Southeastern Fertility
Center for Fertility and Reproductive Surgery

25 QUESTIONS & ANSWERS ABOUT IVF

1. How long has IVF been performed?
In vitro fertilization (IVF) was first successfully performed in Oldham, England, in 1978, resulting in the birth of Louise Brown, who was conceived using Natural Cycle IVF (NC-IVF).

2. How many children have been born after IVF?
More than 7 million children have been born using IVF.

3. I'm confused about the different types of IVF?
The 3 types of IVF are distinguished by what drugs (if any) are used and how many eggs/embryos will be produced. Natural Cycle IVF uses no fertility medications and results in a single egg and embryo. Mini-Stim IVF uses very mild stimulation medications (pills and 2-3 shots) resulting in 2-5 eggs. Stimulated Cycle IVF uses 10-14 days of fertility shots with a goal of 8-15 eggs.

4. Can all patients be treated with all types of IVF?
No, some patients will clearly be candidates only for Natural Cycle IVF whereas others will be best served by Stimulated Cycle IVF.

5. What about couples with male factor?
Severe male infertility is often best treated by IVF combined with Intracytoplasmic Sperm Injection (ICSI).

6. How expensive is IVF?
The cost per cycle (not including medication) ranges from under $5,000 for Natural Cycle IVF to $12,000 for Stimulated Cycle IVF. The medication costs for Stimulated Cycle IVF can be $2,000-5,000.

7. How long is an IVF cycle?

In most cases an IVF cycle lasts about a month, very similar to a regular reproductive cycle. Day 1 is the first day of menstrual bleeding. Most egg collections occur around the 12-14th day of an IVF cycle, but this varies from patient to patient and cycle to cycle. On the day of the egg collection the egg is exposed to sperm (IVF) or a single sperm is injected into the egg (ICSI). The embryo transfer is performed 3-5 days later, and then two weeks after the egg collection a pregnancy test is performed. Some clinics utilize oral contraceptives to manipulate the cycle in order to efficiently schedule patients going through treatment.

8. Do I need to take fertility shots in order to do IVF?

At Southeastern Fertility we offer Natural Cycle IVF and Mini-IVF in addition to traditional Stimulated Cycle IVF. A Natural Cycle IVF treatment does not use any fertility medications to stimulate the growth of extra eggs, but an injection of hCG is used to schedule the egg collection procedure just as is done in traditional IVF. Mini-IVF uses oral fertility medications (Clomiphene or letrozole) along with a couple of days of fertility shots to produce 2-5 follicles prior to the hCG shot. Stimulated Cycle IVF uses daily fertility shots to induce the growth of 8-15 follicles. Some medication protocols use Lupron to induce the final maturation of the follicles as opposed to hCG. This protocol can be much safer in high responder patients, but the rapid drop in estrogen and progesterone in Lupron trigger cycles may necessitate the freezing of all the embryos as opposed to performing an embryo transfer during the initial cycle.

9. Am I a candidate for Natural Cycle IVF?

Natural Cycle IVF can be considered in patients who have relatively regular reproductive cycles. Patients who experience very unpredictable cycles such as women with PCOS or other causes of ovulatory dysfunction may find NC IVF too frustrating as we keep waiting, week after week, for a follicle to grow. Patients whose ovaries cannot be seen on transvaginal ultrasound because of previous surgery or large fibroids may not be good candidates for any form of IVF given the potential difficulty of performing an egg collection in such cases. Patients with poor ovarian reserve may consider NC IVF.

10. Am I a candidate for Mini-IVF?

Young patients with infertility are ideal candidates for Mini-IVF. Patients with irregular cycles from PCOS are also good candidates for Mini-IVF. Patients who have failed to conceive with NC IVF may be good candidates for Mini-IVF. For patients without financial resources to pursue Stimulated Cycle IVF, Mini-IVF and NC IVF may be more reasonably priced.

Our Mission

To provide comprehensive care and unwavering compassion to patients struggling with reproductive health issues.

11. What is a blastocyst transfer?

Embryos on the third day after egg collection are referred to as cleavage-stage embryos. At this point, each embryo contains 6 to 10 discreet cells (blastomeres). When assessing these embryos for quality, the embryologist grades them based on the number and appearance of the blastomeres. Embryos that have equal-size blastomeres with no fragmentation are usually given a high grade (Grade I), whereas embryos that have extensive fragmentation with unequal-size blastomeres are given a low grade (Grade IV). In general, higher-grade embryos have a much better chance of implanting successfully and generating a pregnancy.

If the embryos are maintained in culture beyond day 3, they first form a solid ball containing approximately 30 to 50 cells, called a morula. Over the next day or two, this solid ball of cells becomes a hollow sphere with a clearly defined inner cell mass. This hollow ball of cells is called a blastocyst. Patients who undergo an embryo transfer on day 5 or 6 after egg collection are usually referred to as having a blastocyst transfer, although occasionally the embryo may actually be at the morula stage of development.

12. I was told I need assisted hatching. What is this, and why is it done?

In normal reproduction, the human embryo hatches out of the eggshell (zona pellucida) at the blastocyst stage of development. Assisted hatching involves making a hole in the zona to facilitate the emergence of the embryo following its transfer into the uterus after IVF. Proponents of assisted hatching suggest that it increases implantation and pregnancy rates.

Assisted hatching can be performed chemically or more recently using a laser. In the chemical technique, a dilute acid solution is used to dissolve the external eggshell. Some clinics still perform mechanical hatching, in which a slit is made in the eggshell. There is some controversy regarding which patients benefit most from assisted hatching, and the indications for assisted hatching remain somewhat unclear. Most clinics recommend this procedure in cases where the female partner is older than age 37, has diminished ovarian reserve with increased levels of FSH, or is undergoing a frozen embryo transfer (FET) with previously cryopreserved embryos. Patients who have previously failed IVF following replacement of good-quality embryos may also benefit from assisted embryo hatching.

The risks of assisted hatching are believed to be quite low. There have been reports of increased rates of identical twinning following mechanical hatching (but not after chemical or laser assisted hatching). There is no evidence that assisted hatching harms the embryo or causes any increased rate of birth defects in children.

13. What is embryo freezing, and how successful is it?

Embryos are cryopreserved (frozen) through the use of liquid nitrogen which has a temperature of –196 °C. The freezing process renders them in a state of suspended animation in which they can remain for many years. Embryos that have been stored for more than 20 years have successfully generated pregnancies (although most patients tend to use their frozen embryos within 3 to 5 years after they are produced). The pregnancy rates associated with replacing frozen embryos depend on the age of the patient and the quality of the embryos at the time of cryopreservation. Top-quality embryos from young patients may yield pregnancy rates in excess of 50%, whereas poor-quality embryos may not even survive the thawing process. In some clinics, more than 90% of embryos survive the freeze–thaw cycle. Since most stimulated IVF cycles generate embryos in excess of what would be used in a single embryo transfer, the use of embryo freezing has allowed patients to judiciously limit the number of embryos replaced in any given cycle.

The ability to successfully freeze and thaw blastocyst stage human embryos has improved dramatically over the past decade. In fact, implantation rates for frozen/thawed embryos are now similar to those from fresh embryo transfers.

We Deliver Comprehensive Care with Committed Compassion

14. When can I do a home pregnancy test after IVF?

Laboratory hormone detection of pregnancy may be performed by testing for the presence of the hormone beta-HCG in either the urine or the blood. Both types of tests are reliable and highly accurate. Sometimes, however, pregnancy tests can be misleading and give a spuriously negative or positive test result when performed too early (regardless of whether the desired pregnancy is from an IVF treatment or a spontaneous conception). Performing a pregnancy test within 7 days after the egg collection procedure can result in a false-positive result in patients given HCG to trigger the final maturation of the eggs. In addition, the urine pregnancy test may be spuriously negative if performed less than 14 days after the embryo transfer. In our practice, we have had patients with a serum beta-HCG level of more than 200 mIU/mL who nevertheless reported a negative urine pregnancy test.

We advise patients to obtain a blood pregnancy test 12 to 14 days after an IVF egg collection and to avoid home pregnancy testing. In-office blood pregnancy tests provide the most reliable and accurate result. In addition, the blood pregnancy tests allow us to quantify the amount of HCG present. This is important in following the viability of an early pregnancy and ruling out ectopic pregnancies.

15. My last attempt at Natural Cycle IVF was cancelled because I ovulated before retrieval. Can I do anything to prevent this from happening again?

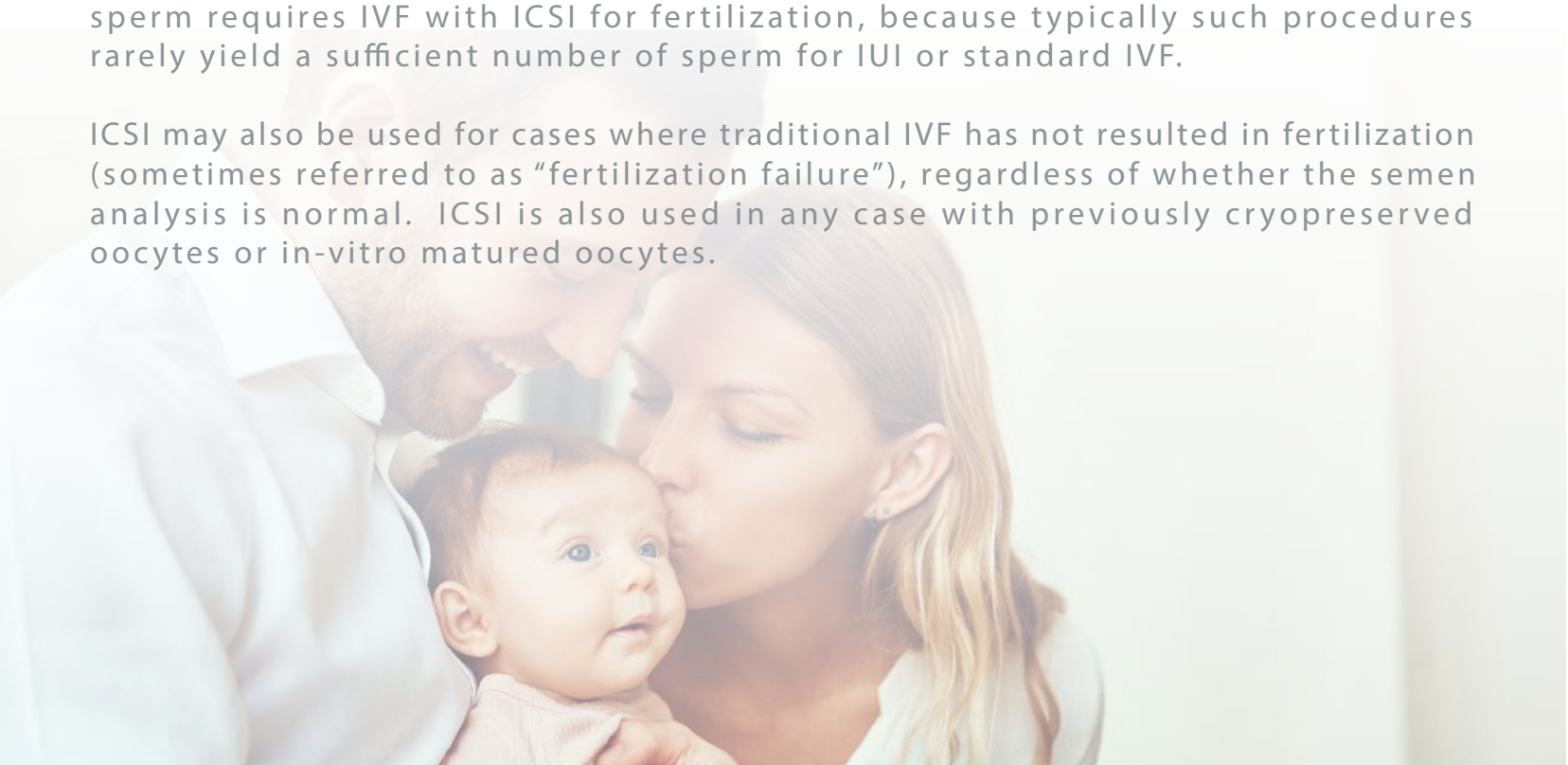
Ovulating prior to egg collection is very disappointing and can occur in 10-15% of Natural Cycle IVF treatment cycles. In Europe, Natural Cycle IVF is frequently performed using GnRH antagonists (such as Antagon or Centrotide) to prevent premature ovulation. The use of GnRH antagonists also necessitates the use of gonadotropin injections (FSH or FSH/LH combination medications, such as Gonal-F and Menopur, respectively) to continue the follicle growth once the GnRH antagonists are started. Most IVF centers refer to this approach as Modified Natural Cycle IVF (MNC-IVF).

We have found that patients who have failed to reach egg collection in two consecutive NC IVF cycles because of a premature LH surge or premature ovulation will reach egg collection 85% of the time with MNC-IVF (whereas historically, only 15% would reach egg collection in a third attempt at traditional Natural Cycle IVF). In our experience, many patients who fail to reach retrieval with NC IVF will opt for traditional Stimulated Cycle IVF to take advantage of the recruitment of multiple follicles, therefore improving their overall chances of success, instead of pursuing MNC-IVF.

16. Who needs ICSI, and how can I be certain that I need it?

The most common indication for ICSI is male factor infertility associated with an abnormal semen analysis. Therefore, men with unproven fertility whose sperm count, motility, or morphology is suboptimal are appropriate candidates for IVF with ICSI to improve the chances of fertilization of the eggs. Some men may have a blockage in their reproductive tract that may keep sperm from getting out, perhaps as a result of a surgical procedure like a vasectomy or because of certain congenital abnormalities. In these and other cases, a specially trained urologist may retrieve sperm directly from the testicles or epididymis. Surgically retrieved sperm requires IVF with ICSI for fertilization, because typically such procedures rarely yield a sufficient number of sperm for IUI or standard IVF.

ICSI may also be used for cases where traditional IVF has not resulted in fertilization (sometimes referred to as “fertilization failure”), regardless of whether the semen analysis is normal. ICSI is also used in any case with previously cryopreserved oocytes or in-vitro matured oocytes.



17. Why would a blocked tube be an issue if I am doing IVF anyway?

Problems that cause tubal disease, such as pelvic infections, usually damage the tubal fimbria—that is, the delicate finger-like projections at the end of the tube that are responsible for capturing the egg when it is released from the ovary. Pelvic infections may also damage the entire thickness of the tube from the tubal muscle to the inner mucosal layer, resulting in a tube that is not amenable to surgical repair.

Damage to the fimbria of a fallopian tube may result in a tube that is blocked at the end farthest away from the uterus. A blocked tube that becomes filled with fluid is called a hydrosalpinx ("hydro" refers to water; "salpinx" refers to the fallopian tube itself). A hydrosalpinx is usually discovered during a hysterosalpingogram (HSG), performed as part of the infertility diagnostic evaluation.

Over the past decade many studies have demonstrated reduced IVF pregnancy rates in patients who have a hydrosalpinx. It has been theorized that the fluid in the tube may flow backward into the uterine cavity. This fluid may contain toxic substances that may adversely affect the receptivity of the endometrium preventing implantation. Alternatively, the fluid may actually flush the embryo out of the cavity or even prove toxic to the embryo itself. Some studies suggest that the presence of an untreated hydrosalpinx will reduce IVF pregnancy rates by 50%.

Treating a hydrosalpinx by either removing the tube or repairing the tube should increase the IVF pregnancy rate. A patient with a single normal fallopian tube and a hydrosalpinx will also have a higher chance of achieving a spontaneous pregnancy after removal or ligation of the damaged tube.

18. Can you have an ectopic pregnancy after IVF?

Unfortunately, a tubal or ectopic pregnancy can occur after IVF. The incidence of ectopic pregnancy following IVF ranges from 0.5 % to 3%. Patients with a history of a prior ectopic pregnancy who become pregnant on their own or with a non-IVF fertility treatment like an intrauterine insemination (IUI) have a 15% risk of a recurrent ectopic pregnancy. So, although IVF cannot eliminate the risk of an ectopic, it may be the best choice for many patients with a previous ectopic who are fearful of experiencing another ectopic pregnancy. Although embryo transfer is routinely performed using ultrasound to properly guide the embryo catheter to the optimal uterine location, even ultrasound-guided embryo transfer cannot eliminate the possibility of an ectopic pregnancy after IVF.

19. What is the most important factor that determines IVF success?

Age is probably the most important factor influencing the outcome of an IVF cycle. In general, women older than age 40 have a markedly lower chance for a live birth compared with women younger than 40 years old. According to the most recent CDC statistics from 2016, the percentage of IVF cycle starts that resulted in live births was 31.0% for women < 35 years of age, 24.0% for women 35-37 years old, 15.5% for women 38-40 years old, 8.0% for women 41-42 years old and 3.2% for women > 42 years old. Clinics and physicians have the autonomy to decline treatment for women with whom they believe that fertility treatment may be futile or represent a poor prognosis at their center. However, patients with even a very poor prognosis may sometimes be permitted to enter into treatment, provided they acknowledge the risks and are realistic about the overall chances of pregnancy for their individual case.

20. How does ovarian reserve affect IVF outcome?

Levels of antimullerian hormone (AMH), FSH and estradiol levels on cycle day 3 and antral follicle count on ultrasound are the most commonly utilized tests for ovarian reserve. Patients with diminished ovarian reserve often fail to respond to the drugs used to stimulate the ovary and may not even make it to egg collection in spite of spending thousands of dollars on medications. Such patients may pursue IVF with donor eggs or embryo adoption, but it is important to bear in mind that no single value can predict with complete certainty a woman's ability or inability to conceive and even patients with poor ovarian reserve may end up conceiving on their own.

Natural Cycle IVF has emerged as another treatment alternative for patients with diminished ovarian reserve. Tests of ovarian reserve predict a patient's response to fertility medications. NC IVF does not use fertility medications, but instead relies upon the single follicle produced in a natural reproductive cycle. Success rates with NC IVF demonstrate that even patients with poor ovarian reserve may be able to conceive with this approach. Unfortunately, no test exists to predict the presence or absence of a healthy egg in a given patient. The only true means to determine the presence of a healthy egg is the delivery of a healthy child – proving that the patient had at least one good egg!

21. I was told to take estradiol (estrogen) pills as part of my IVF or FET protocol, but is it safe to take this hormone if I am pregnant?

Estrogen and progesterone are hormones that are critical for the normal development of the endometrial lining of the uterus. Both medications are frequently used in patients undergoing a frozen embryo transfer (FET) with their own or an adopted embryo. Estrogen thickens the lining and then progesterone causes the lining to mature, ultimately allowing for the embryo's implantation. The use of these medications also provides the physician and patient with flexibility in scheduling and synchronizing the transfer procedure with the ideal implantation window, a particularly crucial component of treatment in patients utilizing a 3rd party for reproduction such as an egg donor or gestational carrier. There is no evidence that the estrogen used to synchronize these cycles presents any risk to the developing fetus or baby.

22. If there are no risks, then why do the labels of these medications carry such a strong warning?

The labeling is an overreaction to previous experience in the United States with the use of a synthetic estrogen called diethylstilbestrol (DES). During the 1960s, this synthetic estrogen, markedly different than the natural estrogen used today, was given to women who were threatening to miscarry. Unfortunately, DES did not function in a normal fashion in terms of how it interacted with the estrogen receptors in the cells of the developing female reproductive tract in the unborn daughters of mothers who were prescribed DES. As a result, many of those women whose mothers took DES during their pregnancy were found to have significant reproductive tract abnormalities. In addition to cervical and uterine abnormalities, they were at a higher risk for an unusual form of vaginal cancer called clear cell carcinoma. Appropriately, DES was taken off the market. At this point in time, the impact of previous DES exposure in the U.S. population has greatly waned as most of the DES daughters have passed beyond childbearing age.

Following the DES debacle, the U.S. government decided that all reproductive steroids should be labeled as being contraindicated in pregnancy. This mandate applies to both progesterone and estrogen compounds. Today, however, the estrogens and progesterones prescribed by fertility physicians are exactly equivalent to the body's own natural estrogen and progesterone produced by the ovary and by the placenta. Women who are prescribed these medications by their physician can take them without any worry that somehow these medications will have an adverse impact on their unborn children.

Southeastern Fertility
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The Southeastern Center for Fertility and Reproductive Surgery is the oldest and best-established medical practice in East Tennessee dedicated to the treatment of infertility.

23. What is ICSI, and how does it differ from IVF?

In routine IVF, eggs are placed in a laboratory dish in culture media together with prepared sperm. The eggs and sperm are allowed to spontaneously fertilize overnight. The fertilized eggs then develop in the incubator until the embryo transfer procedure, which is usually performed 3 to 5 days after the egg retrieval.

Intracytoplasmic sperm injection (ICSI) differs from IVF in that each egg is individually injected with a single sperm using a tiny needle under microscopic guidance. The resulting embryo is then cultured similarly to an embryo produced in a non-ICSI IVF treatment. ICSI was initially introduced by the IVF team working at the Brussels Free University in Belgium. At that time, assisted fertilization was being attempted through the insertion of the sperm under the eggshell (zona pellucida). The Belgian group took the extra step of injecting the sperm not only under the eggshell but actually into the middle of the egg itself. The first ICSI pregnancies were reported in 1992. Since then, hundreds of thousands of children have been born as a result of this unique procedure.

24. How many eggs should I fertilize?

Our recommendation to all patients is that they consider fertilizing only as many eggs as embryos that they are willing to transfer either now or in a future FET cycle. Since we are very comfortable with freezing unfertilized eggs, we recommend that patients carefully consider this decision so as to avoid the difficulties inherent in deciding what to do with frozen embryos once a couple no longer wishes to use them to have additional children. Although the National Embryo Donation Center (NEDC) has matched thousands of donated embryos with recipients, there are estimated to be over 1 million frozen embryos stored in IVF clinics across the United States. At Southeastern Fertility we are committed to helping resolve the problem inherent in storing these embryos indefinitely by avoiding the creation of too many surplus embryos.

25. How do I decide how many embryos to transfer?

Determining the number of embryos to transfer in an IVF cycle is very important as the goal of every treatment cycle should be the delivery of a full-term, healthy, singleton baby. Several European countries have eliminated all discussion of how many embryos to transfer by mandating that all patients undergo only single-embryo transfers.

The ASRM has published guidelines for making the decision of how many embryos to transfer (see below). Patients who fall into the excellent prognosis category are recommended to transfer only one embryo, whereas those with an exceedingly poor prognosis—because of the woman's age or multiple failed IVFs, for example—may undergo embryo transfer of many more embryos.

Recommendations for the limit to the number of embryos to transfer.

	AGE (y)			
Prognosis	**<35**	**35-37**	**38-40**	**41-42**
Cleavage-stage embryos [a]				
Euploid	1	1	1	1
Other favorable [b]	1	1	1	1
All others	<2	<3	<4	<5
Blastocysts [a]				
Euploid	1	1	1	1
Other favorable [b]	1	1	1	1
All others	<2	<3	<4	<5

a See text for more complete explanations

b Other favorable = Any ONE of these criteria: Fresh cycle: expectation of 1 or more high-quality embryos availible for cryopreservation, or previous live birth after an IVF cycle; FET cycle: availability of vitrified day-5 or day-6 blastocysts, euploid embryos, 1st FET cycle, or previous live birth after an IVF cycle.

Please note: Justification for transfering additional embryos beyond recommended limits should be clearly documented in teh patient's medical records.

Practice Committee for the American Society for Reproductive Medicine. Guidance on the limits to the numbers of embryos to transfer: a committee opinion. Fetil Steril. 2017 Apr;107(4):901-903