In Vitro Fertilization (IVF) is a treatment for that removes eggs from a woman’s ovary or ovaries to achieve a pregnancy either at that time or at a later time. A patient can use sperm provided by her partner or from a donor for the insemination of her eggs, and have the resulting embryos transferred to her uterus or use a gestational carrier.

**In Vitro Fertilization Process & Risks**

An IVF cycle typically includes the following steps or procedures:

- Taking medicine to grow several follicles (fluid filled sac that may contain an egg) at once
- Removing the eggs from the ovary or ovaries
- Mixing eggs and sperm together to attempt fertilization
- Growing 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

Sometimes, other IVF steps may be included:

- Injecting individual sperm into each egg, called Intracytoplasmic Sperm Injection (ICSI)
- Cryopreservation (freezing) of eggs or embryos that are not transferred to the uterus
- Genetic testing of the embryos for abnormal genes or number of chromosomes (PGT=Preimplantation Genetic Testing).
Medications for IVF Treatment

- The success of IVF largely depends on growing several follicles at once.
- Injections of the natural hormones FSH and/or LH (gonadotropins) are used for this purpose.
- Other medications are used to keep ovulation from occurring too soon.
- Sometimes the ovaries respond too strongly—and sometimes not strongly enough.

Some medicines commonly used in an IVF cycle:

- **Gonadotropins, or injectable “fertility drugs”** (Follistim®, Gonal-F®, Menopur®, low dose hCG or human chorionic gonadotropin): These are all-natural hormones that help the ovary to grow several follicles at once over an average of 10 days. These injections may be given either just under the skin or directly into muscle.

  Risks/side effects of administering any medication by injection can include bruising, redness, swelling, or pain at the injection site. In rare cases, there may 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 (OHSS) [see “Risks to the Woman” section]. Other side effects may include headaches, weight gain, feeling tired, mood swings, nausea, or clots in blood vessels.

  If testing prior to the IVF cycle has shown that the woman is thought to have a lower number of eggs available, the medications may not help multiple follicles to grow. There may be very few or no eggs harvested at the egg retrieval procedure, or the cycle may be canceled before egg retrieval can be attempted.

- **GnRH-agonists (leuprolide acetate) (Lupron®):** This injectable medication comes 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. Leuprolide can also be used to start the growth of follicles containing eggs, or trigger the final stages of their growth. Leuprolide is approved by the FDA (U.S. Food and Drug Administration), but not approved for use in IVF. Because it has been studied in IVF patients, the medicine has been used in IVF for more than 20 years.

  Leuprolide may cause several side effects including a skin reaction at the injection site, 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. No long term or serious side effects are known. If Leuprolide is given in a cycle after ovulation has occurred, condoms should be used for birth control during 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 acetate or cetrorelix acetate) (Ganirelix®, Cetrotide®):** These drugs are used to prevent premature ovulation. Side effects may include stomach pain, headaches, skin reactions at the injection site, and nausea.

- **Human chorionic gonadotropin (hCG)** (Profasi®, Novarelin®, Pregnyl®, Ovidrel®): hCG is a natural hormone used in IVF to help the eggs become mature, ready to harvest, and be fertilized. This drug must be taken at an exact time prior to retrieving the eggs. Side effects can include breast tenderness, bloating, and pelvic pain.

- **Progestosterone, and in some cases, estradiol:** These two hormones are normally produced by the ovaries after ovulation, however, after egg retrieval, the ovaries will not produce enough of these hormones to support a pregnancy. Adding them helps improve the chances of getting pregnant and maintaining the pregnancy. Progesterone can be taken as a daily intramuscular injection (injection into muscle), or by placing a suppository or gel (Endometrin®, Crinone®, Prochieve®, Prometrium®, or pharmacist-compounded suppositories) directly into the vagina as frequently as three times per day after egg retrieval. Progesterone is often continued for some weeks after you become pregnant. Progesterone has not been shown to cause birth defects. Side effects of progesterone can include depression, sleepiness, an allergic reaction, infection or pain at the injection site. Estradiol can be taken orally, in a patch, as an 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):** Occasionally your physician may ask you to take birth control pills for 2 to 4 weeks before starting hormone stimulation injections. This is to slow down 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.

- **Growth Hormone:** This medicine is used in some regimens in hopes of improving embryo quality. It is given as a daily injection, and may cause some local irritation.

- **Testosterone or DHEA:** This medicine is used in some treatments in hopes of increasing the number of eggs retrieved. It is often given as a pill, patch, or cream, for one to three months before ovarian stimulation begins.

- **Clomid or Letrozole:** These oral medicines are used in some treatments to increase the number of growing eggs or reduce the estrogen level in the bloodstream. Short-term side effects in some women include headache, hot flashes, or increased moodiness.

- **Coenzyme Q10:** This supplemental medicine is often recommended to improve egg quality, and is taken by mouth for one to three months before ovarian stimulation begins.

- **Other medications:** Antibiotics may be given for a short time during the treatment cycle to reduce the risk of infection from egg retrieval or embryo transfer. Antibiotic use may cause several side effects, including vaginal yeast infection, nausea, vomiting, diarrhea, rashes, sensitivity to the sun, or allergic reactions.

Your doctor may suggest using anti-anxiety medications or a muscle relaxant before the embryo transfer. The most common side effect of these medicines is drowsiness.

Other medicines such as steroids, heparin, low molecular weight heparin, or aspirin may also be recommended.

I/We have read and understand the foregoing Medications for IVF Treatment

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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 and infection are rare.

Oocyte retrieval is the removal of eggs from the ovary. Anesthesia is generally used to reduce or eliminate pain. 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 attached to the ultrasound probe, guiding the needle into the ovaries so that the physician can draw out fluid, eggs, and egg-supporting cells from the follicles. On rare occasions, the ovaries cannot be reached through the vagina, in which case, the eggs might be removed by guiding the needle through the abdomen.

Risks of egg retrieval:

**Infection:** Antibiotics may be used before the egg retrieval to help reduce the chance of infection. Bacteria from the vagina may be transferred into the pelvis or ovaries by the needle causing an infection of nearby 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.

**Bleeding:** The needle passes through the vaginal wall and into the ovary to obtain the eggs. Both structures contain blood vessels; therefore, small amounts of blood may be lost while removing the eggs. The risk of major bleeding is small (< 0.1%). Major bleeding may require a blood transfusion, surgery to stop, and could result in the removal of an ovary. If bleeding occurs and is not noticed (also rare), it can lead to death.

**Trauma:** The risk of damage during egg retrieval is very low. Even with ultrasound guidance, nearby organs can be damaged, including damage to the intestines, appendix, bladder, ureters, and ovary. In some cases, a damaged organ may need to be fixed or removed through surgery.

**Anesthesia:** The use of anesthesia while removing eggs can cause an allergic reaction, low blood pressure, nausea or vomiting and in rare cases, death.

**Failure:** Sometimes no eggs are found during the retrieval process. In other cases, the eggs are not normal, or are of poor quality, preventing you from having a successful pregnancy.

I/We have read and understand the foregoing Transvaginal Oocyte (Egg) Retrieval

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In vitro fertilization and embryo culture

- Sperm and eggs are placed together in culture media.
- The dish is incubated under special conditions to promote fertilization.
- The fluid in the dish (culture medium) helps the sperm fertilize the egg and aids in embryo grow. Each clinic may have its own media for growing embryos.
- In most cases, the embryologist chooses the best embryos for embryo transfer by the way they look under a microscope.

After eggs are retrieved, they are moved 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”, fluid made to resemble the conditions in the Fallopian tubes and uterus, to support development of the embryos. The eggs are then placed into incubators, which keep the temperature, humidity, gas, and light at controlled 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 for progress at intervals over the next few days.

Embryo development usually proceeds along the following schedule:
- **Day 1**: The lab checks 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**: Normally developing 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**: Normally developing embryos now have 100 cells or more and are called blastocysts. They have a fluid-filled cavity (blastocoel) a small cluster of cells on the inside (inner cell mass), and an outer layer of cells that develop into the placenta (the trophectoderm).

It is important to understand that many eggs and embryos are abnormal, meaning 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, after being tested for genetic abnormalities (“preimplantation genetic testing, or “PGT”), an additional lab procedure. The best embryo(s) for transfer are usually selected by the way they look under the microscope.

Although we take great care of all eggs, embryos, and sperm in the lab, there are many reasons why pregnancy may not occur with IVF:
- The eggs may fail to fertilize.
- One or more eggs may fertilize abnormally, leading to an abnormal number of chromosomes in the embryo. These abnormal embryos will not be transferred and will be destroyed.
- The fertilized eggs may fall apart (fragment) before dividing into embryos, or the embryos may not develop normally.
- On rare occasions the eggs or embryos may be harmed by contact with bacteria in the lab.
- In spite of 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 may 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 optimal for embryos growth. 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 abnormal embryos—will be used to create a pregnancy or a cell line.

I/We have read and understand the foregoing In vitro fertilization and embryo culture

__________________________  __________________________  ____________
Signature of Patient         Print Name                   Date

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Signature of Partner         Print Name                   Date

Embryo transfer

- After a few days of development, the best-developed embryos are chosen for transfer.
- The number of embryos transferred affects the pregnancy rate and the risk of twins or other multiple pregnancies.
- The woman’s age and the quality of the developing embryo(s) have the greatest effect on pregnancy outcome.
- Embryos are placed in the uterus using a thin tube.
- Extra, 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 future use. One or more embryos are placed in the thin tube called a catheter, placed through the cervix into the uterus under ultrasound guidance to assist in guiding the catheter. Although this is a simple process, there are some very rare risks, including infection, loss of the embryo(s), or damage to the embryo(s). Not all embryos become pregnancies, and not all pregnancies are normal or grow in the correct place – tubal pregnancies can occur.

The number of embryos to transfer is an important decision. A woman’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.
Guidelines for the maximum number of embryos to transfer are given below.

**RECOMMENDED LIMITS ON THE NUMBER OF EMBRYOS TO TRANSFER**

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<td><strong>Cleavage-stage</strong></td>
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<td>Normal # chromosomes</td>
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<td>From Egg Donor &lt;35</td>
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<td>Other favorable*</td>
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<td>≤3</td>
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<td>Not known</td>
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<td>All others</td>
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<td><strong>Blastocyst-stage embryos</strong></td>
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*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; Frozen Embryo Transfer (FET) cycle: availability of vitrified day-5 or day-6 blastocysts, Euploid (correct number of chromosomes) embryos, 1st FET cycle, or previous live birth after an IVF cycle.

**NOTE:** IN THE EVENT OF A DIVORCE OR DISSOLUTION OF RELATIONSHIP, MLFC REQUIRES A VALID, FINAL, NON-APPEALABLE ORDER/DECREE BY A COURT OF COMPETENT JURISDICTION AND/OR A VALID SETTLEMENT AGREEMENT (AS DETERMINED IN MLFC’S SOLE DISCRETION), SPECIFICALLY ADDRESSING THE DISPOSITION OF EMBRYOS STORED WITH MLFC. PRIOR TO ANY EMBRYO TRANSFER A DISPOSITION OF EMBRYOS AGREEMENT MUST BE SIGNED BY ALL PARTIES.

I/We have read and understand the foregoing Embryo Transfer and Recommended Limits on Numbers of Embryos to Transfer

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**Hormonal support of the uterine lining**

- For pregnancy to occur, the embryo(s) must attach to the lining of the uterus, a process called *implantation*.
- Implantation has a better chance of occurring if extra progesterone hormone is taken.

The most important hormones to support implantation are progesterone and estrogen. Normally, the ovaries make these hormones to support pregnancy, however, in IVF cycles, retrieving the eggs causes reduced production of progesterone and estrogen by the ovaries. Therefore, in most cases, progesterone and sometimes estrogen are routinely taken for several weeks to help support the pregnancy. Progesterone is most commonly taken as an injection or as a vaginal suppository. Estrogen can be taken as pills, an injection, vaginal suppositories, or a skin patch.

www.mainlinefertility.com
I/We have read and understand the foregoing Hormonal Support of the Uterine Lining

Signature of Patient __________________________ Print Name __________________________ Date __________________________

Signature of Partner __________________________ Print Name __________________________ Date __________________________

Additional Elements

Intracytoplasmic Sperm Injection (ICSI)

- In some cases, fertilization may not happen when eggs and sperm are placed together in a lab dish. Injecting a sperm into each egg (ICSI, or intracytoplasmic sperm injection) may 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 injection of a single sperm into the interior of an egg using an extremely thin glass needle. The sperm must be healthy, and the egg must be mature.

ICSI is utilized when the sperm count, movement (motility), and/or morphology is poor. Live birth rates are very similar to those after IVF for men with normal sperm counts.

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 low (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 differences in the development of children born after ICSI, regular IVF, or natural conception.

Children conceived by ICSI have slightly increased problems with their sex chromosomes (the X and Y chromosomes) compared to 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, but may be caused by the ICSI procedure itself, or by the sperm. Men with sperm problems such as very low count and low motility are more likely to have genetic abnormalities, and often produce sperm with abnormal chromosomes, especially with abnormal sex chromosomes (X and Y). If sperm with abnormal chromosomes produces 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.

Some men with extremely low sperm counts or no sperm have small deletions on their Y chromosomes. In some of these cases, sperm can be obtained from the testicles via a surgical procedure to fertilize eggs with ICSI. Any sperm containing a Y chromosome microdeletion will pass on the deletion to any male child. These male children will also carry the microdeletion and may be infertile. A Y chromosome microdeletion can often, but not always, be detected by a blood test. This is because the chromosomes in the sperm may not always be the same as those seen when tested in the blood.
Some men are infertile because the tubes connecting the testes to the penis did not form correctly (congenital bilateral absence of the vas deferens [CBAVD]). These men can still father children, but sperm must be taken directly from the testicles or the tubes (epididymis) next to them, and ICSI must be used. These men have a mild form of cystic fibrosis (CF), which can be passed on to their children. Men with CBAVD and their partners should be tested for CF gene mutations before treatment. However, some CF mutations may not be detected by current tests, so that some parents who test negative for CF mutations can still have children affected by CF.

I/We have read and understand the foregoing Intracytoplasmic Sperm Injection (ICSI), and I/we consent to ICSI, if indicated

Signature of Patient _____________________________
Print Name _____________________________
Date _____________________________

Signature of Partner _____________________________
Print Name _____________________________
Date _____________________________

Preimplantation Genetic Testing (PGT)

- Preimplantation genetic testing of embryos requires removal of cells from the embryo (embryo biopsy).
- This test is most often done on Day 5 or Day 6 of embryo development, but it may be done sooner or later in some circumstances.
- The cells removed from the embryo may be sent to an off-site lab for the testing, while embryos remain at the clinic.
- In most cases, the tested embryos will need to be frozen (cryopreserved) while the test is being run.
- Test results may not be 100% correct.

There are several reasons that some patients choose to do PGT. Current reasons include:
- determining whether the embryo has the incorrect number of chromosomes (“PGT-A”).
- determining whether the embryo has a structural rearrangement of its chromosomal material (“PGT-SR”).
- determining whether the embryo has a specific disease-causing mutation (“PGT-M”)
- determining the gender of the embryo.

PGT does not guarantee that a pregnancy will occur, even if embryo tested is normal. Factors other than the genes influence pregnancy rates.

Screening the embryo’s chromosomes (PGT-A), or testing for one specific genetic disease (PGT-M), 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. Some birth defects may also occur even if chromosome screening is normal. An example of this would be a cleft lip or palate (failure of the lip and upper mouth to join properly).

It is always a possibility that PGT will show that there are NO chromosomally normal embryos available to transfer.

Risks of embryo biopsy
- Damage. There is a small risk of damage to the embryo.
- No result. The test may not give a result. It may be possible to repeat the biopsy and try again to test the embryo.
- Misdiagnosis. The test may give an incorrect result, indicating that a normal embryo is actually abnormal, or that an abnormal embryo is actually normal, however, most testing is very accurate. Not all embryos are made up of cells with identical genetics. Some embryos can be “mosaic”, which is when patches of cells within the
same embryo have different genetic makeup. Therefore, it is possible that test results of the biopsied cells do not reflect the genetics of the entire embryo. Consequently, the current recommendation is to confirm the result in early pregnancy.

Separate consents and agreements must be signed by patient and partner (if applicable) for PGT:
- Main Line Fertility and Reproductive Medicine Embryo Biopsy for Preimplantation Genetic Testing (PGT) Consent Form
- Genetics Lab Consent for PGT

I/We have read and understand the foregoing Preimplantation Genetic Testing (PGT)

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Assisted Hatching

- Assisted hatching involves making a hole in the outer shell (zona pellucida) that surrounds the embryo.
- Hatching may make it easier for embryos to be released from the shell and implant in the uterus.

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 thins. This allows the embryo to be released or “hatch” from the shell. Only after hatching can the embryo implant in the uterus for the pregnancy to continue.

Assisted hatching makes it easier for the embryo to escape the shell. This is done in the lab, by making a small hole in the shell with a laser. The procedure is usually done on the day of transfer, before placing the embryos into the transfer catheter.

Some programs use assisted hatching because of the belief that it improves implantation and birth rates, however there is no absolute evidence of this. In most cases, assisted hatching is believed to be helpful in women who are over 38 years old when their eggs are harvested, if they have failed to get pregnant in a previous IVF cycle, and/or when the shell around the embryo is extra thick. The thickness of the shell is checked on all embryos before embryo transfer.

Assisted hatching does have some risks. Very rarely, the embryo can be damaged, lose cells, or even be destroyed. There is also a higher chance of having identical twins (a riskier pregnancy) if the embryos are cleavage stage (Day 3). There may also be other risks not yet known.

I/We have read and understand the foregoing Assisted Hatching, and I/we consent to Assisted Hatching, if indicated.

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Cryopreservation (freezing)

- Freezing of eggs and embryos provides additional chances for pregnancy in the future.
- Frozen eggs and embryos do not always survive the process of freezing and thawing.
- Freezing of eggs before fertilization does not work as well as freezing of embryos.
- 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, as well as in the case of death.
- A person or couple with frozen eggs or embryos MUST be in touch with the clinic once a year.
- There are yearly fees for keeping embryos or eggs frozen.

Sometimes there are normally developing embryos left after embryo transfer which can be frozen for future use. In some cases, the original plan may be to freeze all embryos from an IVF cycle (for example, for PGT). On the other hand, some women 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 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, saving the others for a frozen cycle, thus reducing 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.
- Allows you to freeze embryos while waiting for test results from PGT.
- Protects you if your future fertility is at risk because of surgery or other treatments such as cancer therapy.

There are different ways to freeze embryos. The most common are “slow” freezing and “rapid” freezing (called vitrification). You should know that embryos do not always survive the freezing and thawing process. There is always a risk that no embryos will survive. If this happens, the transfer will be cancelled. Transferring a thawed embryo into the uterus does not guarantee a pregnancy. 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.

Foreseen and unforeseen circumstances (e.g. natural disasters, storage tank malfunctions, equipment failure, and power loss) may cause the eggs or embryo(s) to thaw, be damaged, and/or not survive.

If you choose to freeze eggs or embryos, you MUST complete, and notarize the Disposition of Eggs or Disposition of Embryos agreement before freezing. The statement explains the choices you have for the disposition of the eggs or embryos in a variety of situations. You can submit a new statement later if you change your mind about your choices. For frozen embryos, any change requires that both parties -- you and your partner-- agree in writing to the change. Be sure to let us now if you change your address. You must also pay storage fees as they come due.

I/We have read and understand the foregoing Cryopreservation (freezing)

Signature of Patient ___________________________ Print Name ___________________________ Date ____________

Signature of Partner ___________________________ Print Name ___________________________ Date ____________

www.mainlinefertility.com
Risks to the Woman

Medical Clearances

If you are under the care of a physician for a medical or psychological condition, you will need to obtain a letter of medical clearance from your treating physician. Our goal is to ensure that you are medically and/or psychologically stable to undergo IVF procedures, including egg retrieval, embryo transfer and epididymal aspiration/testicular biopsy, and that the medications you are prescribed are safe during pregnancy. The clearance letter must contain the following information:

- The condition for which you are being treated
- A statement that you are stable to undergo IVF procedures under anesthesia
- A statement that you are stable to attempt pregnancy.

Ovarian Hyperstimulation Syndrome (OHSS)

OHSS is a side effect of stimulating the ovaries. Signs of mild OHSS include lower abdominal discomfort and distention, mild nausea/vomiting, diarrhea, shortness of breath on exertion. Moderate OHSS may cause increasing abdominal bloating and discomfort, ovarian enlargement, and rapid weight gain. With severe OHSS you may note decreased urination, shortness of breath, large distended abdomen, abdominal pain, and excessive weight gain. Changes in the level of red blood cells and electrolytes may cause kidney and liver problems, and in the most severe cases, blood clots, kidney failure, or death. These complications occur very rarely (in only 0.2% of all treatment cycles).

OHSS occurs at two stages:
- early, 1 to 5 days after egg retrieval (as a result of the hCG trigger injection); and
- late, 10 to 15 days after retrieval (because of the natural rise of hCG if pregnancy occurs).

The risk of severe problems from OHSS is much higher if you become pregnant. For this reason, your doctor may suggest that all of your embryos be frozen for later use instead of transferring them in the fresh cycle. A frozen transfer can be done later, when there is reduced risk of OHSS.

Cancer

There is some concern that using fertility drugs can cause breast, ovarian, or uterine cancer. These cancers are more common in women with infertility, so it is difficult to know whether the reason for the cancer is infertility or 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 studies need be done to confirm whether there is an association of cancer with use of fertility drugs.

Risks of Pregnancy

Getting pregnant through IVF comes with certain risks. There may be other risks linked to IVF that are not known at this time. Please see the table below for certain known risks.
### Risks of Pregnancy with IVF

<table>
<thead>
<tr>
<th>Risk</th>
<th>Singleton Pregnancies</th>
<th>Twin Pregnancies</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Incidence in IVF Pregnancies (%)</strong></td>
<td>Risk compared to other infertile women</td>
<td>Risk compared to fertile women</td>
</tr>
<tr>
<td>Gestational diabetes</td>
<td>8.2% No difference</td>
<td>41% higher</td>
</tr>
<tr>
<td>Pregnancy-induced hypertension</td>
<td>12.6% No difference</td>
<td>No difference</td>
</tr>
<tr>
<td>Placental complications</td>
<td>5.2% 95% higher</td>
<td>281% higher</td>
</tr>
<tr>
<td>Primary cesarean delivery</td>
<td>32.2% 10% higher</td>
<td>20% higher</td>
</tr>
<tr>
<td>Low birthweight (&lt;5.5 pounds)</td>
<td>7.7% 21% higher</td>
<td>65% higher</td>
</tr>
<tr>
<td>Preterm birth (&lt;37 weeks gestation)</td>
<td>10.3% 26% higher</td>
<td>70% higher</td>
</tr>
</tbody>
</table>

In 2015 approximately 25% of IVF pregnancies were multiple pregnancies (twins, triplets, or greater), of which less than 1% are triplets or more. Identical twins occur in less than 5% of all IVF pregnancies and may happen more often after blastocyst (Day 5 or 6) transfers. Multiple pregnancies in general have an increased risk of pregnancy problems, including but not limited to: early delivery, pre-eclampsia (high blood pressure and protein in the urine), excess bleeding with delivery, and diabetes of pregnancy (gestational diabetes, and problems with the placenta (afterbirth). Other issues common with multiple pregnancy include gall bladder problems, skin problems, and the need for extra weight gain.

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

I/We have read and understand the foregoing Risks to the Woman

__________________________                  ____________________________
Signature of Patient                  Print Name                  Date

__________________________                  ____________________________
Signature of Partner                  Print Name                  Date
Risks to Your Baby

- IVF babies may be at a slightly higher risk for birth defects and genetic defects.
- IVF has a greater chance of multiple pregnancy, even when only one embryo is transferred.
- A multiple pregnancy is the greatest risk to your baby when using IVF.

Overall Risks

The first IVF baby was born in 1978. Since then, more than 5 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 couples do not have normal reproductive function, meaning that a baby they have through IVF may have more health problems than a baby conceived naturally.

IVF single babies are often born about 2 days earlier than naturally conceived babies, and 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 has been checked in animal and human data for several generations. 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 through normal birth is about 4.4%, and it is about 3% for severe birth defects. In IVF 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 due to older mothers and to having infertility. No higher risk is seen in frozen embryo or donor egg cycles.

Imprinting Disorders. These are rare disorders caused by whether the genes from the mother or the genes from the father are working. Studies do not agree on whether these disorders are associated with IVF. Even if they are, these disorders are extremely rare (1 out of 15,000 people).

Childhood cancers. Most studies do not suggest any extra risk, except 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.

Infant development. Most studies of long-term developmental outcomes have been reassuring so far. Most children are doing well, however, these studies are hard to complete and have some limitations. A more recent study using better methods shows an extra risk of cerebral palsy and developmental delay, however, this arose mostly from prematurity and low birth weight that was a result of multiple pregnancy.

Risks of a Multiple Pregnancy

More than 30% of IVF pregnancies are multiple pregnancies (twins, triplets, or greater). Identical twins occur in less than 5% of all IVF pregnancies. Identical twins may happen more often after blastocyst (Day 5) transfers, and with assisted hatching of cleavage stage embryo (Day 3) transfers.

Early delivery accounts for most of the problems 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, where the circulation is not equal between the fetuses, may occur in up to 20% of twins who share a placenta. Twins sharing the same placenta have a higher frequency of birth defects compared to twins with two placentas. 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. No one knows how much multiple pregnancies affect neurological or behavioral development, even when none of the other problems occur.

Fetal death rates for single 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. Loss of a fetus in the first trimester does not usually affect the surviving fetus.

The Option of Multifetal Pregnancy Reduction (Selective Reduction): The more fetuses there are in the uterus, the greater the chance of problems. 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 mother and remaining fetus(s).

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.

I/We have read and understand the foregoing Risks to Your Baby

__________________________________________  __________________________  ______________________
Signature of Patient                        Print Name                                    Date

__________________________________________  __________________________  ______________________
Signature of Partner                       Print Name                                    Date
Ethical and Religious Considerations in Infertility Treatment

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 pregnancy with 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.

Psychosocial Effects of Infertility Treatment

Finding out that you or your partner are infertile or have low fertility can be very painful. Infertility and its treatment can affect your emotions, health, finances, and social life. During treatment, you may feel anxious, helpless, depressed, or all alone and 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 expert. Here are some of the warning signs you should watch out for:

- 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.
- 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.

Raising twins or higher multiples may cause physical, emotional, and financial stresses. The chance of having depression and anxiety is higher in women 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](http://www.path2parenthood.org)).

Reporting Outcomes

In 1992, the Fertility Clinic Success Rate and Certification Act was passed. This law 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 success rates which are reported each year.

Main Line Fertility Center 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), it will also be reported to SART. Information reported to SART about your cycle may be used for research or quality assessment according to HIPAA guidelines; your name will never be connected to your cycle information in any research that is published by ASRM or SART.
Research Conducted by SART

Since 2006, the Society for Assisted Reproductive Technology has participated in a series of studies looking at the health of women and children after IVF. Many of these studies are still being conducted. The studies compare women who have not had trouble conceiving and their children with women who used IVF and their children. The studies also compare women who had trouble conceiving but did not do IVF, and their children, to women and their IVF children. IVF children who have siblings form 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”.
Additional Information

General IVF overviews available on the internet
www.reproductivefacts.org
www.sart.org/
www.cdc.gov/art/
www.resolve.org/site/PageServer

Effect of Woman’s Age

Effect of Number of Oocytes Retrieved

Effect of Infertility Diagnoses


Effect of Maternal Obesity


Number of Embryos to Transfer


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.

Culturing Embryos to the Blastocyst Stage
Informed Consent for Assisted Reproductive Technology (ART)

Main Line Fertility Center

Intracytoplasmic sperm injection


Embryo hatching


Ovarian Hyperstimulation


Risks of pregnancy


Risks to offspring


We (I) acknowledge that we have read and understood the information provided above regarding the IVF process and its risks, and agree to go forward with this treatment as our signatures below testify.

Our (my) signatures below also constitutes our(my) acknowledgment that we (I) have read, understood, and agree to the processes, procedures, and risks detailed herein.

We (I) have had the opportunity to ask any questions that we (I) may have regarding the processes/procedures that may be performed, the benefits or purposes of those processes/procedures, the potential complications and associated risks, in addition to the likelihood of achieving the goals contemplated by the processes/procedures detailed herein.

We (I) also acknowledge and understand that Main Line Fertility cannot guarantee or warrant that any of the ART processes/procedures detailed herein will result in a successful pregnancy.

In the event that any provision of this consent is deemed unenforceable as a matter of law, then that provision will be deemed to be deleted, but the rest of this consent will otherwise remain in effect.

SIGNATURE PAGE TO FOLLOW
X
____________________________
Patient Signature

____________________________
Date

Patient Name

____________________________
Date of Birth

Notary Public
Sworn and subscribed before me on this _____ day of _______, __________.

____________________________
Notary Signature

____________________________
Date

X
____________________________
Spouse / Partner Signature

____________________________
Date

Spouse / Partner Name

____________________________
Date of Birth

Notary Public
Sworn and subscribed before me on this _____ day of _______, __________.

____________________________
Notary Signature

____________________________
Date

If signed in the office:

Statement by Witness (must be employee of Clinic and at least 18 years of age)

I declare that the person(s) who signed this document is/are personally known to me and appear(s) to be of sound mind and acting on their own free will. They signed this document in my presence.

_____ Photo ID checked
_____ Form of photo ID:  valid Driver’s License  Passport  Non-Driver’s License

Patient

____________________________
Witness Name:

Witness Signature:

____________________________
Date:

Partner

____________________________
Witness Name:

Witness Signature:

____________________________
Date: