BOSTONIVF

IVF Treatment Guide

People come to Boston IVF from all walks of life, carrying hope and often heartbreak, with one common goal: to fulfill their dream of having a chance to expand their family.

At Boston IVF, the science of fertility is our passion – it is work that we're exceptionally skilled at, in a field in which we are pioneers.

But what keeps us striving in science, research and technology is our commitment to excellent patient care.

Whether you're attempting to become a parent for the first time, to further expand your family or to pursue parenthood in the future, we are here to help and support you through this very personal journey.

The pineapple is a powerful symbol of hope and resiliency within the infertility community and for those trying to conceive. Strong on the outside and sweet on the inside, the pineapple adds a sense of protection, awareness, and support to the often isolating experience of building a family through fertility treatments.

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Instructions

Please read this document carefully. If you do not understand the information provided, please speak with your treating physician. This material is being presented so you can make an informed decision regarding the elements of IVF treatment you agree to undertake in your upcoming IVF treatment cycle.

Overview

In Vitro Fertilization, Intracytoplasmic Sperm Injection, Assisted Hatching, Egg Cryopreservation, Embryo Cryopreservation, Preimplantation Genetic Testing

Please be sure to read all of the content in this IVF guide as it directly supports our treatment consents.

In Vitro Fertilization (IVF) has become an established treatment for many forms of infertility. The main goal of IVF is to afford a patient or couple the opportunity to build their family. This may involve the use of patient/partner eggs/sperm or donor eggs/sperm.

This consent book reviews the IVF process from start to finish, including the risks that this treatment might pose to you or your partner and your offspring. While best efforts have been made to disclose all known risks, there may be risks of IVF that are not yet clarified or even suspected at the present time.

An IVF Cycle Typically Includes the Following Steps or Procedures:

- Taking hormonal medications to develop several eggs at once
- Removing the eggs from the ovary or ovaries
- Fertilizing egg(s) with sperm
- Growing any resulting fertilized eggs into embryos in the lab
- Placement ("transfer") of one or more embryo(s) into the uterus
- Taking hormonal medications to support a successful pregnancy

Sometimes Other IVF Steps May Be Included:

- Injecting individual sperm into each egg, called ICSI (intracytoplasmic sperm injection)
- Cryopreservation (freezing) of eggs or embryos that are not transferred to the uterus
- Genetic testing of embryos for abnormal number of chromosomes or particular genes (called PGT or preimplantation genetic testing)

Important Medication Reminder

Ingestion of aspirin or aspirin-like products (e.g. Motrin®, Advil®, Anaprox®, Naprosyn®, Aleve®, etc.) should be avoided during treatment unless your doctor recommends these medications. Tylenol® is generally considered to be safe to take during treatment.

The use of all other prescription or over-the-counter medications including herbal remedies requires discussion with your physician before starting a treatment cycle as they may have adverse effects.

Suboptimal Stimulation Response Acknowledgement

There is a chance during any IVF treatment cycle that stimulation medication does not result in the development of mature follicles/oocytes (eggs) to move on to egg retrieval. In this case, it may be medically indicated to cancel the IVF cycle and sometimes convert to intrauterine insemination (IUI), or timed intercourse.

Additional Reasons for Cancellation

While most ART cycles proceed as planned, some cycles may need to be cancelled/postponed if it is not optimal for the best outcome. This could include, but are not limited to the list below.

1. Poor ovarian stimulation evident by few follicles growing or low estradiol levels – potential for few eggs
2. Premature ovulation evident by an LH surge or lost follicle prior to retrieval
3. No oocytes upon retrieval
4. No available sperm for fertilization
5. Failed fertilization
6. No embryo development for transfer
7. Abnormal uterine lining
8. Active infectious disease during ART cycle (including but not limited to respiratory or febrile illnesses (COVID, flu, etc)
9. Change in medical status that warrants evaluation and treatment.

If your treatment cycle is cancelled, your care team with follow up with instructions for next step.

Abstinence/Contraception Consent

Until completion of the IVF/embryo transfer cycle (including frozen embryo transfers), we advise that you abstain from intercourse or use condoms if you have a partner with sperm. The reason is to avoid a high-risk multiple gestation pregnancy from a concurrent natural conception.

Production of a Fresh Sperm Sample for IVF (if applicable):

The directors of the embryology/andrology labs along with your physician recommend that if you have <90 minutes travel time to your procedure center, the production of your sperm sample should be completed at home prior to arriving for the procedure. Collection of a sperm sample will require a sterile specimen container; these are available to pick up prior to egg retrieval day at all Boston IVF centers. Other containers that are not considered sterile specimen containers will NOT be accepted.

NOTE: The person who produced the sperm sample must bring the sample to Boston IVF with an unexpired photo ID; handing off the sample to a partner is *NOT* acceptable. You will be asked to produce the sperm sample at the IVF Center if your commute from home to the surgical center is more than 90 minutes or if specifically recommended by your doctor.

Core Elements of IVF, Benefits & Risks
Medications for IVF Treatment

Medications may include the following (not a complete list):

Gonadotropins, or Injectable "Fertility Drugs"

The core medication used in IVF is the hormone **Follicle Stimulating Hormone (FSH)**. It comes under different brand names: Follistim®, Gonal-F®, Menopur®. These natural hormones (called **gonadotropins**) stimulate the ovaries – typically over the course of 8-12 days – with the goal of growing multiple follicles or **oocytes** (eggs). These hormonal medications are given by subcutaneous injection, just under the skin. The doctor will monitor response to medication using blood tests and ultrasound examinations during stimulation.

- The success of IVF largely depends on growing and retrieving multiple eggs in one cycle
- Injections of gonadotropins/FSH stimulate multiple eggs to develop
- Note that eggs cannot be seen on an ultrasound. Instead, follicle number and size are used to infer egg number
- Not every follicle may have an egg developing within
- Other medications may be used to prevent ovulation from happening too soon, before the eggs are retrieved surgically *[see below]*
- Sometimes the ovaries over-respond and sometimes not enough

As with all injectable medications, bruising, redness, swelling, or discomfort can occur at the injection site. Rarely, there can be an allergic reaction to these drugs. The intent of giving these medications is to cause multiple follicles to grow and develop. Many patients experience some bloating and minor discomfort as the follicles grow and the ovaries become temporarily enlarged. Up to 2% of patients will develop **Ovarian Hyperstimulation Syndrome (OHSS)** *[see full discussion of OHSS in the Risks to Patients section which follows]*. Other risks and side effects of gonadotropins include, but are not limited to, fatigue, headaches, weight gain, mood swings, nausea, and (very rarely) clots in blood vessels.

Sometimes, especially when testing prior to the IVF cycle has shown that the patient has a lower number of eggs (diminished ovarian reserve), the medications may result in very few follicles developing. The end result may be few or no eggs obtained at egg retrieval or even cancellation of the IVF cycle prior to egg retrieval. This scenario is sometimes called a "poor responder."

Some older research initially suggested that the risk of ovarian tumors may increase in women who take any fertility drugs over a long period of time. These studies had significant flaws, which limited the strength of the conclusions. More recent studies have not confirmed this risk. A risk factor for ovarian cancer is infertility itself, suggesting that early reports may have falsely attributed the risk associated with infertility to the use of medications to overcome infertility. In these studies, successful conception and live birth following treatment for infertility lowered the risk of ovarian tumors to the risk level of fertile patients.

Medications to Prevent Ovulation

Two types of medications are used to prevent the release of the eggs (ovulation) pre-maturely. One class of medications is called **GnRH agonists** and include the medication Lupron® and the other types of medications are called **GNRH antagonists** and include Cetrotide® and Ganarelix®. Your care team will instruct you when to begin these medications during the IVF cycle.

Core Elements of IVF, Benefits & Risks
Medications for IVF Treatment

GnRH-agonists: Leuprolide acetate (Lupron®)

This medication may be used in two forms during IVF: by daily low-dose injection to prevent premature ovulation before they are ready to be retrieved, or to cause ovulation to occur at the correct time using a much higher dose ("trigger shot"). Although Lupron is an FDA (Federal Drug Administration) approved medication, it has not been approved for use in IVF, although it has been used in this way since 1988. Potential side effects experienced with long-term use include, but are not limited to, hot flashes, vaginal dryness, bone loss, nausea, vomiting, skin reactions at the injection site, fluid retention, muscle aches, headaches, and depression.

No long term or serious side effects are known with short term use of this medication.

GnRH-antagonists: Ganirelix Acetate or Cetrorelix Acetate (Cetrotide®)

These are the other classes of medications used to prevent premature ovulation. These tend to be used most commonly in IVF now. The brands available in the USA are Cetrotide®. Ganarelix®, and Fyremadel®.

These medications are taken by injection and are started by your doctor part way through stimulation. The potential side effects include, but are not limited to, abdominal pain, headaches, skin reaction at the injection site, and nausea.

Human chorionic gonadotropin (hCG) (Profasi®, Novarel®, Pregnyl®, Ovidrel®)

Human chorionic gonadotropin (hCG) is a natural hormone used in IVF to induce the eggs to become mature and fertilizable. hCG may be used in low doses daily during the stimulation phase or as a one-time injection in much higher doses that causes the eggs to mature and be retrievable from the follicle. We often call this injection the "Trigger Shot" since it triggers final egg maturation and takes about 35-40 hours for its full effect. The timing of this medication is critical to retrieve mature eggs. Typically, you will be asked to take your trigger shot 36 hours prior to your scheduled egg retrieval time. Potential side effects include, but are not limited to, breast tenderness, bloating, and pelvic discomfort.

Progesterone & Estradiol

Progesterone and **estradiol (estrogen)** are hormones normally produced by the ovaries. They are critical for pregnancy support. After egg retrieval and in preparation for embryo transfer, supplemental progesterone is commonly prescribed.

Progesterone is usually given by injection or by the vaginal route (Endometrin®, Crinone®, Prometrium®, or pharmacist-compounded suppositories) after egg retrieval. Progesterone is often continued for some weeks after a pregnancy has been confirmed. Progesterone has not been shown to cause birth defects. Side effects of progesterone include depression, sleepiness, allergic reaction and, if given by intra-muscular injection, includes the additional risk of infection or pain at the injection site. Supplemental Estrogen (known as estradiol) is also sometimes prescribed in addition to progesterone. It may be administered by pill, patch, intramuscular, or vaginal suppository. Side effects of estradiol include nausea, irritation at the injection site if given by intramuscular injection and, although very rare, an increased risk of blood clots or stroke.

Oral Contraceptive Pills

Many treatment protocols include oral contraceptive pills (birth control pills) to be taken for 2 to 4 weeks before gonadotropin injections are started in order to slow down hormone production and synchronize egg production. Side effects include unscheduled bleeding, headache, breast tenderness, nausea, swelling and an increased risk of blood clots or stroke.

Other Medications

Anti-anxiety medications or muscle relaxants may be offered prior to the embryo transfer; the most common side effect is drowsiness, and you will need a ride home. Other medications such as steroids, heparin, low molecular weight heparin or low dose aspirin may also be included in the treatment protocol.

Transvaginal Oocyte (Egg) Retrieval

Oocyte retrieval is the removal of eggs from the ovary usually performed under general anesthesia.

The procedure is performed on an empty stomach, i.e. you should have nothing to eat or drink after midnight the night before the procedure. A transvaginal ultrasound probe is used to visualize the ovaries and the egg-containing follicles within the ovaries. A long needle, which can be seen on ultrasound, is used to puncture each follicle to aspirate the contents. The aspirated material includes **follicular fluid**, **oocytes** (eggs), and **granulosa** (egg-supporting) cells. On occasion the ovaries are not accessible by the transvaginal route.

These procedures and risks will be discussed with you by your doctor, if applicable. Anesthesia is generally used to reduce, if not eliminate, discomfort.

It is important to recognize that not all **follicles** contain eggs. In general, 50-70% of follicles are likely to provide an egg. Follicles larger than 15 mm are the most likely to yield eggs. Not all eggs retrieved will be mature. Only mature eggs can be fertilized.

Risks of Egg Retrieval Include:

Infection:

Bacteria normally present in the vagina may be transferred into the abdominal cavity by the needle. These bacteria may cause an infection of the uterus, fallopian tubes, ovaries, or other intra-abdominal organs. The estimated incidence of infection after egg retrieval is less than 0.001%. Treatment of infections could require the use of oral or intravenous antibiotics. Severe infections (rarely) require hospitalization or surgery to remove infected tissue. Infections can reduce your chances of getting pregnant in the future. The vagina is cleaned, and antibiotics are routinely administered before the egg retrieval procedure to reduce the risk of pelvic or abdominal infection. Despite these measures, there is no way to completely eliminate this risk.

Bleeding:

The needle passes through the vaginal wall and into the ovary to obtain the eggs. Both structures contain blood vessels.

In addition, there are other blood vessels nearby. A small amount of bleeding is common and expected during egg retrievals. The risk of major bleeding problems has been estimated to be less than 0.1%. Major bleeding may require surgery and possibly loss of the ovary. The need for blood transfusion is possible; however, the risk of this is very low. Although extremely rare, unrecognized bleeding can lead to death.

Trauma:

Even with ultrasound guidance, it is possible to damage nearby organs during the egg retrieval. This includes damage to the bowel, appendix, bladder, uterus, and ovary. Damage to internal organs may result in the need for additional treatment such as surgery for repair or removal of the damaged organ. However, the risk of such trauma is extremely low.

Anesthesia:

The use of anesthesia during the egg retrieval can produce unintended complications such as an allergic reaction, low blood pressure, nausea or vomiting and in rare cases, death. Complications are more likely to occur in those who have pre-existing medical diseases such as obesity, asthma, high blood pressure, and heart disease. If your doctor considers you to be at higher risk for complications, they may ask that you meet with the anesthesia team in advance of your procedure to ensure adequate preparation for the procedure.

Failure:

It is possible that no eggs may be retrieved at the time of aspiration of follicles or that the eggs may be abnormal or of poor quality and otherwise fail to produce a successful pregnancy.

In Vitro Fertilization & Embryo Culture

After eggs are retrieved, they are transferred to the embryology laboratory where they are kept in conditions that support their needs and growth. The eggs are placed in small dishes containing **"embryo culture medium"** which is special fluid made to resemble that found in the fallopian tubes to support development of the embryos. The dishes containing the eggs are then placed into incubators, which control temperature, humidity, gas, and light at just the right levels.

A few hours after egg retrieval, sperm is placed in the culture medium with the eggs, or individual sperm is injected into each mature egg in a technique called **ICSI (Intracytoplasmic Sperm Injection)**. The eggs are then returned to the incubator, where they remain to develop. The dishes are inspected periodically so that fertilization and embryo development can be assessed.

The day after the eggs have been inseminated, they are examined for signs of normal fertilization. At this stage, normal development is evident by the fertilized egg having 2 pronuclei; this is called a **zygote** or early embryo. Two days after insemination, normally developing embryos would have divided into between 2 to 4 cells. Three days after insemination, normally developing embryos would have divided into between 4 to 8 cells. At 5 to 7 days after insemination, normal embryos would have developed to the blastocyst stage, which is typified by an embryo that has 200 or more cells, an inner fluid-filled cavity and two groups of cells called the inner cell mass (that develops into the baby) and **trophectoderm cells** (that develop into the placenta).

It is important to note that since many eggs and embryos are abnormal, it is expected that not all eggs will fertilize and not all embryos will divide at a normal rate. Some embryos may stop growing in the laboratory. Even if your embryo(s) develop normally in the lab and you have an embryo transfer, you still may not get pregnant. One reason for this is that not all embryos developing at the normal rate are also genetically normal. Nonetheless, their visual appearance (grade) is the most common and useful guide in the selection of the most appropriate embryo(s) for transfer when not doing PGT.

In spite of reasonable precautions, any of the following may occur in the laboratory that would prevent the establishment of a pregnancy:

- Fertilization of the egg(s) may fail to occur.
- One or more eggs may fertilize abnormally resulting in an abnormal number of chromosomes in the embryo; these abnormal embryos cannot be transferred.
- The fertilized eggs may fail to develop into embryos, or the embryos may not develop normally.
- Rarely, the eggs or embryos may be harmed by contact with bacteria.
- Laboratory accidents or human errors can occur which could lead to the loss of eggs, sperm and/or embryos.
- Other unforeseen circumstances may prevent any step of the procedure to be performed or prevent the establishment of a pregnancy.
- Hurricanes, tornadoes, floods, earthquakes, fires, or other natural disasters (as well as bombings or other terrorist acts) could destroy the laboratory or its contents, including any sperm, eggs, or embryos being stored there.

Quality control is the process of running tests to ensure lab conditions are the best they can be to help embryos grow. Sometimes immature or abnormal eggs or embryos that have not developed normally can be used for quality control checks before they are discarded.

None of the material that would normally be discarded will be utilized to establish a pregnancy or a cell line unless you sign other consent forms to allow the clinic to use your eggs, sperm, or embryos for research purposes.

Embryo Transfer

Embryos may be transferred into the uterus several days after the egg retrieval (**fresh transfer**) or frozen and subsequently thawed for transfer at a later date (**frozen transfer**). Embryos are placed in the uterine cavity with a thin tube (catheter). Ultrasound guidance is used to help guide the catheter and confirm placement of the embryo in the uterine cavity. Although the possibility of a complication from the embryo transfer is very rare, risks include infection and damage to or loss of the embryos. Not all embryos become pregnancies and not all pregnancies are normal or grow in the correct place. Even though the embryo is placed in the uterine cavity, they may implant in the fallopian tube and **tubal (ectopic) pregnancy** can occur.

The number of embryos to transfer is an important decision. The age of the patient and the stage/grade or chromosome status after PGT of the developing embryo are factors which have significant influence on the likelihood of pregnancy and the risk of a multiple pregnancy. It is possible to develop more fetuses than the number of embryos transferred if one (or more) of the transferred embryo(s) split into "identical" twins. The risk of one embryo splitting into a twin pregnancy after embryo transfer is approximately 2-3%. The discussion with your doctor of the number of embryos to transfer happens prior to your IVF/transfer cycle and is based on national guidelines to minimize the chance of a riskier multiple gestation pregnancy.

- After a few days of development, the best developed embryo(s) may be selected for transfer.
- The number of embryos transferred influences the likelihood of pregnancy and the risk of multiple pregnancy.
- The age of the patient who provided the oocytes (eggs) and the appearance of the developing embryo(s) have significant influence on pregnancy outcome.
- In general, Boston IVF aims to transfer fewer embryos with the goal of achieving one healthy full term baby at a time.
- Extra, normally developing embryos that are not transferred can be frozen for potential use in the future.

In an effort to help curtail the problem of multiple pregnancies, national guidelines published in 2017 recommend the number of embryos to transfer *(see Tables below)*. These guidelines differ depending on the developmental stage of the embryos and the appearance of the embryos and consider the patient's personal history.

In some cases, there will be additional embryos remaining in the lab after the transfer is completed. Depending on their developmental progress, it may be possible to freeze them for later use.

Guidelines for the maximum number of embryos to transfer are given in the chart below.

(See Cryopreserved Embryo Storage on pages 15 & 16).

Recommended Limits on the Number of Embryos to Transfer

Age:	<35	35-37	38-40	41-42	>42
CLEAVAGE-STAGE EMBRYOS					
Other Favorable*	1	1	≤3	≤4	No Limit
All Others	≤2	≤3	≤4	≤5	No Limit
BLASTOCYST-STAGE EMBRYOS					
Euploid (PGT tested normal)	1	1	1	1	1
Other Favorable*	1	1	≤2	≤3	No Limit
All Others	≤2	≤2	≤3	≤3	No Limit

1 Practice Committee of the American Society for Reproductive Medicine, and the Practice Committee of the Society for Assisted Reproductive Technology. Guidance on the limits to the number of embryos to transfer: A committee opinion. *Fertility and Sterility* 2017; 107:901-3.

Additional Elements of IVF Benefits & Risks

Intracytoplasmic Sperm Injection (ICSI)

The use of **ICSI (Intracytoplasmic Sperm Injection)** provides an effective treatment for male factor infertility, in the majority of cases. The negative effects of low sperm count, or motility may be overcome with ICSI if viable sperm are available because the technique penetrates the shell (**zona pellucida**) around the egg and the egg membrane (**oolemma)** to deliver the sperm directly into the egg. ICSI involves the direct injection of a single normal-appearing sperm into the interior of an egg using an extremely thin glass needle.

ICSI allows couples with severe male factor infertility to achieve fertilization and live birth rates similar to those achieved with in vitro fertilization (IVF) using conventional methods of fertilization in patients with normal sperm counts. ICSI can be performed even in patients with no sperm in the ejaculate if sperm can be successfully collected from the epididymis or the testis via surgery.

ICSI has been reported to be associated with a slightly higher risk of birth defects in some studies. However, it was unclear in those studies whether the association is due to the ICSI procedure per se or to inherent defects in the sperm from patients who have severely abnormal sperm, thus requiring ICSI. The risk of birth defects after ICSI is quite small (4.2% versus ~3% of those conceived naturally). Experts are still debating the impact of ICSI on the intellectual and motor development of children. Most recent studies have not detected any differences in the development, or the abilities of children born after ICSI, conventional IVF, or natural conception.

The prevalence of sex chromosome abnormalities in children conceived via ICSI is higher than observed in the general IVF population, but the absolute difference between the two groups is very small (0.8% to 1.0% in ICSI offspring vs. 0.2% in the general IVF population). The reason for the increased prevalence of chromosomal anomalies observed in ICSI offspring is not clear. It appears to be related to the genetics of the patient producing the sperm, rather than the ICSI procedure itself. Patients with sperm problems (low count, poor motility, and/or abnormal shape) are more likely themselves to have genetic abnormalities and often produce sperm with abnormal chromosomes; the sex chromosomes (X and Y) in the sperm of patients with abnormal semen parameters appear especially prone to abnormalities. If sperm with abnormal chromosomes produce pregnancies, these pregnancies will likely carry these same defects. **Translocations** (a rearrangement of chromosomes that can cause birth defects, or miscarriage) may be more common after ICSI.

Some patients are infertile because of an obstructive problem, causing no sperm to be found in the ejaculate. For example, the tubes connecting the testes to the penis may not form correctly. This condition, called **congenital bilateral absence of the vas deferens (CBAVD)**, can be bypassed by aspirating sperm directly from the testis or epididymis and using them in IVF with ICSI to achieve fertilization. However, patients with CBAVD may also be affected with a mild form of cystic fibrosis (CF), and this gene could be passed on to their offspring. All patients with CBAVD, as well as their partners, should be tested for CF gene mutations prior to treatment, so that the risk of their offspring having CF can be estimated and appropriate testing performed. It is important to understand that there may be CF gene mutations that are not detectable by current testing and parents who test negative for CF mutations can still have children affected with CF.

Some patients with extremely low sperm count or no sperm may have abnormalities (**microdeletions**) in their Y chromosome. Testicular biopsy and successful retrieval of viable sperm can be used to fertilize eggs with ICSI. However, any sperm containing a Y chromosome microdeletion will be transmitted to the male child. Thus, the risk that genetically male offspring might later manifest disorders including infertility is very real. However, patients without a detectable deletion by blood testing can generate offspring having a Y chromosome microdeletion.

Additional Elements of IVF Benefits & Risks

Rescue ICSI:

In some cases, unexpectedly none of the eggs fertilize by regular insemination (placing the eggs and sperm in a dish together). When this lack of fertilization is discovered the next day, an attempt may be made to inseminate some of these unfertilized eggs with ICSI.

Embryos resulting from rescue ICSI appear to have reduced potential for pregnancy, compared to embryos created with a prior ICSI.

Assisted Gamete Treatment

The vast majority of sperm samples contain many millions of moving (motile) sperm. However, in rare cases (and this is generally known ahead of time), the IVF sperm sample may not contain any motile sperm. If this happens, there is a high risk that no eggs will fertilize, resulting in no embryos to transfer. In order to increase the chance that some eggs will fertilize, the sperm may be stimulated to gain some motility by adding a motility enhancer. This motility enhancer is temporary and simply aids the embryologist in selecting the best sperm for insemination.

There are also very rare situations where sperm have very low or no motility and there has been a problem with fertilization in previous cycles. In these cases, the eggs may receive a medication that can help facilitate fertilization. Both of these treatments are safe and your doctor can explain them in more detail if they are needed.

Assisted Hatching

The cells that make up the early embryo are enclosed within a flexible shell called the zona pellucida. During normal development of the embryo, a portion of the **zona pellucida** dissolves, allowing the embryonic cells to exit or “hatch” out of the shell. Only upon hatching can the embryonic cells implant within the **endometrium** (lining of the uterus) to result in pregnancy.

Assisted hatching makes it easier for the embryo to exit the zona pellucida. The opening can be made by a needle, a laser, or with chemicals. It is unclear if assisted hatching improves live birth rates and therefore it is not routinely performed at Boston IVF. There may be instances where it is suggested by your physician, however.

Risks that may be associated with assisted hatching include (very rarely) damage to the embryo resulting in loss of cells, or destruction of the embryo. Artificial manipulation of the embryo may increase the rates of identical twinning which results in a higher risk pregnancy. There may be other risks not yet known.

Genetic Carrier Screening

Genetic carrier screening is done to determine if one or both parents carry abnormal genes that may increase the chance that their child will have a specific genetic disease. For many genetic diseases, if an individual has a single abnormal gene/mutation, that person is considered a carrier for that genetic disease. Carriers are typically normal and healthy. If this abnormal gene is passed to the child, the child will usually not be affected by that genetic disease but will also be a carrier for that genetic disease. If both parents are carriers of the abnormal gene for the same genetic disease, there is a 25% chance that their child will be affected with the genetic disease. The severity of these genetic diseases varies, but some can be severe or even life threatening. Genetic carrier screening is typically done by prospective parents to identify whether they are at risk for having a child affected by a common genetic condition.

The American College of Obstetricians and Gynecologists (ACOG) and the American College of Medical Geneticists (ACMG) recommend routine screening for certain genetic diseases and additional screening when indicated due to ethnicity, family history, or other known risk factors. Two of the recommended standard genetic carrier screening tests are for Cystic Fibrosis (CF) and Spinal Muscular Atrophy (SMA). Many physicians now recommend full carrier screening panels via blood samples on both partners pre-conceptually. There is no one genetic carrier test that detects all genetic diseases. During your evaluation and treatment, you may consider screening for specific genetic disease(s) which may be indicated based on your medical history and/or family history to determine whether you are a carrier for that specific genetic disease(s). You may be asked to sign a consent to be tested or a waiver if you decline routine testing for CF, SMA, and any other genetic screening tests recommended by your physician.

Preimplantation Genetic Testing (PGT)

Preimplantation Genetic Testing for aneuploidy (PGT-A) is testing for an abnormal number of chromosomes in the embryo, and this test also provides information on the sex of the embryo (male or female).

Preimplantation Genetic Testing for a structural rearrangement in the chromosomes (PGT-SR) is testing for a structural chromosomal abnormality.

Preimplantation Genetic Testing for monogenic disorders (PGT-M) is testing for an abnormal gene in the embryo.

- Preimplantation genetic testing of embryos requires sampling of 4-8 cells from the part of the embryo that becomes the placenta (embryo biopsy).
- The embryo biopsy is most often done on Day 5, 6 or 7 of embryo development.
- The cells removed from the embryo are typically sent to an off-site genetics laboratory for the testing, while embryos remain in storage at the clinic.
- In most cases, the tested embryos will need to be cryopreserved (frozen) while the genetic test is being done.
- Test results may be incorrect (rarely).

PGT cannot guarantee that a pregnancy will occur, even if the genetic test result is normal. Factors other than the chromosomes and genes also influence the ability of embryos to implant and result in a successful pregnancy.

Testing the embryo's chromosomes, or testing for one specific genetic disease, does not guarantee that the embryo will be healthy and free of ***other*** disorders. For example, some common disorders that cannot be checked with PGT are autism and diabetes, which are multifactorial.

Birth defects can also occur even if chromosome testing is normal. An example of this would be a cleft lip or palate (failure of the lip and upper mouth to develop properly). The risk of having a baby with a minor or major birth defect is the same with spontaneous conception or with IVF and is approximately 2-3%. PGT does not prevent isolated birth defects not related to a major chromosomal abnormality.

There is also a possibility that PGT will show that there are NO normal embryos suitable to transfer.

Risks of Embryo Biopsy

- **Damage.** There is a small risk of damage to the embryo. This may result in no viable embryos suitable for transfer.
- **No result.** The test may not give a result. Sometimes, there is not enough genetic material retrieved to run the test. It may be possible to repeat the biopsy and try again to test the embryo.
- **Misdiagnosis.** The test may give the wrong result, and say that a normal embryo is actually abnormal, or that an abnormal embryo is actually normal.

The accuracy of testing is determined by the genetics laboratory. If an embryo is reported as chromosomally normal (euploid), the chance of misdiagnosis is very low (<1%). However, if an embryo is reported as abnormal (aneuploid), there is a chance that this embryo could still result in a healthy live birth. This is due to a phenomenon known as "mosaicism". Because cells with different genetics may coexist in the embryo, the small number of cells biopsied may not reflect the genetics of the entire embryo. Consequently, the current recommendation is to confirm the genetics of the fetus in early pregnancy using routine genetic screening as recommended by your obstetrician.

Sex Selection & Family Balancing

PGT-A for determination of the sex of an embryo has multiple applications. There are certain genetic diseases that are caused by a mutation of a gene in the X chromosome. Because the genetically normal male sex chromosome complement is XY, any gene mutation present on the X chromosome will result in the male individual being affected by the genetic disease, since there is not a complementary normal X chromosome to offset the expression of the mutated gene as there is in females (whose genetically normal complement is XX). Hemophilia (a bleeding disorder) is an example of an X-linked disease. In this case, if a couple is at risk for passing Hemophilia on to their male offspring, they may choose to transfer only female embryos to avoid a male affected with the disease.

Another reason a patient(s) may choose to determine the sex of their embryos is to balance their family. Patients who have one or more children of the same sex may wish to have a child of the opposite sex to "balance" their family.

Cryopreservation

- **Cryopreservation** (freezing) of eggs/sperm and embryos provides opportunities for pregnancy in the future.
- Cryopreserved sperm/eggs and embryos do not always survive the process of freezing and thawing.
- Ethical and legal questions can arise when couples separate or divorce. It is vital to agree on what will be done with cryopreserved embryos in those cases. Consultation with a reproductive attorney may assist in maintaining appropriate intended disposition directives.
- A person or couple with cryopreserved sperm/eggs or embryos MUST contact the clinic once a year. It is critical that any and all contact or status changes are reported to Boston IVF.
- There are yearly storage fees for keeping sperm/eggs or embryos cryopreserved.

Sometimes there are normally developing embryos remaining after embryo transfer. Additional normal-appearing embryos may be cryopreserved (frozen) for future use. In some cases, it may be planned for all embryos from an IVF cycle to be cryopreserved (for example, when PGT is being done). On the other hand, some patients may wish to cryopreserve their eggs or sperm because they are not ready to conceive now, or because they are planning to have medical treatments (such as treatment for cancer) that affect their ability to produce eggs or sperm in the future.

Benefits of Cryopreservation

- May allow use of eggs or embryos in the future, thereby avoiding another stimulation cycle.
- Allows for fewer embryos transferred in the fresh cycle. This can reduce the risk of a multiple pregnancy (twins, triplets, or greater).
- Allows the cryopreservation of all embryos in following the stimulation cycle and egg retrieval which prevents or reduces the risk of developing severe **ovarian hyperstimulation syndrome (OHSS)**.
- Allows storage of embryos while waiting for genetic test results from PGT.
- Protects you if your future fertility is at risk because of surgery or other medical treatments that could damage your eggs or sperm.

The most common method to freeze embryos is called **vitrification** (rapid freeze). Cryopreserved embryos do not always survive the freezing and thawing process. When using vitrification, approximately 2-4% of embryos frozen will not survive this process. There is always a risk that none of the embryos will survive. If this happens, the planned frozen embryo transfer will be canceled. Studies of animals and humans indicate that children born from cryopreserved embryos do not have any greater chance of birth defects than children born after transfer of embryos which have not been previously cryopreserved. However, until very large numbers of children have been born from cryopreserved embryos, it is not possible to be absolutely certain that there are no increased risks. If eggs are frozen by vitrification, >90% of eggs will survive.

Donated Reproductive Materials or Research Embryo Fate

If you choose to cryopreserve eggs or embryos, be sure to let us know if you change your address or contact information. You must also pay storage fees as they come due.

Cryopreserved Embryo/Egg Storage

There are fees associated with cryopreserving and maintaining cryopreserved embryo(s). Patients/ couples who have cryopreserved embryo(s) must remain in contact with Boston IVF on an annual basis in order to inform the clinic any change in their desire to maintain their cryopreserved embryos in storage, update any changes to their contact information, and to pay fees associated with the storage of their embryo(s).

Cryopreserved embryos will be maintained in storage until specific directives and authorization for those directives are provided. When the disposition has been decided, Boston IVF requires that a consent form specific to the method of disposition be signed and approved by the Laboratory Manager. Boston IVF reserves the right at its sole discretion to make decisions regarding the final disposition of cryopreserved embryos if fee obligations are not met. Disposition fees may apply and are subject to change.

Failure to maintain proper contact information and/or pay storage fees may lead to cryopreserved embryos being deemed abandoned. Abandoned embryos may be discarded at Boston IVF's discretion without further notice to the patient.

Disposition Options

Options for cryopreserved embryo disposition provide that they can be:

- Remain in storage with storage fees
- Thawed and transferred for pregnancy attempt
- Donated to research
- Discarded
- Transferred to another storage facility
- Released to an outside embryo donation agency

Changes in a relationship may affect the options available for disposition. It is important that Boston IVF is notified of any changes in relationship status so that you may be advised of any necessary actions, which may include referral to a reproductive attorney, submission of legal documentation, and/or notarized consents.

You may decide to donate your unused cryopreserved eggs, sperm, or embryo(s) to research or to another infertile person or couple for reproductive purposes. In certain situations, donating embryo(s) for research or to another person or couple may not be possible or may be restricted by law, but every effort will be made to abide by your wishes.

If after 5 years, no recipient couple/individual or research project can be found, or your embryos are not eligible, your embryo(s) may be discarded by the lab in accordance with laboratory procedures and applicable laws.

In some cases, discarded sperm, eggs or embryos may be used for future studies conducting research that leads to a better understanding of infertility and to improve techniques used in the treatment of infertility. These discarded embryos will not be used for any other purposes.

Donation to another couple may have additional requirements and may require additional actions by the donor or donor couple, which may include, not limited to additional blood testing, counseling, or legal referral. Medical information may need to be shared with recipients or donation agencies, as directed.

Additionally, Boston IVF cannot be responsible for changes in the political climate that restricts or prohibits future use or disposition options. Reproductive laws vary state-by- state and may require individual consideration based on which states are involved in treatment, transport, and/or disposition.

Risks to Patients Undergoing Ovarian Stimulation

Ovarian Hyperstimulation Syndrome (OHSS)

This is the most severe side effect of stimulating the ovaries. **Ovarian hyperstimulation syndrome (OHSS)** causes fluid to leak from blood vessels. Signs of OHSS include increased ovarian size, nausea, vomiting, and a buildup of fluid (ascites) in the abdomen (belly). You may also have difficulty breathing. In some cases, OHSS increases the concentration of red blood cells, and may cause kidney and liver problems. In the most severe cases, OHSS may result in blood clots, kidney failure, or death. All these complications occur extremely rarely (less than 0.2% of all IVF treatment cycles).

OHSS Occurs in Two Stages:

- Early, 1 to 5 days after egg retrieval (as a result of the hCG trigger); and
- Late, 10 to 15 days after retrieval (because of the hCG when pregnancy results following embryo transfer).

The risk of severe problems from OHSS is much higher if you become pregnant. For this reason, your doctor may suggest that all your embryos be cryopreserved (frozen) for later use instead of transferring them during the fresh IVF cycle. A frozen embryo transfer would be done later, when there is little to no risk of OHSS.

Venous Thromboembolisms (Blood Clots)

The use of ovarian stimulation medication leads to a small increased risk of blood clots. If your doctor considers you at high risk for blood clots, they may prescribe a blood thinning medication (e.g., heparin/Lovenox®) during the stimulation and/or following embryo transfer.

Cancer

There is some concern that using fertility drugs can cause breast, ovarian, or uterine cancer. These cancers are more common in patients with infertility, so it is difficult to know whether the reason for the cancer is infertility or the drugs used for IVF. In current studies that take into consideration the increased risk of cancer due to infertility, there does not seem to be an increased risk of cancer due to the fertility drugs. More studies are needed to confirm whether there is an association of cancer with use of fertility drugs. Overall, the data we currently have seems reassuring.

Risks of Pregnancy

Getting pregnant following IVF may be associated with risks. This is partly because patients using IVF are often older than those who conceive on their own without infertility treatment. In addition, the cause of infertility itself may contribute. There may be other risks linked to IVF that are not known at this time. Please see the table below for certain known risks. It is important to be mindful that these numbers are not adjusted, meaning that the differences may be partially attributed to differences in the population and not necessarily IVF itself.

Multifetal pregnancies (twins, triplets or more) in general have an increased risk of complications during pregnancy. In addition to preterm (early) delivery, problems for the patient include pre-eclampsia (high blood pressure and protein in the urine), diabetes of pregnancy (gestational diabetes), and excess bleeding at the time of childbirth. Problems with the placenta (afterbirth) are also more common. Other problems more common with multifetal pregnancy include gallbladder problems during pregnancy, skin problems, and the need for extra weight gain.

Following IVF, embryos are transferred directly into the uterus. However, tubal, cervical, or abdominal ectopic pregnancies can sometimes occur. These abnormal pregnancies may need to be treated with medication or surgery. Abnormal pregnancies within the uterus can also occur.

Risks of Pregnancy with IVF[1]

	Fertile population	Subfertile population[2]	IVF singleton pregnancies	Difference in pregnancies conceived with IVF (cases per 1,000 women)
Gestational Diabetes	5.6%	8.5%	8.2%	- 3
Pregnancy Induced High Blood Pressure	8.6%	10.2%	12.6%	+ 24
Placental Complications	1.7%	2.7%	5.4%	+ 27
Primary Cesarean Delivery	18.0%	20.5%	32.2%	+ 117
Low Birthweight (<5.5 pounds)	5.4%	5.7%	7.7 %	+ 20
Preterm Birth (<37 weeks gestation)	6.3%	7.7 %	10.3%	+ 26

[1] Table adapted from Luke B, Gopal D, Cabral H, Et al. Pregnancy, birth, and infant outcomes by maternal fertility status: the Massachusetts Outcomes Study of Assisted Reproductive Technology. Am J Obstet Gynecol. 2017 Sep;217(3):327.e1-327.e14
[2] Patients with a diagnosis of infertility that conceived without IVF
[3] Compared to the subfertile population
[4] These incidences may also be related to differences in the populations such as age and comorbidities

Risks of Pregnancy

Risks to Your Baby

- Babies born following IVF may be at a slightly higher risk for birth defects and genetic defects.
- IVF has a slightly greater chance of twin pregnancy, even when only one embryo is transferred.

Overall Risks

The first IVF baby was born in July 1978. Since then, almost 8 million children around the world have been born through IVF. Studies have shown that these children are quite healthy. In fact, some experts believe having a child through IVF is now just as safe as having a child naturally. Still, one must be careful when making this claim. Infertile patients or couples do not have normal reproductive functions. This means that a baby they have through IVF may have more health problems than a baby conceived naturally.

IVF singleton babies are often born about 2 days earlier than spontaneously conceived babies. They are about 5% more likely to weigh less than 5 pounds, 8 ounces (2,500 grams) than a spontaneously conceived single baby.

IVF twins are not born earlier or later than spontaneously conceived twins. In general, all twin pregnancies (and beyond) are at higher risk of preterm labor and preterm birth, compared to singleton pregnancies.

The risks of embryo **cryopreservation** (freezing) have been studied in animal tests over several generations. Human data has also been studied. There is no evidence that children born from cryopreserved and thawed embryos or cryopreserved, and thawed eggs or sperm have any more health problems than those born from fresh embryos/eggs.

Birth Defects

The risk of birth defects in babies conceived spontaneously is about 4.4%, and it is about 3% for severe birth defects. In IVF- conceived babies, the risk for any birth defect is about 5.3%, while the risk for a severe birth defect is about 3.7%. Most of the increased risk with IVF seems to be related to the fact that women going through IVF are often older and having infertility may also be associated with increased risk of birth defects. No higher risk has been seen in frozen embryo or donor egg cycles.

Imprinting Disorders

These are extremely rare disorders caused by whether the genes from the egg or the genes from the sperm are activated. Studies do not agree on whether these disorders are associated with IVF or ICSI or not. Even if they are, these disorders are extremely rare (1 out of 15,000 people).

Childhood Cancers

Most studies do not suggest any increased risk of childhood cancer in babies born from IVF, except possibly for retinoblastoma (a cancer behind the eye). One study did report an increased risk after IVF treatment, but further studies did not find an increased risk. Overall, the data we currently have is reassuring.

Infant Development

Most studies of long-term developmental outcomes have been reassuring so far. Most children are doing very well. However, these studies are hard to do, and they have some limitations.

Risks of Pregnancy

Risks of a Multiple Pregnancy

In the past, more than 30% of IVF pregnancies were multifetal pregnancies (twins, triplets, or greater). More recently, due to a concerted effort to transfer only one embryo at a time, less than 15% of IVF pregnancies are multiple pregnancies. Identical twins, also called monozygotic twins, occur in less than 3% of all IVF pregnancies. Identical twins may happen more often after **blastocyst** (Day 5) transfers, and with assisted hatching after cleavage stage (Day 3) transfers. These techniques may increase the chance of a single embryo splitting after transfer (to 2-3%), likely accounting for the slightly increased risk of identical twinning in IVF.

Preterm (early) delivery accounts for most of the complications associated with twins and higher order multiple pregnancies. IVF twins deliver an average of three weeks earlier than IVF singleton babies, and they weigh about 2 pounds less than IVF singleton babies. Triplet (and greater) pregnancies deliver before 32 weeks (7 months) in almost half of cases. Fetal growth problems and unequal growth among the fetuses can also result in perinatal illness and death before or shortly after delivery.

Multiple fetuses that share the same placenta (monochorionic twins), such as most identical twins, have additional risks. **Twin-to-twin transfusion syndrome**, where the circulation is not equal between the fetuses, may occur in up to 20% of twins who share a placenta (although this is rare overall because monochorionic twinning is rare). Twins sharing the same placenta have a higher frequency of birth defects compared to twins with two placentas (dichorionic; by far the most common type of twinning). Death of one fetus in a twin pregnancy after the first trimester is more common with a shared placenta; this may cause harm to the remaining fetus.

Other problems babies can face include cerebral palsy, retinopathy of prematurity (eye problems that result from early delivery), and chronic lung disease. Premature birth associated with multiple pregnancies may also affect neurological or behavioral development (e.g., Autism, learning disabilities, etc.), even when none of the other problems occur.

Fetal death rates for singleton pregnancies are 4.3 per 1,000. For twins, that number is higher at 15.5 per 1,000; and for triplets, the fetal death rate is 21 per 1,000. The death of one or more fetuses in a multiple pregnancy ("vanishing twin") is more common in the first trimester and may happen in up to 25% of IVF pregnancies.

The Option of Multifetal Pregnancy Reduction (Selective Reduction)

The more fetuses there are in the uterus, the greater the chance of complications related to preterm delivery and others. Patients with twins or more have 3 choices:

- Continue with the pregnancy (with all the risks that have already been stated).
- End the pregnancy.
- Reduce the number of fetuses (terminate one or more of the fetuses) to lower the health risks to the patient carrying and to the remaining fetus.

Reducing the number of fetuses lowers the risk of early delivery. This can be a difficult decision to make. The main danger is losing the entire pregnancy. The odds of losing the entire pregnancy are about 1 in 100 (1%). The odds of losing the entire pregnancy are greater if there are more than 3 fetuses present before the procedure is done. This should be discussed with your infertility doctor and with a high-risk obstetrician (maternal-fetal medicine physician).

As previously stated, the majority of embryo transfers are now single embryo transfers (due to significant improvements in IVF lab technology), therefore higher order multiple pregnancies like triplets or more are now quite rare in IVF.

Ethical & Religious Considerations In Infertility Treatment

Psychosocial Effects of Infertility Treatment

Finding out that you or your partner is infertile or have a lower fertility can be very painful. Infertility and its treatment can affect your emotions, your health, your finances, and your social life. During treatment, you may feel anxious, helpless, depressed, or isolated. You may go through highs and lows. Be sure to notice if these feelings get severe. In some cases, you may want to seek the help of a mental health professional. Here are some of the warning signs you should watch out for, and seek help immediately if you experience:

- Losing interest in the things you usually like to do.
- Feeling depressed most of the time.
- Strained feelings with your partner, family, friends, or those with whom you work with.
- Thinking about infertility all the time.
- Feeling extremely anxious or nervous.
- Having trouble finishing tasks.
- Finding it hard to focus or concentrate.
- Having changes in your sleep patterns, such as having a hard time falling asleep or staying asleep, waking up early every morning, or sleeping more than normal.
- Having a change in your appetite or weight (increase or decrease).
- Using drugs or alcohol more than before.
- Thinking about death or suicide.
- Staying away from other people.
- Feeling negative, guilty, or worthless much of the time.
- Feeling bitter or angry much of the time.

Infertility treatment can raise ethical or religious concerns for some patients. IVF involves the creation of embryos outside the human body. It can also involve the production of extra embryos, and can lead to a high number of fetuses (triplets or more). Patients who have concerns should speak with their counselor or religious leader, or with someone else they trust. This can be a helpful step in infertility treatment.

Raising twins or higher multiples may cause physical, emotional, financial, and marital stresses. The chance of having depression and anxiety is higher in patients raising multiples.

Patients may consider working with mental health professionals who are specially trained in infertility care, as well as with their health care team, to minimize the emotional impact of infertility treatments.

National support groups are also available, such as RESOLVE, **(www.resolve.org)** or Path2Parenthood **(www.path2parenthood.org)**.

Reporting Outcomes

In 1992, the **Fertility Clinic Success Rate and Certification Act** was passed. This federal law requires the Centers for Disease Control and Prevention (CDC) to gather facts about IVF cycles and pregnancy outcomes in the U.S. each year. These facts and success rates are reported every year.

De-identified information from your IVF procedure will be reported to the CDC. It will also be reported to the Society of Assisted Reproductive Technologies (SART) of the American Society for Reproductive Medicine (ASRM) if your clinic is a member of this organization. The CDC may ask for more information from the treatment center or contact you directly for additional follow up. Information about your cycle may be used for research or quality control according to HIPAA guidelines. Your name will never be connected to your cycle information in any research that is published.

Research Conducted by SART

Since 2006, the Society for Assisted Reproductive Technology (SART) has participated in a series of studies looking at the health of patients and children after IVF. Many of these studies are still being conducted. The studies compare patients who have not had trouble conceiving and their children with patients who used IVF and their children. The studies also compare patients who had trouble conceiving but did not do IVF, and their children, to patients and their IVF children. IVF children who have siblings from another study group. They are compared with their siblings who were conceived with IVF, conceived with non-IVF fertility treatment, or conceived spontaneously. The items studied are problems related to pregnancy or birth, and the risk of birth defects. Children are also followed to find out if they have developmental delays, problems in school, or increased risk of childhood or adult cancer. You can see the results of many of these studies in the information given below. Results can also be found on the SART website **(www.sart.org)** under "Research."

Research & Innovation at Boston IVF

Boston IVF is affiliated with Harvard Medical School and Beth Israel Deaconess Medical Center.

Boston IVF has conducted 100+ clinical trials which have led to improved fertility care, including the first ICSI/IVF pregnancy in New England, the first baby born in Massachusetts from a frozen egg, recent advancements in transgender family building, and more.

Before you start treatment, your doctor or a member of the research team may approach you to participate in a research study. These studies can help further the field of reproductive medicine and help patients in the future.

Some studies may offer free or discounted treatment or medications. Some studies may offer monetary incentive. These studies are entirely optional and declining to participate will not affect your treatment in any way.

Research involving discarded material

In some cases, Boston IVF may have surplus biological samples including discarded sperm, eggs, embryos follicular fluid and blood. These may be used for future studies conducting research that leads to a better understanding of infertility and to improve techniques used in the treatment of infertility. If these discarded samples are studied as part of a human research project, the study will be conducted in compliance with an Institutional Review Board (IRB) approved protocol. No discarded samples will ever be used to create embryos or establish a pregnancy.

Research involving deidentified data

De-identified information related to your treatment at Boston IVF may also be used to perform quality control and identify trends that improve patient care and advance the field of infertility. These research projects would only be done in compliance with an Institutional Review Board (IRB) approved protocol. Boston IVF may present research findings at meetings, conferences and in publications.

Please ask your clinician if you have any concerns.

Additional Information

General IVF Overviews Available on the Internet

www.reproductivefacts.org
www.sart.org
www.cdc.gov/art
www.resolve.org

Birth Defects

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Culturing Embryos to the Blastocyst Stage

Blastocyst culture and transfer in clinical-assisted reproduction: A committee opinion. The Practice Committee of the American Society for Reproductive Medicine and the Practice Committee of the Society for Assisted Reproductive Technology. Fertil Steril 2013; 99:667-72.

Effect of Infertility Diagnoses

Stern JE, Luke B, Tobias M, Gopal D, Hornstein MD, Diop H. Adverse pregnancy and birth outcomes by infertility diagnoses with and without ART treatment. Fertility and Sterility 2015; 103:1438-45.

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Effect of Maternal Obesity

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Obesity and reproduction: A committee opinion. Practice Committee of the American Society for Reproductive Medicine. Fertility and Sterility 2015; 104:1116-26.

Effect of Number of Oocytes Retrieved

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The role of assisted hatching in in vitro fertilization: a guideline. A Committee opinion. The Practice Committee of the American Society for Reproductive Medicine and the Practice Committee of the Society for Assisted Reproductive Technology. Fertil Steril 2014; 102:348-51.

Luke B, Brown MB, Wantman E, Stern JE. Factors associated with monozygosity in assisted reproductive technology (ART) pregnancies and the risk of recurrence using linked cycles Fertility and Sterility, 2014; 101:683-9.

Intracytoplasmic Sperm Injection (ICSI)

Genetic considerations related to intracytoplasmic sperm injection (ICSI). The Practice Committee of the American Society for Reproductive Medicine and the Practice Committee of the Society for Assisted Reproductive Technology. Fertility Sterility 2006; 86 (suppl 4): S103-S105.

Intracytoplasmic sperm injection (ICSI) for non-male factor infertility: a committee opinion. Practice Committees of the American Society for Reproductive Medicine and Society for Assisted Reproductive Technology. Fertility and Sterility 2012; 98:1395-9.

Wen J, Jiang J, Ding C, Dai J, Liu Y, Xia Y, Liu J, Hu Z. Birth defects in children conceived by in vitro fertilization and intracytoplasmic sperm injection: a meta-analysis. Fertility and Sterility 2012; 97(6): 1331-1337 e4.

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Additional Information

Number of Embryos to Transfer

Elective single-embryo transfer. Practice Committee of the American Society for Reproductive Medicine and the Practice Committee of the Society for Assisted Reproductive Technology. Fertility and Sterility 2012; 97:835-42.

Criteria for number of embryos to transfer: a committee opinion. The Practice Committee of the American Society for Reproductive Medicine and the Practice Committee of the Society for Assisted Reproductive Technology. Fertil Steril 2013; 99(1):44-6.

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Multiple pregnancy associated with infertility therapy: an American Society for Reproductive Medicine Practice Committee opinion. Practice Committees of the American Society for Reproductive Medicine Fertil Steril 2012; 97:825-34.

Imprinting diseases and IVF: A Danish National IVF cohort study. Lidegaard O, Pinborg A and Anderson AN. Human Reproduction 2005; 20(4):950-954.

Amor DJ and Halliday J. A review of known imprinting syndromes and their association with assisted reproduction technologies. Human Reproduction 2008; 23:2826-34.

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Luke B, Brown MB, Spector LG, Missmer SA, Leach RE, Williams M, Koch L, Smith Y, Stern JE, Ball GD, Schymura MJ. Cancer in women after assisted reproductive technology. Fertility and Sterility 2015; 104:1218-26.

Glossary

A

Adhesions: Scar tissue that may be located in the abdominal cavity, fallopian tubes, or inside the uterus. Can can tubal factor infertility or Asherman's syndrome (intrauterine adhesions that can impact ongoing implantation).

Amenorrhea: Lack of a menstrual period for 6 months or more.

Andrology: A medical specialty that evaluates male fertility.

Aneuploid: A chromosomally abnormal embryo (wrong number of chromosomes).

Anovulation: The failure to ovulate and the most common cause of female subfertility. There are many different causes for the failure to ovulate, including problems with the central nervous system or pituitary gland, and abnormalities within the follicles or ovaries (PCOS is a common example).

Assisted Hatching (AH or AZH): A micromanipulation procedure in which an opening is made into the hard outer surface of the early embryo (zona pellucida) with the use of chemicals, mechanical techniques, or lasers to potentially improve implantation after the embryo is transferred into the uterus.

Assisted Reproductive Technology (ART): A group of treatment methods used to improve fertility, which involves collecting the eggs and putting them in direct contact with sperm. ART is an umbrella term that includes IVF, ICSI, Assisted Hatching, egg freezing, and more.

Azoospermia: Semen that contains no sperm, either because the testicles cannot make sperm (non-obstructive) or because the individual's reproductive tract is blocked (obstructive).

B

Basal Body Temperature (BBT): The body temperature when taken at its lowest point, usually in the morning before getting out of bed. Charting an individual's BBT is used to monitor ovulation. If the BBT pattern rises about a half degree during the latter half of the menstrual cycle, it suggests that ovulation has taken place.

Beta hCG Test (BhCG): A blood test used to detect very early pregnancies and to evaluate the development of the embryo. The test measures hCG, which is secreted by early placental cells after implantation. We often repeat this test serially, looking for an appropriate rise in early pregnancy.

Blastocyst: A stage of embryonic development that occurs about 5 days after fertilization, when the embryo consists of two different cell types (those that will form the placenta and those that will form the fetus) and a central cavity.

Blastocyst Transfer: The placement of blastocysts into the uterus during IVF.

Blighted Ovum (Egg): Older term for an embryo that attaches itself to the uterine wall, but the embryo does not develop. Now more often called "anembryonic pregnancy." The amniotic sac may only contain fluid and no fetal tissue when a miscarriage occurs.

Bromocriptine: A medication used to reduce the prolactin secreted from the pituitary in those women with high prolactin levels, which may impact ovulation. Brand names include Parlodel and Dostinex.

C

Cervical Mucus: The mucus produced by glands in the cervical canal that plugs the opening of the cervix. Most of the time this thick mucus plug prevents sperm and bacteria from entering the uterus except around the time of ovulation (the "fertile window"). At this time, under the influence of estrogen, the mucus becomes thin, watery, and stretchy so that sperm can pass into the uterus.

Cervix: The opening into the uterus.

Chemical Pregnancy: A pregnancy verified by blood hCG test, but which results in an early loss before a gestational sac is seen on an ultrasound. Also called biochemical pregnancy.

Chocolate Cyst: A cyst in the ovary that is filled with old blood. It is known medically as an "endometrioma." The term chocolate cyst is used because it resembles melted chocolate. A chocolate cyst forms when endometriosis implants invade the ovary and bleed.

Clomiphene (or Clomid): Often a first line of treatment to stimulate and induce ovulation. Clomid binds to estrogen receptors in the hypothalamus. When their sites are occupied, the hypothalamus responds by telling the pituitary to release more Follicle Stimulating Hormone (FSH).

Glossary

Conception: The fertilization of an egg by sperm that leads to the creation of a baby.

Congenital Bilateral Absence of the Vas Deferens (CBAVD): A condition where the tubes that connect the testes to the penis did not form correctly. These patients have azoospermia, or no sperm in the ejaculate, and associated infertility. Patients with CBAVD may also suffer from a mild form of Cystic Fibrosis.

Congenital: Conditions present from birth, either hereditary or environmental.

Corpus Luteum: A yellow-colored cyst that forms from the ovarian follicle after it releases an egg. Once formed, the cyst produces estrogen and progesterone to prepare and support the uterine lining for implantation.

Cryopreservation: The freezing of eggs and embryos to provide opportunities for pregnancy in the future. Also known as egg or embryo freezing.

D

Diminished Ovarian Reserve (DOR): Low remaining egg reserve (typically age-based). DOR is typically diagnosed with ovarian reserve testing, such as AMH, FSH, and/or antral follicle count. Patients with DOR typically respond less to ovarian stimulation.

Donor Sperm: Sperm from a known or (more typically) anonymous donor who does not intend to parent the future child.

E

Ectopic Pregnancy: A condition in which the embryo implants outside of the uterus, usually in the fallopian tube, although it can also occur in the ovary, cesarean section scar, cervix, or abdominal cavity. If such a pregnancy is allowed to continue, it may eventually rupture the fallopian tube and cause life-threatening hemorrhage. Such a pregnancy can never be sustained and often leads to decreased or complete loss of function in the affected tube. Also known as a tubal pregnancy.

Egg: Female reproductive cell.

Egg Donation: Process in which eggs from a person of young reproductive age are donated to an individual/couple, i.e. intended parent(s), for use in an Assisted Reproductive Technology (ART) procedure.

Egg Retrieval: An outpatient procedure to collect eggs from stimulated ovaries, typically performed under IV sedation with trans-vaginal ultrasound and needle aspiration.

Embryo: A term that describes the time from fertilization of the egg up to 10 weeks of pregnancy.

Embryo Culture Medium: Special fluid made to resemble that found in the fallopian tubes to support development of the retrieved embryos.

Embryo Grade: A method used by embryologists to determine which embryos to transfer, based on their appearance. At Boston IVF, we use the Gardner grading system, used by many IVF clinics around the world.

Embryo Transfer: Placement of one or more embryos into the uterus through the cervix, typically performed with ultrasound guidance.

Endometrial Biopsy: A small sampling of endometrial cells for microscopic study.

Endometriosis: A chronic condition in which some of the normal cells that line the internal cavity (endometrial tissue) are found outside the uterus, most often in the pelvic area involving the ovaries, fallopian tubes, bladder, bowel, and rectum. Endometriosis may interfere with fertility in multiple ways, including egg quality, tubal scarring, and implantation.

Endometrium: The lining of the uterus.

Epididymis: A coiled, tubular organ attached to and lying on the testicle that stores the sperm before ejaculation.

Estradiol (E2): A hormone normally produced by the ovaries, important in multiple different reproductive and health functions. Estradiol, or estrogen, supports bone health before menopause, and thickens the uterine lining for pregnancy.

Euploid: A chromosomally normal embryo.

Glossary

F

Fallopian Tubes: The passageway through which a fertilized egg must travel to reach the uterus and implant in a spontaneous conception.

Fertility Clinic Success Rate and Certification Act (1992): A federal law that requires the Centers for Disease Control and Prevention (CDC) to gather and report facts about IVF cycles and pregnancy outcomes in the U.S. each year.

Fertility Clinic: A program of fertility specialists offering a range of fertility services, usually including Assisted Reproductive Technology (ART).

Fertility Drugs: A group of medications given to people to improve fertility, depending on infertility diagnosis.

Fertilization: Penetration of the egg by the sperm cell with subsequent evidence of 2PN (pronuclear) and 2 polar bodies, signaling normal fertilization.

Fetal Reduction: A technique that reduces the number of fetuses in a multifetal pregnancy to reduce the associated risks.

Fetus: A term used to describe a human in utero development, from the period when the embryo is fully formed at around 8-10 weeks, until birth.

Fibroid/Myoma: Benign tumors of the uterine muscle and connective tissue.

Fimbria: Fingerlike projections at the end of the fallopian tube nearest the ovary. When stimulated by the fluid released from the follicles during ovulation, the fingerlike ends should grasp the egg and sweep it into the tube.

Follicle Stimulating Hormone (FSH): Produced by the pituitary gland in the brain. Measurements of FSH with estradiol (E2) early in the menstrual cycle is a part of assessing current ovarian reserve. A high FSH indicates a low ovarian reserve. Injectable FSH is also used to stimulate the ovaries during fertility treatment. Medications include Bravelle, Follistim, and Gonal-F.

Follicle: A fluid-filled sac in the ovary that contains an egg.

Follicular Fluid: The contents aspirated during an egg retrieval.

Follicular Phase: The portion of an individual's cycle before ovulation during which a follicle grows and increasing levels of estrogen cause the lining of the uterus to thicken.

Fresh Embryo Transfer: An embryo transfer that occurs 3 or 5 days after the egg retrieval.

Frozen Embryo Transfer: Embryos frozen and thawed for transfer at a later date.

G

Gamete Intra-Fallopian Tube Transfer (GIFT): A technique in which the egg and the sperm are brought together by retrieving the eggs, placing them with sperm into a catheter, and immediately delivering them into the fallopian tube for fertilization using laparoscopy. This is rarely done in a modern IVF clinic.

Gamete: Term for either a sperm or egg.

Genetic Carrier Screening: A procedure that determines if one or both parents may carry abnormal genes that increase the chance that their child will have a specific genetic disease.

Gestation: The medical term for pregnancy.

Gestational Carrier: A person with prior healthy pregnancy who elects to carry a pregnancy for another person or couple who cannot carry the pregnancy for various reasons. A gestational carrier (or "surrogate") carries a pregnancy genetically unrelated to them for the intended parent(s).

Gn-RH Agonist: Drugs sometimes used in an IVF cycle that inhibit premature ovulation. Medications include Lupron and Synarel.

Gn-RH Antagonist: Drugs often used in an IVF cycle that inhibit premature ovulation. Medications include Cetrotide and Ganirelix.

Gonadotropins: Natural hormones that stimulate the ovary over the span of typically 8 to 12 days, with the intention of growing several eggs. Examples include Luteinizing Hormone (LH) and Follicle Stimulating Hormone (FSH).

Gonads: The umbrella term for the ovaries and testicles, i.e., glands that produce sex steroids for reproductive function.

Granulosa: Cells in the ovary that support eggs.

Gynecologist: A physician whose specialty is health care for people with female reproductive organs, like a uterus and ovaries.

Glossary

H

Hormone: A chemical substance that travels via the bloodstream and carries a signal from one part of the body to another.

Human Chorionic Gonadotropin (hCG): A natural hormone used in IVF to induce the eggs to become mature and fertilizable. Medications include Ovidrel, Novaryl, and Pregnyl.

Human Menopausal Gonadotropin (hMG): Fertility medication that stimulates follicle growth. Medications include Menopur, Repronex and Luvens.

Hypothalamus: A part of the brain that sends signals to the pituitary gland and is critical for normal menstrual cycle function, as part of the HPO (hypothalamic-pituitary-ovarian) axis.

Hysterectomy: Surgical removal of the uterus and typically the cervix and fallopian tubes, but not necessarily the ovaries.

Hysterosalpingogram (HSG, Hysterogram, Tubogram): An X-ray of the pelvic organs while a radio-opaque dye is injected through the cervix into the uterus and fallopian tubes. This test is used to check for malformations of the uterus or blocked fallopian tubes in suspected infertility.

I

Implantation: The cellular process of attachment of the embryo to the maternal uterine wall.

Imprinting Disorders: Extremely rare disorders caused by whether the genes from the egg or the genes from the sperm are activated.

In Vitro Fertilization (IVF): Literally meaning "in glass," a method of assisted reproductive technology where an egg and sperm are combined outside the body. One or more eggs may fertilize and be transferred into the uterus to further develop.

Infertility: The inability to conceive after a year (or 6 months, depending on age) of unprotected, well-timed intercourse, or the inability to carry a pregnancy to term.

Inner Cell Mass: The cluster of cells in an early embryo that forms the future fetus.

Intracytoplasmic Sperm Injection (ICSI): An IVF technique that involves the direct injection of a single normal appearing sperm into the interior of an egg using an extremely thin glass needle. This allows patients with severe sperm factor infertility to achieve higher fertilization and live birth rates.

Intrauterine Insemination (IUI): Placing a concentrated pellet of washed sperm directly into the uterus, bypassing the cervix, with the goal of fertilizing an egg in the fallopian tube.

L

Laparoscopy: A minimally invasive surgical procedure in which a telescope-like instrument is inserted through a small incision in the abdominal wall to view the inner organs in order to diagnose and sometimes treat suspected reproductive problems.

Leuprolide Acetate: A fertility drug containing a Gonadotropin-releasing hormone analog that, following an initial stimulation, suppresses premature ovulation. Medication includes Lupron.

Luteal Phase: The second half of the menstrual cycle that occurs between the release of an egg (ovulation) and the menstrual period. Progesterone is the dominant hormone of the luteal phase.

Luteinizing Hormone (LH): A pituitary hormone that stimulates the ovaries or testicles.

LH Surge: A sudden large release of luteinizing hormone from the pituitary gland that triggers ovulation about 36 hours after the surge begins.

M

Menstrual Cycle: The monthly series of physiologic reproductive changes in the uterus and ovaries that averages about 28 days, measured from day one of a period to the next day one.

Microdeletions: A genetic abnormality due to a small missing section of a chromosome, sometimes resulting in disease.

Glossary

Micromanipulation: The use of high magnification and special instruments to manipulate sperm, eggs, and embryos during IVF.

Miscarriage: The spontaneous loss of an embryo or fetus before the 20th week of pregnancy. Most miscarriages occur during the first trimester of pregnancy, with the majority occurring before 9-10 weeks of gestation.

Mosaicism: The phenomenon of having 2 or more genetically distinct cell types co-existing; in this case, within a single embryo.

Myomectomy: The surgical removal of fibroids from the uterus.

O

Oligomenorrhea: An irregular menstrual cycle that occurs in intervals longer than 35 days. This condition is usually caused by abnormal coordination between the hypothalamus, the pituitary gland, and the ovaries.

Oligospermia: The term for a low sperm count in the ejaculate.

Oocyte: The biological term for an egg.

Oocyte Retrieval: Removal of eggs from the ovary, most often under anesthesia.

Oolemma: Egg membrane.

Ovary: The reproductive gland that contains eggs (oocytes) and produces sex hormones such as estrogen.

Ovarian Cyst: A fluid-filled sac within or on the surface of the ovary. The majority of ovarian cysts are not related to any disease and disappear without treatment within a few months.

Ovarian Failure: A condition involving a loss of normal ovarian function in which the ovaries do not produce eggs, so estrogen levels drop and follicle-stimulating hormone levels rise. In patients under age 40, this is called POI (primary ovarian insufficiency) or "early menopause."

Ovarian Hyperstimulation Syndrome (OHSS): The most severe side effect of stimulating the ovaries, OHSS causes fluid to leak from blood vessels. Signs of OHSS include increased ovarian size, nausea, vomiting, severe abdominal distention, shortness of breath, and a buildup of fluid in the abdomen or around the lungs.

Ovulation: The release of a mature egg from a follicle.

Ovulation Induction: Drug treatment that stimulates the development and release of one or more mature eggs from the ovaries.

P

Pap Smear: A microscopic examination of cells sampled from the cervix to detect cancerous or precancerous conditions of the cervix.

Pelvic Inflammatory Disease (PID): A general term for infection of the female reproductive organs.

Pituitary Gland: The small gland found at the base of the brain that secretes many hormones, including Follicle Stimulating Hormone (FSH) and Luteinizing Hormone (LH).

Polycystic Ovary Syndrome (PCOS): A metabolic condition associated with irregular or absent ovulation. The condition may include obesity, infertility, and excess hair growth.

Pre-Eclampsia: A complication of pregnancy that involves high blood pressure and protein in the urine. Patients that are carrying a multifetaletal pregnancy are more likely to develop pre-eclampsia.

Preimplantation Genetic Testing for a Structural Rearrangement in the Chromosomes (PGT-SR): Embryo biopsy and specialized testing for when a partner carries a translocation, aimed at selecting a chromosomally normal embryo.

Preimplantation Genetic Testing for Aneuploidy (PGT-A): Testing for an abnormal number of chromosomes in the embryo; this test also provides information on the biological sex (not gender) of the embryo: XX female or XY male.

Preimplantation Genetic Testing for Monogenic Disease (PGT-M): Testing for a specific, known genetic disease caused by a single gene mutation. Typically, this is offered when it is found that both partners are a carrier of the same disease, putting future offspring at risk.

Progesterone: A hormone normally produced by the ovaries and is critical for pregnancy support. After egg retrieval and in preparation for embryo transfer, supplemental progesterone is commonly prescribed.

Glossary

Prolactin: The pituitary hormone that stimulates the production of milk in those who breastfeed. It also circulates at low levels in the bloodstream of non-pregnant people. High levels of prolactin in non-pregnant people can cause anovulation.

Pyospermia: A high white blood cell count in the semen, indicating infection.

Q

Quality Control: Process of running tests to ensure lab conditions are the best they can be to help embryos grow.

R

Reproductive Endocrinologist: A doctor who specializes in the diagnosis and treatment of infertility. Also known as a fertility specialist.

Rescue ICSI: When low or no fertilization is observed the day after egg retrieval after normal insemination is used. In this case, it is sometimes appropriate to offer rescue ICSI in attempt to fertilize the eggs successfully.

S

Salpingectomy: Surgical removal of one or more fallopian tubes. Salpingectomy is usually performed if the tube has become infected or to treat an ectopic pregnancy.

Salpingitis: Inflammation of the fallopian tube.

Semen: Fluid of the male reproductive tract, containing sperm and a number of other substances such as water, simple sugars, alkaline chemicals, and prostaglandins.

Semen Analysis (SA): A laboratory test used to assess the amount and quality of the sperm and semen.

Sperm: Male reproductive cell.

Sperm Bank: A service that maintains frozen sperm samples.

Sperm Count: The number of sperm in the ejaculate, also called sperm concentration and given as the number of sperm per milliliter. A low sperm count is called oligospermia. A sperm count of 20 million/ml or above is considered normal.

Sperm Morphology: The evaluation of the size and shape of sperm in a semen analysis.

Sperm Motility: The proportion of sperm that moves in a forward motion.

Sperm Wash: A technique used to separate sperm cells from the seminal fluid, resulting in a small volume of highly concentrated sperm used for IUI treatments.

Sterility: A condition that results in the absolute inability to reproduce.

Swim-Up Test: A useful diagnostic procedure that also can be used to remove sperm from semen. It has some advantages to sperm washing because the live sperm will swim up to the culture media leaving behind most of the debris.

T

Testicles: Also known as testes, the male sex glands located in the scrotum. Testicles store and produce sperm and are the main source for the secretion of the male sex hormone testosterone.

Testicular Biopsy: A surgical procedure in which a small sample of testicular tissue is removed for microscopic examination to see if sperm is present and able to be retrieved.

Testosterone: The primary male hormone responsible for secondary sex characteristics and for supporting the sex drive. Testosterone is also necessary for sperm production.

Therapeutic Donor Insemination (TDI): A type of insemination using donor sperm not from a partner.

Translocations: A rearrangement of chromosomes that can cause birth defects or miscarriage.

Trophectoderm: The cells of a blastocyst that become the future placenta.

TTC: An abbreviation for "Trying to Conceive."

Glossary

Tubal Ligation: Female sterilization. The fallopian tubes are blocked to prevent the egg from meeting sperm. Commonly known as "having the tubes tied."

Tubal Pregnancy: A condition in which the embryo implants outside of the uterus, usually in the fallopian tube, although it can also occur in the ovary, cesarean section scar, cervix, or abdominal cavity. If such a pregnancy is allowed to continue, it may eventually rupture the fallopian tube and cause life-threatening hemorrhage. Such a pregnancy can never be sustained and often leads to decreased or complete loss of function in the affected tube. Also known as an ectopic pregnancy.

Twin-to-Twin Transfusion Syndrome: A condition where circulation is not equal between the fetuses of twins that share a placenta.

U

Ultrasound: Use of high-frequency sound waves that are reflected off solid tissues to give an image of internal body structures. This device is used to detect and count follicle growth in many fertility treatments and to detect and monitor pregnancy.

Uterus: Part of the female reproductive system that carries and nourishes a fetus prior to birth.

V

Vanishing Twin: The death of one or more fetuses in a multifetaletal pregnancy.

Venous Thromboembolism: Medical term for a blood clot.

Vitrification: The modern laboratory technique used to "flash freeze" eggs or embryos, which has led to much higher survival and success rates.

Z

Zona Pellucida: A flexible shell that encloses the cells that make up the early embryos.

Zygote: An embryo in the early stages of development that has two nuclei.