

INSTRUCTIONS:

This consent form provides a description of the treatment that you are undertaking and its benefits, risks, and alternatives.

- Read this informed consent document completely before signing the **Consent Signature Packet**. If you have any questions, please speak with your doctor.
- Do not make any additions or deletions to the consent. Treatment **cannot** be started until all consents are signed.
- Consents must be signed in front of a Genetics & IVF (GIVF) staff member or a Notary Public, or through a GIVF-initiated ID verified DocuSign.

In-Vitro Fertilization (IVF) has become an established treatment for many forms of infertility. IVF is a treatment that removes oocytes (eggs) from a patient's ovary or ovaries to achieve a pregnancy at that time or at a later time. The main goal of IVF is to allow a patient the opportunity to become pregnant using her own eggs, and sperm provided by her partner or from a donor.

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

An IVF cycle typically includes the following steps or procedures:

- Ovarian stimulation: taking medications to grow multiple eggs which are contained in small sacs called follicles within the ovaries
- Monitoring of ovarian response (follicular/egg development) performed with serial blood hormone tests and/or vaginal ultrasound exams
- Retrieval of eggs from the ovary or ovaries
- Insemination: Combining eggs and sperm together for fertilization
- Growing (culturing) any resulting fertilized eggs (embryos) in the lab
- Placement (transfer) of one or more embryo(s) into the uterus
- Taking hormone medications to help you have a successful pregnancy

In certain cases, these additional elements might be used or recommended:

- Intracytoplasmic Sperm Injection (ICSI) to increase the chance for fertilization
- Assisted hatching of embryos to increase the chances of embryo attachment ("implantation") or as part of the embryo biopsy protocol for preimplantation genetic testing
- Preimplantation Genetic Testing (PGT)
- Oocyte or Embryo Cryopreservation – freezing of unfertilized or fertilized eggs for later use
- Use of Gestational Carrier

GENERAL PRE-TREATMENT RECOMMENDATIONS

During treatment, the patient should avoid any activity, behavior, or medications that could reduce the chance of conceiving and having a healthy baby. These recommendations should be followed:

- A prenatal vitamin with at least 0.8 mg of Folic Acid should be taken daily before beginning treatment, optimally for at least one month prior to conception. This will reduce the risk of a neural tube defect (e.g., spina bifida), which is a birth defect that affects the development of the spine.
- Smoking and the use of smokeless tobacco or nicotine products (e.g.: cigarettes, vaping, nicotine gum, etc.) must be avoided before and during treatment, and pregnancy.
- Recreational drugs should not be used before or during treatment or pregnancy.
- The use of alcohol should be avoided during treatment and pregnancy.
- Aspirin or aspirin-like products (e.g., Motrin, Advil, Anaprox, Naprosyn, Aleve, etc.) should be avoided during treatment. However, in certain circumstances you may be advised to take low dose aspirin (baby aspirin, 81 mg). Tylenol is safe to take before and during treatment.
- The use of all prescription and over-the-counter medications, including herbal remedies, should be discussed with your care team before starting a treatment cycle.

IVF TREATMENT: CORE COMPONENTS

MEDICATIONS FOR IVF

- The success of IVF largely depends on growing several eggs at once.
- Injections of the natural hormones FSH and/or LH (gonadotropins) are used to stimulate the ovaries; Other medications are used to prevent early or premature ovulation.
- Sometimes the ovaries respond too strongly, and sometimes they don't respond enough.

The basic strategy of IVF relies upon the induction of the development of a large number of ovarian follicles simultaneously. Medications are administered to increase the number of follicles that develop, which will increase the number of eggs that are obtained at the egg retrieval, which will increase the number of embryos that will be available for transfer. FSH (follicle stimulating hormone) and/or LH (luteinizing hormone) injections are used for this purpose. These hormones are known as gonadotropins. Other medications are also used to prevent premature ovulation. The use of injectable gonadotropins requires careful monitoring to avoid either inadequate or excessive response.

Commonly used medications in an IVF cycle include but are not limited to:

- **Gonadotropins, or injectable “fertility drugs”** (Follistim®/Gonal-F®/Menopur®, or human chorionic gonadotropin – Ovidrel®/Pregnyl®/Novarel®): These are hormones that stimulate the ovary to grow several eggs (oocytes) at once over the span of 8 or more days or trigger the final development/maturation of the eggs. These injections may be given either just under the skin or directly into muscle. Monitoring ovarian response through blood tests and ultrasound during ovarian stimulation

is required to assure proper dosage of drugs and the timely recovery of eggs. Taking any medicine by injection can cause bruising, redness, swelling, or pain at the injection site. In rare cases, there can be an allergic reaction. Some women have bloating or minor discomfort as the ovaries briefly become enlarged. About 1% of women will develop Ovarian Hyperstimulation Syndrome (see *Risks of Ovarian Stimulation with Fertility Drugs* section, below.) Other side effects can include headaches, weight gain, feeling tired, mood swings, nausea, or clots in blood vessels. Sometimes, especially when hormone testing prior to the IVF cycle has shown that the patient has a lower number of eggs available, the medications may not help multiple eggs to grow. There may be very few or even no eggs harvested at the egg retrieval procedure, or the cycle may be canceled prior to egg retrieval.

- **GnRH-agonists (leuprolide acetate) (Lupron®):** This medication is an injection available in two forms. One is a short-acting form that needs to be injected daily, and the other is a long-acting form that lasts for 1-3 months. Leuprolide is often given to help prevent the release of eggs (by ovulation) before they can be retrieved. It can also be used to start the growth of eggs or trigger the final stages of their development and maturation. Leuprolide is approved by the U.S. Food and Drug Administration (FDA), but not approved for use in IVF. However, it has been extensively studied and used in IVF patients for more than 20 years. Leuprolide side effects include hot flashes, vaginal dryness, nausea, headaches, and muscle aches. Some women may retain fluid or feel depressed, and long-term use can result in bone loss. Since it is taken as an injection, skin reactions can also occur where the injection is given. No serious side effects are known. If Leuprolide is given in a cycle after ovulation has occurred, you should use condoms for birth control in that month. Leuprolide has not been linked with any birth defects, but it should be stopped if you become pregnant while taking it.
- **GnRH-antagonists (Ganirelix®, Cetrotide®):** These medications are used to prevent premature ovulation. Side effects may include stomach pain, headaches, skin reactions at the injection site, and nausea.
- **Progesterone, and in some cases, estradiol:** These two hormones are normally produced by the ovaries after ovulation. In some women, after egg retrieval, the ovaries will not produce enough of these hormones to support a pregnancy. Adding them helps improve your chances of getting pregnant and staying pregnant. Progesterone can be taken as a daily intramuscular injection or as a vaginal suppository (Endometrin®, Crinone®, Prochieve®, Prometrium®, or pharmacist-compounded suppositories) as frequently as three times per day after egg retrieval. Progesterone is often continued for a few weeks after you become pregnant and has not been shown to cause birth defects. Side effects can include depression, sleepiness, or an allergic reaction. The intra-muscular injection can cause infection or pain at the injection site. Estradiol can be taken by pill, patch, intramuscular shot, or as a vaginal suppository. Side effects of estradiol include nausea, irritation at the site of the injection or patch, and the risk of blood clots or stroke.
- **Oral contraceptive pills (birth control pills):** Many treatment protocols include birth control pills for 2 to 4 weeks before starting hormone stimulation injections to suppress hormone production or to schedule a treatment cycle. Side effects include bleeding, headache, breast tenderness, nausea, and swelling. There is also a risk of blood clots or, very rarely, stroke.
- **Clomid or Letrozole (oral pills):** These medicines are used in some treatments as part of the ovarian stimulation protocol or to reduce the estrogen level in the bloodstream. Short-term side effects in some women include headache, hot flashes, or increased moodiness.
- **Other medications:** Antibiotics may be given for a short time during the treatment cycle to reduce the risk of infection from egg retrieval. Antibiotic use may cause a number of side effects including vaginal yeast infection, nausea, vomiting, diarrhea, rashes, sensitivity to the sun, or allergic reactions. Anti-

anxiety medications or a muscle relaxant may be recommended prior to the embryo transfer. The most common side effect of these medicines is drowsiness. Other medicines such as steroids, heparin, low molecular weight heparin, or low dose aspirin may also be recommended.

Risks of Ovarian Stimulation with Fertility Drugs:

The use of the above listed medications can cause side effects such as nausea, vomiting, hot flashes, headaches, mood swings, abdominal bloating and cramping, visual symptoms, memory difficulties, joint problems, weight gain and weight loss, all of which are temporary. Rare allergic reactions are also possible. Other possible side effects include the following:

- **Ovarian Hyperstimulation Syndrome (OHSS):** Ovarian Hyperstimulation Syndrome is the most severe possible side effect of stimulating the ovaries and is more of a concern when using injectable medications than oral medications. Signs of OHSS include increased ovarian size, nausea, vomiting, a buildup of fluid in the abdomen/pelvis, and breathing difficulties. In some cases, OHSS increases the level of red blood cells, and causes kidney and liver problems. In the most severe cases, it can cause blood clots, kidney failure, or death. These complications occur very rarely (in only 0.2% of all treatment cycles) and close monitoring can help identify patients at higher risk which could result in cycle cancellation.
- **Torsion:** Ovarian torsion is a rare condition when the ovary and portions of the fallopian tube twist around the ligaments that hold it in place. This can cut off the blood flow to the ovary and fallopian tube. If the blood supply is cut off long enough, the tissue in the ovary may die, potentially impacting fertility. The symptoms of ovarian torsion include fever, severe lower abdominal/pelvic pain, cramping, nausea, and vomiting. It is important for anyone experiencing these symptoms to seek medical care immediately. Ovarian torsion is diagnosed by physical exam including a transvaginal ultrasound. Treatment requires emergency surgery to untwist the ovary to restore blood flow and avoid necrosis, or in severe cases, to remove the ovary.
- **Cancer:** There is some concern that using fertility drugs can cause breast, ovarian, or uterine cancer. These cancers are more common in infertile patients, so it is difficult to know whether the reason for the cancer is the infertility itself, or the use of the drugs. 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 alone. More research is needed to confirm whether there is an association of cancer with use of fertility drugs.

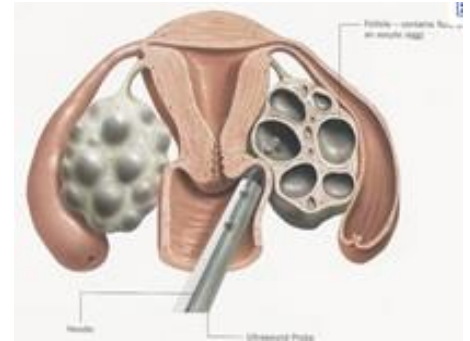
MONITORING

During the ovarian stimulation phase of treatment, monitoring of ovarian response (follicular development) is performed using periodic blood hormone tests and/or vaginal pelvic ultrasound exams. Monitoring helps the physician determine the appropriate dose of the fertility medications and the timing of the egg retrieval. Blood drawing may be associated with mild discomfort and, possibly, bruising, bleeding, infection, or scar at the needle sites. Vaginal ultrasound examinations are usually painless and generally considered to be safe; however, the possibility of harm cannot be excluded.

TRANSVAGINAL OOCYTE (EGG) RETRIEVAL

- Eggs are removed from the ovary with a needle under ultrasound guidance. Anesthesia is given to make this more comfortable.
- Complications such as injury, bleeding, and infection are rare.
- Not every follicle yields an egg and not every egg is mature/healthy.

Oocyte retrieval is the removal of eggs from the ovary. Before removing the eggs, the doctor will look at your ovaries using an ultrasound probe placed into the vagina. A long needle, which can be seen on ultrasound, is then attached to the ultrasound probe. Guiding the needle into the ovaries, the doctor will aspirate fluid, eggs, and egg-supporting cells. Very rarely, the ovaries are not accessible through the vagina. In that case, the eggs might be removed by guiding the needle through the abdomen to reach the eggs. Anesthesia with IV sedation is used to reduce discomfort. It is important to note that not every follicle will yield an egg and not every egg may be mature and healthy for fertilization.



Risks of egg retrieval:

- **Infection:** Bacteria from the vagina may be inadvertently transferred into the abdominal cavity or ovaries by the needle. This can cause an infection of the uterus, fallopian tubes, ovaries or other intra-abdominal organs. The incidence of infection after egg retrieval is very small (less than 0.1%). If you do get an infection, you may be given antibiotics. Severe infections sometimes require surgery to remove infected tissue. Infections can reduce your chance of getting pregnant in the future. Antibiotics may be used before the egg retrieval to help reduce the chance of infection. Still, there is no way to remove the risk completely.
- **Bleeding:** The needle passes through the vaginal wall and into the ovary to obtain the eggs. Both structures contain blood vessels and there are other blood vessels nearby. This means that small amounts of blood may be lost while removing the eggs. The risk of major bleeding is small (< 0.1%). Major bleeding may require surgical repair and could result in the removal of an ovary. The need for blood transfusion is rare. Although very rare, review of world experience with IVF indicates that unrecognized bleeding has led to death.
- **Trauma:** Even with ultrasound guidance, it is possible to damage nearby organs during the egg retrieval. This includes damage to the intestines, appendix, bladder, ureters, and ovary. In some cases, a damaged organ may need to be surgically repaired or removed. Such risk of trauma during egg retrieval is very low.
- **Anesthesia:** For the egg retrieval, medications are usually administered intravenously by an anesthesiologist. You will have a discussion prior to the procedure to review your medical history as well as the risks and benefits of anesthesia. The use of anesthesia during the egg retrieval can cause unintended complications such as an allergic reaction, low blood pressure, nausea, vomiting, and in rare cases death.
- **Failure:** It is possible that no eggs are found during the retrieval process. In other cases, the eggs may be abnormal, or are of poor quality. These situations can prevent you from having a successful pregnancy.

IN VITRO FERTILIZATION AND EMBRYO CULTURE

- Sperm and eggs are placed together in a petri dish under special conditions to promote fertilization.
- The fluid in the dish (culture medium) helps the sperm fertilize the egg and helps embryos to grow. Each clinic may have its own blend of fluids in which to grow the embryos.
- In most cases, the embryologist chooses the best embryos for pregnancy by the way they look under a microscope. It is important to note that many eggs and embryos are abnormal.

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

Three to four hours after the eggs are retrieved, sperm are placed in the culture medium with the eggs. In some cases, individual sperm are injected into each mature egg in a technique called Intracytoplasmic Sperm Injection (ICSI) (see *ICSI* section). The eggs are then returned to the incubator, where they remain to develop and grow. They are inspected at intervals over the next few days to check their progress.

Embryo development usually proceeds along the following schedule:

- **DAY 0:** Day of retrieval or egg thaw when eggs and sperm are placed together by ICSI or just co-incubation.
- **DAY 1:** This is the day that the eggs and sperm come together, and we can check for signs of fertilization. At this stage, the normally fertilized egg is still a single cell with 2 nuclei, called a 2PN or zygote.
- **DAY 2:** Normal embryos will divide into 2 to 4 cells.
- **DAY 3:** Normally developing embryos will continue to divide and contain 4 to 8 cells.
- **DAY 4:** The cells of the embryo begin to merge to form a solid ball of cells called a morula (named because it looks like a mulberry).
- **DAY 5:** Normal embryos now have 100 cells or more and are called blastocysts with an inner fluid-filled cavity and a small cluster of cells on the inside called the inner cell mass. Embryos can be incubated up to Day 7 to monitor for progress and development to the blastocyst stage.

It is important to understand that many eggs and embryos are abnormal. This means that some eggs will not fertilize, some embryos will not divide at a normal rate, and some embryos may stop growing. Even if your embryo(s) develop normally in the lab, you still may not get pregnant. Some embryos end up being genetically abnormal. Testing for genetic abnormalities is possible with preimplantation genetic testing (PGT) (see “PGT” consent form), but genetic testing is not routinely done. If you do not opt for PGT, the best embryo for transfer will be selected by the way it looks under the microscope.

We take great care of all eggs, embryos, and sperm in the lab. Still, there are many reasons why pregnancy may not happen with IVF:

- The eggs may fail to fertilize.

- One or more eggs may fertilize abnormally. This can lead to an abnormal number of chromosomes in the embryo. These abnormal embryos cannot be transferred.
- The fertilized eggs may degenerate before dividing into embryos, or the embryos may not develop normally.
- Rarely, the eggs or embryos may be harmed by contact with bacteria in the lab.
- Despite having multiple backup systems in place, lab equipment may fail, or power may be lost. Both can lead to the destruction of eggs, sperm, and embryos.
- A lab accident or human error can happen and can lead to embryo loss.
- Other unplanned events may prevent any step of the process from being performed or prevent a pregnancy from occurring.
- Hurricanes, floods, or other “acts of God,” including bombings or other terrorist acts, could destroy the laboratory or its contents, including any sperm, eggs, or embryos.

Quality control is the process of running tests to ensure that lab conditions are the best they can be to help embryos grow. Systems in the lab are frequently checked to make sure conditions are optimal. 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--blood, tissues eggs, sperm or embryos--will be used to create a pregnancy or a cell line.

EMBRYO TRANSFER

- The number of embryos transferred affects the pregnancy rate and risk of twins or other multiples.
- Embryos are placed into the uterine cavity using a catheter and ultrasound guidance. Not all embryos transferred become pregnancies
- Normally developing embryos that are not transferred can be frozen for future use.

After a few days of development, the embryo transfer takes place, or the embryos are frozen for transfer at a later time. One or more embryos are placed in the uterus using a thin tube called a catheter. Ultrasound guidance is used to help guide the catheter and confirm placement through the cervix and into the uterus. Although this is a simple process, there are some very rare risks. These risks include infection, loss of the embryo(s), or damage to the embryo(s). Not all embryos become pregnancies, and not all pregnancies are normal or lead to a healthy live birth. Some patients may experience miscarriage (which is an age-related risk) or ectopic pregnancy where the embryo implants outside the uterus (e.g., implants in the tube).

The number of embryos to transfer is an important decision. A patient’s age and the quality of the embryo affect both the chance for pregnancy as well as the chance for multiple embryos to implant. If multiple embryos implant, a multiple pregnancy (twins, triplets, or more) will result. In some cases, an embryo can split into two (identical twins) after transfer. Before the transfer, it is critical to discuss with your doctor how many embryos to transfer. To limit the multiple pregnancy rate, elective single embryo transfer is strongly recommended when appropriate, such as in cases where the embryo has been genetically tested or in younger patients.

As a member of the Society of Assisted Reproductive Technologies (SART), GIVF is obligated to follow the ASRM guidelines:

**AMERICAN SOCIETY FOR REPRODUCTIVE MEDICINE (ASRM)
GUIDELINES ON THE MAXIMUM NUMBER OF EMBRYOS TO TRANSFER**

| Age | <35 | 35-37 | 38-40 | 41-42 | >42 |
|---------------------------------|-----|-------|-------|-------|-----------|
| Cleavage-stage embryos | | | | | |
| Normal # chromosomes | 1 | 1 | 1 | 1 | 1 |
| From Egg Donor <35 | 1 | 1 | 1 | 1 | 1 |
| Other favorable* | 1 | 1 | ≤3 | ≤4 | Not Known |
| All others | ≤2 | ≤3 | ≤4 | ≤5 | Not Known |
| Blastocyst-stage embryos | | | | | |
| Normal # chromosomes | 1 | 1 | 1 | 1 | 1 |
| From Egg Donor <35 | 1 | 1 | 1 | 1 | 1 |
| Other favorable* | 1 | 1 | ≤2 | ≤3 | Not Known |
| All others | ≤2 | ≤2 | ≤3 | ≤3 | Not Known |

* Other favorable = any ONE of these criteria: Fresh cycle: expectation of 1 or more high-quality embryos available 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.

IVF TREATMENT: ADDITIONAL ELEMENTS

INTRACYTOPLASMIC SPERM INJECTION (ICSI)

- In some cases, fertilization will not happen when eggs and sperm are placed together in a lab dish. Injecting a sperm into each egg with ICSI can help fertilization occur.
- ICSI does not guarantee normal fertilization.
- There may be an increased risk of genetic problems in children born from ICSI.
- ICSI will not improve any defects in the eggs.

ICSI involves the direct injection of a single sperm into the interior of an egg using an extremely thin glass needle, allowing the sperm to enter the egg without having to break through the shell around it (the zona pellucida). The sperm must be healthy, and the egg must be mature for this technique to be successful.

ICSI is recommended and medically indicated when the sperm count, movement, or quality is poor, or in cases of prior poor fertilization rates. Live birth rates using ICSI are very close to those of IVF for men with normal sperm counts. Other indications for ICSI include the use of previously frozen eggs and/or when Preimplantation Genetic Testing (PGT) is planned.

ICSI may be associated with a slightly higher risk of birth defects. It is hard to know if the increased risk is due to the ICSI procedure itself or to defects in the sperm. The risk of birth defects after ICSI is still quite small (4.2% compared with 3% in children conceived naturally). Experts are still debating the impact of ICSI on the mental and physical development of children. Most recent studies have not detected any differences in the development of children born after ICSI, regular IVF, or natural conception.

Children conceived by ICSI have slightly more problems with their sex chromosomes (the X and Y chromosomes) than children conceived by IVF alone, but only by a very small margin (0.8% to 1.0% for ICSI pregnancies compared to 0.2% for IVF pregnancies). The reason for the difference is not clear. It may be caused by the ICSI procedure itself, or by the father. Men with sperm problems such as very low count and low motility are more likely to have genetic abnormalities. They often produce sperm with abnormal chromosomes, especially with abnormal sex chromosomes (X and Y). If sperm with abnormal chromosomes produce pregnancies, the pregnancies will likely carry the same defects. Translocations (a re-arrangement of chromosomes that can cause miscarriage or birth defects) may be more common after ICSI.

ASSISTED HATCHING

- Assisted hatching is used to facilitate the embryo hatching and implantation process. It involves making a hole in the outer shell surrounding the embryo.
- Assisted hatching is a standard component of the Preimplantation Genetic Testing (PGT) protocol.

The cells that make up the early embryo are coated with a membrane (shell) called the zona pellucida. Normally, as the embryo grows, this shell dissolves, allowing the embryo to be released or “hatch” from the shell; hatching is required before an embryo can implant in the uterus. Assisted hatching helps encourage the embryo to hatch by making a small hole in the shell with a special laser.

Studies suggest that assisted hatching might help improve pregnancy chances for some patients, including those transferring embryos that have previously been frozen. At GIVF we perform assisted hatching on non-PGT embryos as routine protocol.

If embryos undergo Preimplantation Genetic Testing (PGT) prior to vitrification, assisted hatching is performed before the embryo biopsy. Thus, these embryos do not need assisted hatching after subsequent thawing since it has already been done.

There is a slight increased risk for identical twins in embryos that have undergone assisted hatching. Very rarely, an embryo can be damaged from the assisted hatching process.

PREIMPLANTATION GENETIC TESTING

Patients considering Preimplantation Genetic Testing (PGT): please refer to separate informed consent for PGT.

CRYOPRESERVATION (freezing of eggs and/or embryos)

- Freezing of eggs and/or embryos provides other chances for pregnancy in the future.
- Frozen eggs and/or 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 remaining eggs or embryos in those cases.
- Patients with frozen eggs or embryos MUST be in touch with the clinic once a year.
- There are yearly fees for storing frozen embryos/eggs.

Sometimes there are normally developing embryos left after embryo transfer. Additional normal-appearing embryos can be frozen for future use. In some cases, it may be planned for all embryos from an IVF cycle to be frozen (for example, when PGT is used or if a fresh transfer is not recommended). On the other hand, some patients may wish to freeze their eggs because they are not ready to conceive now, or because they are planning to have therapy such as cancer treatment that could damage their eggs.

Benefits of cryopreservation/freezing:

- Saves you from going through ovarian stimulation again if you need eggs or embryos in the future.
- Allows you to transfer fewer embryos in the fresh cycle and keep the others for a frozen cycle. This can reduce the risk of a multiple pregnancy (twins, triplets, or greater).
- Allows you to freeze all embryos in the fresh cycle to prevent over-stimulation of the ovaries or if other conditions are present that might compromise implantation.
- Allows you to freeze embryos while waiting for PGT test results.
- Can be an option for fertility preservation especially if your future fertility is at risk due to surgery, medical conditions, or other treatments such as cancer therapy.

Studies of animals and humans indicate that children born from frozen embryo cycles do not have any greater chance of birth defects than children born after fresh embryo transfers. However, until very large numbers of children have been born from frozen embryos, it is not possible to be absolutely certain that there are no increased risks.

Risks of cryopreservation/freezing:

The entire cryopreservation process -freezing, storage, and thawing - can damage or destroy some or all cryopreserved eggs or embryos, resulting in the inability to proceed with further treatment or transfer.

It is also possible that cryopreserved eggs and embryos may be damaged, destroyed, lost, or fail to develop, and therefore be unavailable for further treatment or transfer due to a number of potential factors, including but not limited to: patient-specific differences in tolerance of gamete freezing; accidents; power outages; mechanical or equipment failure (including but not limited to loss of nitrogen or other tank failures); materials (including vials, straws and other containers used to freeze and store the samples and their labels); changes of any applicable law or regulations; human error; labelling errors; inventory record loss; natural and man-made disasters; sabotage; transportation or shipping accidents or other events which may be beyond the control of Genetics & IVF Institute (GIVF) or its laboratory.

In accordance with its protocols, GIVF makes reasonable efforts to handle and maintain its patients' eggs and embryos, including, but not limited to maintenance and monitoring of its equipment, materials, and laboratory. Despite such efforts, I understand that, as a result of one or more of these potential factors, my eggs and/or embryos may become unavailable for further treatment or transfer or that the likelihood of a pregnancy resulting from any treatment or transfer may be reduced.

In the event my eggs or embryos are damaged, destroyed, lost, or are otherwise unavailable for further treatment or transfer, or fail to result in a pregnancy, I hereby agree not to sue and agree to hold harmless, GIVF, and any of GIVF's physicians, employees, or agent except in the event of willful misconduct or gross negligence on the part of GIVF, or any of GIVF's physicians, employees, contractors, or agents.

ADDITIONAL RISKS TO THE PATIENT AND/OR OFFSPRING

Assisted reproductive technologies in most cases leads to successful delivery of healthy singleton pregnancies. However, there are complications of pregnancy that may develop more frequently in those conceived using IVF techniques.

IVF single babies are often born about 2 days earlier than naturally conceived babies. They are about 5% more likely to weigh less than 5 pounds, 8 ounces (2,500 grams) than a naturally conceived single baby. IVF twins are not born earlier or later than naturally conceived twins.

The risks of freezing eggs and embryos have been checked in animal tests over several generations. Human data has also been checked. There is no proof that children born from frozen and thawed embryos or frozen and thawed eggs have any more health problems than those born from fresh embryos. Still, it is hard to know for sure if the rate of health problems is the same as the normal rate.

Birth Defects: The risk of birth defects in the general population is 2%-3% and is slightly higher among infertile patients. Most of this risk is due to delayed conception and the underlying cause of infertility. Whether or not IVF alone is responsible for birth defects remains under debate and study. When intracytoplasmic sperm injection (ICSI) is done along with IVF, there may be an increased risk of birth defects. Rare genetic syndromes called imprinting disorders may be slightly increased with IVF.

Miscarriage and ectopic pregnancy: The rate of miscarriage after IVF is similar to the rate following natural conception, with the risk going up with the mother's age. The rate of miscarriage may be as low as 15% for women in their 20s to more than 50% for women in their 40s. There is a small risk (1-2%) of an ectopic (tubal, cervical, or abdominal) pregnancy with IVF. These abnormal pregnancies outside of the uterus may need to be treated with medication or surgery. There is less than 1% risk for a heterotopic pregnancy after IVF, typically in cases where multiple embryos are transferred. This is when an embryo implants and grows in the uterus while another embryo implants in the tube or elsewhere, leading to a simultaneous ectopic pregnancy. Heterotopic pregnancies usually require surgery to remove the ectopic pregnancy. In most cases, the pregnancy in the uterus can continue to develop and grow safely after the tubal pregnancy is removed.

Risks of Multiple Pregnancy: Having a multiple pregnancy (pregnancy with more than one baby) is more likely with IVF, particularly when more than one embryo is transferred. These pregnancies carry significant risks, including:

- Preterm labor and/or delivery: premature babies (regardless of whether they were conceived naturally or with IVF) are at higher risk for health complications such as lung development problems, intestinal infections, cerebral palsy, learning disabilities, language delay, and behavior problems
- Maternal hemorrhage
- Delivery by cesarean section (C-section)
- Pregnancy-related high blood pressure
- Gestational diabetes

Early delivery accounts for most of the higher risk of complications associated with babies from multiple pregnancies. IVF twins deliver an average of three weeks earlier than IVF single babies, and they weigh about 2 pounds less than IVF single 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, such as most identical twins, have additional risks. Twin-to-twin transfusion syndrome, a condition of the placenta where the blood circulation is not equal between the fetuses, can occur in up to 20% of identical twins that share a placenta. Twins sharing the same placenta have a higher frequency of birth defects. Death of one fetus in a twin pregnancy after the first trimester is more common with a shared placenta and may cause harm to the surviving fetus.

Your doctor will transfer the minimum number of embryos necessary to provide a high likelihood of pregnancy with the lowest risk of multiple pregnancy. The more embryos that are transferred into the uterus, the greater the risk of multiple pregnancy and chances of a problem during pregnancy or delivery. Patients with twins or more may choose to continue with the pregnancy (with all the risks that have already been stated); end the pregnancy; or reduce the number of fetuses (selective reduction), as clinically appropriate and/or permitted by state law. Selective reduction 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%) and the odds are greater if there are more than 3 fetuses present.

OTHER CONSIDERATIONS

Psychosocial Effects Treatment: Infertility and its treatment can affect intended parent's emotions, health, finances, and relationships with others. During evaluation and treatment, patients may feel anxious, helpless, depressed, lonely, or moody. Intended parents are encouraged to consider meeting with a counselor or other mental health professional who is specially trained in infertility care. Support groups, such as RESOLVE or Path2Parenthood, are also available.

Ethical And Religious Considerations: Infertility treatment can raise ethical or religious concerns for some; patients who have concerns should speak with their clinical care team, counselor, or someone else they trust.

Legal Considerations and Legal Counsel: The laws regarding embryo cryopreservation, subsequent thaw and use, and parent-child status of any resulting child(ren) is, or may be, unsettled in the state in which either the patient, spouse, partner, or any donor lives, or the state in which the ART program is located. GIVF will not provide legal advice. Intended parents are encouraged to consult a lawyer who is experienced in the areas of reproductive law if there are any questions or concerns about the present or future status of their eggs/embryos, individual or joint access to them, individual or joint parental status as to any resulting child, or any other aspect of this consent and agreement.

Alternatives To IVF: Additional alternatives to IVF treatment include intrauterine insemination, adoption, or not pursuing treatment.

REPORTING OUTCOMES

In 1992, the Fertility Clinic Success Rate and Certification Act was enacted into law which requires the Centers for Disease Control and Prevention (CDC) to gather information about IVF cycles and pregnancy outcomes in the U.S. each year. This information is used to calculate and report annual success rates by IVF clinic.

GIVF will report the required information from your IVF procedure to the CDC. Since our Clinic is a member of the Society of Assisted Reproductive Technologies (SART) of the American Society for Reproductive Medicine (ASRM), this information will also be reported to SART. The information reported may be used for research or quality assessment according to the Health Insurance Portability and Accountability Act (HIPAA) guidelines; your name will never be connected to your cycle information in any research that is published by ASRM or SART.

Since 2006, SART has participated in a series of studies, some of which are still being conducted, looking at the health of women and children after IVF including problems related to pregnancy and birth defects. IVF children are also followed and monitored for developmental delays, problems in school, or increased risk of childhood or adult cancer. Results are on the SART website (www.sart.org) under "Research."