collection. If the husband is absent on the day of egg collection or he cannot produce a sample under stress, he can make an appointment previously for freezing the sperm.

Step6: Freezing of Collected Oocytes

At this point of time if you have surplus amount of eggs we can do egg freezing which will help you to attempt a repeat cycle without stimulation. Yet another occasion we encounter often is the hyperstimulation in which the response of the ovary is too much to these hormonal injections. During these situations also we can freeze the eggs to avoid dreaded complication of OHSS later.

Step 7: Fertilization of Collected Oocytes Following egg collection, when you are planned to have an IVF, the egg and sperm will be placed in a dish allowing fertilization to occur naturally. If you are having ICSI, an embryologist will insert one single sperm directly into the egg, allowing fertilization to occur.

Step 8: Embryo Development The day after egg collection a nurse will contact you to let you know the time for embryo transfer the following day. The embryos will grow under the care of the embryologists for normally two days.

Step 9: Embryo Transfer The embryos are returned to the woman's uterus in a simple procedure called an Embryo Transfer, a simple procedure similar to a PAP smear, performed by a fertility specialist under ultrasound guidance. No anesthetic is usually used for the procedure, which involves a speculum being inserted into the vagina, and a soft silicone narrow (about 2-3mm diameter) tube called a catheter, gently passed through the opening of the cervix and embryos are placed at an ideal place inside the uterus under USG guidance. Embryo transfer can be on 2 days, 3 days or 5 days after the egg collection which will be decided by the embryologist depending upon the growth number and quality of available embryos. We routinely recommend for day 5 transfer, otherwise known as blastocyst transfer which gives maximum implantation rate.

Step 10: Pregnancy blood test A pregnancy blood test will be organized for two weeks following embryo transfer. A blood test is the only reliable pregnancy test, as urinary pregnancy test kits can provide a false reading due to the hormone medication used in IVF treatment. Should the pregnancy test be positive, the nurses will organize an

appointment with your Fertility Specialist for an ultrasound scan normally at around 6 weeks.

Advantages of Fertility Treatment at Aster IVF

Aster IVF follows the family motto of “We’ll Treat You well ” and the team with a cumulative experience of over 30 years ,assure you that we will provide you with the highest standard of fertility care available - every step of the way - throughout your treatment with us, and encourage you to call us should you have any questions or concerns.

We understand that commencing treatment can be daunting, that there are complicated medical regimes to absorb and that you may not remember everything your fertility specialist or nurse explained in your initial appointments.

We emphasize the importance of patient support throughout the care we provide. We encourage you to access the range of patient support services in a way that suits your individual needs.

Encountering Problems during IVF Cycle

Unfortunately not all IVF cycles are successful. We believe it is important that you are aware of the possible disappointments as well as the joys that IVF can bring. The following is a brief outline of where problems may arise.

Treatment Cycle Cancellation:

A treatment cycle may need to be cancelled due to poor response to fertility drugs. In some cases, the ovaries do not respond well to the drugs and an insufficient number of eggs grow. This is detected by low, or a slow rise in hormone levels or follicle growth as measured by blood tests and ultrasound. Setbacks at this stage teach us more about the hormone patterns and we may be able to amend the treatment plan for subsequent attempts. Cycles cancelled at this stage do not incur the full costs of IVF.

No Egg Recovery After Egg Collection:

In a normal IVF cycle most, but not all follicles, will yield an egg at the time of your egg collection. The usual proportion is that approximately 70% of your follicles will produce an egg. Some follicles will not produce an egg at all. Small follicles may produce an egg but it will not usually be a mature egg. Immature, Post mature and atretic eggs cannot be used for IVF/ICSI. The number of follicles seen on your stimulation cycle scan is not, therefore, the same as the number of eggs expected at your egg collection, particularly if small follicles are included in the count.

Failed Fertilization and Cleavage of Embryos:

In a very small proportion of cycles (1-3%), none of the eggs will fertilize. On average, around 65% of eggs fertilize, as not all eggs collected at the time of egg collection will successfully fertilize and develop into an embryo suitable for transfer or freezing, nor will all eggs fertilize normally. Sometimes this is due to poor sperm quality or poor egg quality. Usually a special technique to inject the sperm directly into the egg (ICSI) can overcome the problem in a future cycle. However it is important to remember that, even

when ICSI is used, fertilization and further division of the egg does not always occur.

Successful Embryo Transfer without Pregnancy:

If the cycle is not going to be successful, embryo implantation is usually the point at which it will not work otherwise known as implantation failure if the quality of transferred embryos are good. Unfortunately, many embryos lack all the genes needed to develop fully and, despite a healthy appearance at the time of transfer, will not subsequently implant and develop.

Patient Support During Treatment

There may be times before or during treatment that you may feel emotional or stressed, or feel like there are times when there is nobody you can talk to who understands what you are going through.

Direct relationships between stress and infertility have not been established. Some people conceive at times of high stress in their lives, while others will respond with ovulation disorders or a decreased libido. However, improving your overall health and wellbeing, and trying to minimize stress in your life, can only help while undergoing treatment.

IVF and trying to achieve a pregnancy

Many patients have found the support of an IVF specialist throughout treatment an invaluable source of strength. The Aster IVF team are experienced in helping individuals and couples deal with difficult emotions and situations and we encourage you to access this service at any stage throughout your treatment.

Genetic Counselling

Some couple who themselves or members of their family, have a specific genetic disease must schedule an appointment with our doctors who will to discuss the options available to the couple and the implications arising from each form of treatment. The option of Preimplantation Genetic Diagnosis (PGD) is then discussed with them accordingly.

FREEZING OF EGGS

Freezing of eggs is rather the latest tool in the Fertility Specialist's armamentarium. After introduction of Vitrification, otherwise known as the ultra rapid freezing technique it has become possible to freeze the eggs routinely in clinical practice with high recovery and success rates. We are also using the Cryotech™ Vitrification for Egg Freezing for both Fertility Preservation as well as IVF Lite. Now we have routinely incorporated egg vitrification in our clinical practice. Most common indications for vitrification now ACCUVIT and Remote Embryo Transfer that we are now recommending as our first line IVF treatment.

FREEZING OF SEMEN

Semen freezing is a simple method of fertility preservation. It can be used for patients

whose partners are have difficulty in producing sample at the time of treatment. It can also be used for fertility preservation in cancer patients. Our success rates are excellent after using frozen sperm for fertility treatment. It can be used for patients who obtain sperm after surgical retrieval (PESA/TESA) for later use if we get excess number of sperm. In our set up we usually do testicular Sperm aspiration (TESA) for patients with complete absence of sperm in the ejaculate as an initial procedure and if sperm are obtained we will freeze them and start ovarian stimulation later so that the treatment cycle will not be futile in cases of patients with problem of azoospermia.

FREEZING OF EMBRYO

As per federal law embryo freezing is banned in UAE and hence we are not doing frozen cycle embryo transfers presently.

New Patient Session with IVF Nurse once your treatment plan is finalized!

An initial appointment with an IVF nurse is required and we recommend that you make this visit for a session with reproductive care nurse about a week before you expect your period. During this session, an IVF cycle (with any specific treatment protocol decided by the fertility specialist) will be explained in detail, like about medications & their duration of intake, injection techniques will be taught, medications discussed and given to you to take home if needed.