

CONSENT TO TREATMENT WITH ASSISTED REPRODUCTIVE TECHNOLOGIES

Overview

Assisted reproductive technology (ART)

The Centers for Disease Control and Prevention (CDC) defines ART to include "all fertility treatments in which eggs or embryos are handled. In general, ART procedures involve surgically removing eggs from a woman's ovaries, combining them with sperm in the laboratory, and returning them to the woman's body or donating them to another woman." According to CDC, "they do not include treatments in which only sperm are handled (i.e., intrauterine or artificial insemination) or procedures in which a woman takes medicine only to stimulate egg production without the intention of having eggs retrieved."

In-vitro Fertilization (IVF)

The term IVF is often used interchangeably with ART because it is the most prevalent form of ART. IVF literally means allowing fertilization of the male and female gametes (sperm and egg) occur outside the female body. IVF is an established treatment for many forms of infertility. The first IVF baby in the world was born in 1978. The goal of IVF is to give a couple an opportunity to become parents, most commonly using eggs and sperm from a couple. There are many variations of the treatment depending on the medical indications and social circumstances, including use of donor eggs, donor sperm and/or gestational surrogates. It is an elective procedure designed to result in a pregnancy leading to a live birth when other treatments have failed or are not appropriate.

This consent reviews the IVF process from start to finish, including the risks that this treatment might pose to all participants in the process as well as the unborn child(ren). 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 time of this writing.

At various points in this document, rates are given which reflect what are believed to be U.S. national averages for those employing IVF treatments. These include items such as pregnancy rates, cesarean delivery rates, and preterm delivery rates. These rates are not meant to indicate the rates of these outcomes within individual practices offering IVF, and are not to be understood as such. Furthermore, patient selection and treatment approaches differ among clinics. The Society for Assisted Reproductive Technology, SART, maintains and the Family Fertility Center concurs that a comparison of clinic success rates may not be meaningful.

Please place your initials at each page to indicate that you have read and understand the information provided. If you do not understand the information provided, please speak with our nurse and/or physician. There are a few locations within the consent form, specifically on pages **14, 19, 20, 21, 28, and 32**, where you must make a decision. Please select your choice, and initial or sign where requested.

This consent form, along with other relevant consent forms for treatment or procedures as determined by your choices, must be completed **before** IVF treatment is started so that we have a mutual understanding of what treatment options you elect and consent to.

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CONSENT TO TREATMENT WITH ASSISTED REPRODUCTIVE TECHNOLOGIES

Outline of Consent to Treatment with Assisted Reproductive Technologies

- 1. Name(s) of party/parties
 - A. Party/parties requesting ART or IVF treatment
 - a. Couple
 - b. Individual
 - B. Party/Parties participating in the process of ART or IVF treatment
- 2. Nature and purpose of IVF
- 3. Specific steps in IVF
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 - I. Indications for ICSI
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 - III. Purpose of ICSI
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 - F. Embryo culture
 - a. Nature of embryo culture
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- c. Limitations of microscopic examination of embryos
 - G. Other ART procedures in conjunction with IVF treatment
 - a. Assisted hatching
 - b. Embryo biopsy and pre-implantation genetic diagnosis
 - c. Embryo freezing
 - H. Embryo transfer
 - a. Number of embryos to transfer
 - b. Twin and higher-order multiple pregnancies
 - c. Limits on the number of embryos to transfer
 - d. Single embryo transfer
 - e. Disposition of extra embryos
 - I. Hormonal support of uterine lining after embryo transfer
 - J. Determine if pregnancy has occurred
- 4. Risks of IVF
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 - B. Risks to the woman undergoing ovarian stimulation
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 - a. Pregnancy resulting from IVF
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 - a. Overall risks
 - b. Birth defects
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 - d. Childhood cancers
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 - i. Preterm labor and delivery
 - ii. Prematurity
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 - iv. Additional risks to multiple fetuses
 - v. Option of selective reduction
- 5. Quality control in the IVF laboratory
- 6. Ethical and religious considerations in infertility treatment
- 7. Legal considerations and legal counsel
- 8. Psychosocial effects of infertility and its treatment
- 9. Alternatives to IVF
- 10. Reporting IVF outcome
- 11. Acknowledgement

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1. Name(s) of party/parties

A. Party/parties requesting ART or IVF treatment

a. Couple

We, _____ and _____
of _____ County, City of _____ in the state of _____ are
_____ (married couple or domestic partners)

and are over the age of twenty-one years. We request and authorize Dr. H. Christina Lee, and/or such assistants as she may designate to use the services of the Family Fertility Center to perform assisted reproductive technologies (ART), also known as in-vitro fertilization (IVF), because we have been unable to become pregnant and/or have a child on our own, and other treatments have failed or are not appropriate.

b. Individual

I, _____, of _____ County, City of _____ in the state of _____ am over the age of twenty-one years. I request and authorize Dr. H. Christina Lee, and/or such assistants as she may designate to use the services of the Family Fertility Center to perform assisted reproductive technologies (ART), commonly known as in-vitro fertilization (IVF), because I have been unable to become pregnant and/or have a child on my own, and other treatments have failed or are not appropriate.

B. Party/Parties participating in the process of ART or IVF treatment

a. Oocyte or eggs will be extracted from _____

b. Sperm will be obtained from _____

c. Eggs from 1.B. a, and sperm from 1.B.b will be fertilized in the laboratory.

d. The resulting normally fertilized eggs (embryo or embryos) will be placed into the uterus of _____.

e. Intended parents

i. Couples

_____ and _____ are the intended parents of any and all child(ren) resulting from this procedure.

ii. Individual

_____ is the sole intended parent of any and all child(ren) resulting from this procedure.

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2. Nature and purpose of IVF

IVF is an established treatment for many forms of infertility where an egg or eggs are extracted from the ovary or ovaries of a woman and mixed or injected with human sperm in the laboratory to achieve fertilization. After normal fertilization is achieved, the fertilized eggs are cultured in the laboratory for an appropriate period of time before they are placed inside a woman’s uterus (womb) with the intent of making the woman pregnant.

An IVF cycle typically includes the following steps or procedures:

- controlled ovarian stimulation: use of medications to grow multiple eggs,
- monitor ovarian and uterine responses,
- procurement of sperm sample,
- retrieval of eggs from the ovary or ovaries,
- fertilization of eggs: insemination or injection of sperm into the egg,
- culturing of any resulting fertilized eggs (embryos),
- placement (transfer) of one or more embryo(s) into the uterus, and
- support of the uterine lining with hormones to facilitate and sustain pregnancy

In some cases, additional procedures are employed. These include:

- Intracytoplasmic sperm injection (ICSI) to increase the chance for fertilization,
- Assisted hatching of embryos to potentially increase the chance of embryo attachment (implantation),
- Embryo Cryopreservation (freezing),
- Embryo Biopsy, and
- Pre-implantation Genetic Diagnosis/Screening (PGD/PGS)

3. Specific steps in IVF

Before IVF can begin, suitability of all parties involved for this procedure will be determined by standard infertility evaluation, screening tests, psychological counseling where indicated, and other medical procedures where required by federal, state or local law or deemed medically necessary by the treating physician.

A. Controlled ovarian stimulation

The party named in Section 1.B.a will self-administer by injection combinations of medications including: Leuprolide acetate (Lupron®), Cetrorelix acetate (Cetrotide®), Ganirelix acetate follicle stimulating hormone (FSH) and/or luteinizing hormone (LH) (Menopur®, Follistim® or Gonal-F®), human chorionic gonadotropin (hCG) (Ovidrel®, Novarel®, Pregnyl®), and progesterone (Endometrin®, Crinone®, or Prometrium®), and/or estradiol for the purposes as described in Sections 3.A.a and 3.A.b below.

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a. Purpose of controlled ovarian stimulation

The success of IVF largely depends on growing multiple mature eggs at once. Injection of the natural hormones, also called gonadotropins or more specifically follicle stimulating hormone (FSH), and/or luteinizing hormone (LH), are used for this purpose. Additional medications are used to prevent premature ovulation. An overly vigorous ovarian response can occur or, conversely, an inadequate response may occur.

b. Nature and side effect of medications for IVF

i. Gonadotropins, or injectable "fertility drugs"

(Follistim®, Gonal-F®, Menopur®): These natural hormones stimulate the ovary in hopes of inducing the simultaneous growth of several oocytes (eggs) over the span of 8 or more days. All injectable fertility drugs have Follicle Stimulating Hormone (FSH), a hormone that will stimulate the growth of your ovarian follicles (which contain the eggs). Some of them also contain Luteinizing Hormone (LH) or LH-like activity. LH is a hormone that may work with FSH to increase the production of estrogen and growth of the follicles. These medications are given by subcutaneous or intramuscular injection. Proper dosage of these drugs and the timing of egg recovery require monitoring of the ovarian response as described in Section 3.C.

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 mature multiple follicles, and many women experience some bloating and minor discomfort as the follicles grow and the ovaries become temporarily enlarged. Up to 2.0 % of women will develop Ovarian Hyperstimulation Syndrome (OHSS) as described in Section 3.B.c.i. below. Other risks and side effects of gonadotropins include, but are not limited to, fatigue, headaches, weight gain, mood swings, nausea, and clots in blood vessels.

Despite pre-treatment attempts to assess response, and particularly when pre-treatment evaluation indicates an abnormal ovarian reserve, the stimulation 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 treatment cycle prior to egg retrieval.

ii. GnRH-agonists (leuprolide acetate) (Lupron®)

This medication is taken by injection. There are two forms of the medication: A short acting medication requiring daily injections and a long-acting preparation lasting for 1-3 months. The primary role of this medication is to prevent a premature LH surge, which could result in the release of eggs before they are ready to be retrieved. Since GnRH-agonists initially cause a release of FSH and LH from the pituitary, they can also be used to start the growth of the follicles or initiate the final stages of egg maturation. Though leuprolide acetate is an FDA (U.S. Food and Drug Administration) approved medication, it has not been approved for use in IVF, although it has routinely been used in this way since 1980's. Potential side effects usually experienced with long-term use include but are not limited to hot flashes, vaginal dryness, bone loss, nausea,

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vomiting, skin reactions at the injection site, fluid retention, muscle aches, headaches, and depression. No long term or serious side effects are known. Since GnRH-a are often administered after ovulation, it is possible that they will be taken early in pregnancy. The safest course of action is to use a barrier method of contraception (condoms) the month you will be starting the GnRH-a. GnRH-a have not been associated with any fetal malformations; however, you should discontinue use of the GnRH-a as soon as pregnancy is confirmed.

- iii. GnRH-antagonists (ganirelix acetate or cetrorelix acetate) (Ganirelix® or Cetrotide®)

These are another class of medications used to prevent premature ovulation. They tend to be used for short periods of time in the late stages of ovarian stimulation. The potential side effects include, but are not limited to, abdominal pain, headaches, skin reaction at the injection site, and nausea.

- iv. Human chorionic gonadotropin (hCG) (Novarel®, Pregnyl®, or Ovidrel®):

hCG is a natural hormone used in IVF to induce the eggs to become mature and fertilizable. The timing of this medication is critical to retrieve mature eggs. Potential side effects include, but are not limited to breast tenderness, bloating, and pelvic discomfort.

- v. Progesterone, and in some cases, estradiol

Progesterone and estradiol are hormones normally produced by the ovaries after ovulation. After egg retrieval in some women, the ovaries will not produce adequate amounts of these hormones for long enough to fully support a pregnancy. Accordingly, supplemental progesterone, and in some cases estradiol, are given to ensure adequate hormonal support of the uterine lining. 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 associated with an increase in fetal abnormalities. Side effects of progesterone include depression, sleepiness, and allergic reaction. If progesterone is given by intra-muscular injection, there is the additional risk of infection or pain at the injection site. Estradiol, if given, can be by oral, trans-dermal, intramuscular, or vaginal administration. Side effects of estradiol include nausea, irritation at the application site if given by the trans-dermal route, and the risk of blood clots or stroke.

- vi. Oral contraceptive pills

Some treatment protocols include oral contraceptive pills to be taken for two to six weeks before gonadotropin injections are started in order to suppress hormone production or to schedule a cycle. Side effects include bleeding, headache, breast tenderness, nausea, swelling and the risk of blood clots or stroke.

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vii. Other medications

Antibiotics may be given for a short time during the treatment cycle or at the time of egg retrieval to reduce the risk of infection associated with egg retrieval or embryo transfer. Antibiotic use may be associated with causing a yeast infection, nausea, vomiting, diarrhea, rashes, sensitivity to the sun, and allergic reactions. Occasionally, anti-anxiety medications or muscle relaxants may be recommended prior to the embryo transfer. The most common side effect is drowsiness. Rarely other medications such as steroids, heparin, low molecular weight heparin or aspirin may also be included in the treatment protocol.

c. Other risks of medications for IVF

i. Ovarian hyperstimulation syndrome (OHSS)

The most serious side effect of ovarian stimulation with fertility medications is OHSS. Its symptoms can include increased ovarian size, nausea and vomiting, accumulation of fluid in the abdomen, breathing difficulties, an increased concentration of red blood cells, kidney and liver problems, and in the most severe cases, blood clots, kidney failure, or death. The severe cases affect only a very small percentage of women who undergo in vitro fertilization—0.2 percent or less of all treatment cycles—and the very severe are an even smaller percentage. Only about 1.4 in 100,000 cycles has lead to kidney failure, for example. OHSS occurs at 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 (as a result of the hCG if pregnancy occurs). To reduce the risk of early stage OHSS, leuprolide acetate is used to trigger oocyte maturation instead of human chorionic gonadotropin. Late onset OHSS is about 4 to 12 times higher if pregnancy occurs. Hence, to avoid late onset OHSS, it is best not to have a fresh embryo transfer

ii. Cancer

Many have worried that the use of fertility drugs could lead to an increased risk of cancer—in particular, breast, ovarian, and uterine (including endometrial) cancers. One must be careful in interpreting epidemiological studies of women taking fertility drugs, because all of these cancers are more common in women with infertility, so merely comparing women taking fertility drugs with women in the general population inevitably shows an increased incidence of cancer. When the analysis takes into account the increased cancer risk due to infertility per se, the evidence does not support a relationship between fertility drugs and an increased prevalence of breast or ovarian cancer. More research is required to examine what the long-term impact fertility drugs may have on breast and ovarian cancer prevalence rates. For uterine cancer, the numbers are too small to achieve statistical significance, but it is at least possible that use of fertility drugs may indeed cause some increased risk of uterine cancer.

B. Monitor ovarian or uterine response

The party named in Section 1.B.a will undergo serial ultrasound examinations and blood testing for reproductive hormones to assist in predicting the time of expected ovulation. As described in

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Section 3. A.b.i above, sometimes when the stimulation results in very few follicles, few or no eggs may be obtained at egg retrieval or treatment cycle may be cancelled prior to egg retrieval.

The party named in Section 1.B.d will undergo serial ultrasound examinations and blood testing for reproductive hormones to assist in preparation of the uterine lining to maximize implantation success. If this party is not the same person named in Section 1.B.a, she will also self administer hormones to prepare the uterine lining in preparation for embryo transfer.

C. Procurement of sperm sample

Unless other arrangement is made, on the day of egg retrieval, party named in Section 1.B.b. will produce by masturbation a fresh sperm specimen which will undergo laboratory preparation for fertilization.

If donor sperm is used for fertilization, the sperm must be procured and sent to the Family Fertility Center prior to the day of retrieval. Furthermore, the donor sperm sample must be determined eligible according to rules and regulations set forth by the Code for Federal Regulations for human cells, tissues and cellular and tissue-based products (CFR, title 21, part 121 HCT/P) and enforced by the Food and Drug Administration (FDA), as well as deemed acceptable by the Family Fertility Center.

In cases where previous semen analysis showed no live sperm, sperm may be isolated from a testicular biopsy or epididymal aspiration obtained from the party named in Section 1.B.b in a separate procedure.

D. Oocyte retrieval

The party named in Section 1.B.a will undergo oocyte retrieval when eggs are removed from the ovary with a needle under ultrasound guidance. Anesthesia is provided to make this comfortable.

a. Nature of oocyte retrieval

Oocyte retrieval is the removal of eggs from the ovary. An ultrasound probe is placed vaginally used to visualize the ovaries and the egg-containing follicles within the ovaries. A long needle, which can be seen on ultrasound, can be guided into each follicle and the contents aspirated. The aspirated material includes follicular fluid, oocytes (eggs) and granulosa (egg-supporting) cells. Generally, all follicles greater than 12 mm in diameter will be aspirated. But it is within the discretion of the physician to determine which particular follicle will be aspirated. Rarely, the ovaries are not accessible via the vaginal route and laparoscopy or transabdominal retrieval may be necessary. Anesthesia is generally used to reduce, if not eliminate, discomfort.

b. Risks of oocyte retrieval

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i. Infection

Bacteria normally present in the vagina may be transferred inadvertently 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 0.5%. Treatment of infections could require the use of oral or intravenous antibiotics. Severe infections occasionally require surgery to remove infected tissue. Infections can have a negative impact on future fertility. Prophylactic antibiotics are routinely used immediately prior to egg retrieval procedure at the Family Fertility Center to reduce the risk of pelvic or abdominal infection. Despite the use of antibiotics, there is no way to eliminate this risk completely.

ii. Bleeding

The needle passes through the vaginal wall and into the ovary to obtain the eggs. Both of these structures contain blood vessels. In addition, there are other blood vessels nearby. Small amounts of blood loss, less than 100ml, are common during egg retrievals. When blood accumulates inside the abdomen, symptoms of lower abdominal pain or cramping, inability to take deep breathes, and pain in the right shoulder or right upper abdomen may develop. On occasion, such symptoms are so severe it may require removal of the accumulated blood with another needle aspiration or, rarely, by a laparoscopy under general anesthesia.

The incidence of major bleeding problems has been estimated to be less than 0.1%. Major bleeding may require surgical repair, possibly loss of the ovary, or the need for blood transfusion. Although very rare, review of the world experience with IVF indicates that unrecognized bleeding has lead to death.

iii. Trauma

Despite the use of ultrasound guidance, it is possible to damage other intra-abdominal organs during the egg retrieval. Previous reports in the medical literature have noted damage to the bowel, appendix, bladder, ureters, 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 low.

iv. 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.

c. Failure to obtain any egg

It is possible that the aspiration will fail to obtain any eggs or the eggs may be abnormal or of poor quality and fail to produce a viable pregnancy.

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- E. Fertilization of the eggs
 - a. Method of fertilization
 - i. Conventional in-vitro fertilization (IVF)

In conventional IVF sperm and eggs are mixed together in a culture dish with specialized conditions (culture media, controlled temperature, pH (acidity), humidity and light) to permit the sperm to fertilize the eggs on their own ability.

- ii. Intracytoplasmic sperm injection (ICSI)

In the alternative, fertilization is achieved by injecting a single sperm into an egg using a technique called intracytoplasmic sperm injection (ICSI)

I. Indications for ICSI

ICSI is performed if no or low fertilization was observed in a previous IVF attempt, fertilization with conventional IVF is anticipated to be poor because sperm parameters are out of normal range in a semen analysis , sperm quality or oocyte quantity is borderline so ICSI is performed to maximize the number of embryos available for transfer, or other indications, e.g. viral infection in the party from whom sperm is used for fertilization.

II. Nature of ICSI

ICSI involves the direct injection of a single sperm into the interior of an egg using an extremely thin glass needle. Manipulation of the egg requires specialized equipment specifically designed to perform the very small intricate movements utilized during the procedure. Prior to injection of the sperm, eggs have to be treated with a solution containing hyaluronidase, an enzyme which removes the cumulus cell surrounding the egg so as to allow visualization of the egg itself. The egg will be held in place with a small glass pipette while a micro glass needle, previously loaded with a single viable sperm, is introduced through the shell (zona pellucida) into the egg. The sperm is released from the micro needle into the inside of the egg. After the egg is injected with the sperm, it is rinsed in fresh culture medium and cultured as described in Section 3.F.a.i.

III. Purpose of ICSI

ICSI is an effective treatment for male factor infertility because the technique delivers the sperm directly into the egg, bypassing the shell around the egg (zona pellucida) and the egg membrane (oolemma), thereby increasing the chance of fertilization when fertilization rates are anticipated to be lower than normal. As long as viable sperm are available, the negative effects of abnormal semen characteristics and sperm quality on fertilization can be overcome with ICSI.

ICSI allows couples with male factor infertility to achieve fertilization and live birth rates close to those achieved with in vitro fertilization (IVF) using conventional methods of fertilization in men

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with normal sperm counts. ICSI can be performed even in men with no sperm in the ejaculate if sperm can be successfully extracted from the epididymis or the testis.

IV. Limitations of ICSI

Despite ICSI, failure to establish a pregnancy may result because of the following reasons: (1) inability of the eggs to withstand the injection procedure, (2) failure of the sperm to activate the egg in spite of injection inside the egg, (3) poor egg quality resulting in inability of the egg to achieve normal fertilization or subsequent cell division or growth, and/or (4) failure of the embryo to implant.

V. Risks of ICSI

Reports on the risk of birth defects associated with ICSI (compared to those associated with conventional fertilization in IVF cycles) have yielded conflicting results. The most comprehensive study conducted thus far, based on data from five-year-old children, has suggested that ICSI is associated with an increased risk of certain major congenital anomalies. However, whether the association is due to the ICSI procedure itself, or to inherent sperm defects, could not be determined because the study did not distinguish between male factor conditions and other causes of infertility. Note that even if there is an increased risk of congenital malformations in children conceived with ICSI, the risk is relatively low (4.2% versus ~3% of those conceived naturally). The impact of ICSI on the intellectual and motor development of children conceived via ICSI also has been controversial. An early report suggested that development in such children lagged significantly behind that of children resulting from conventional IVF or those conceived naturally. However, more recent studies from larger groups, using standardized criteria for evaluation, 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 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. Whereas it may result from the ICSI procedure itself, it might also reflect a direct paternal effect. Men 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 men with abnormal semen parameters appear especially prone to abnormalities. If sperm with abnormal chromosomes produce pregnancies, these pregnancies will likely carry these same defects. The prevalence of translocations (a re-arrangement of chromosomes that increases the risk of abnormal chromosomes in egg or sperm and can cause miscarriage) of paternal origin and of de novo balanced translocations in ICSI offspring (0.36%) also appears higher than in the general population (0.07%).

Some men are infertile because the tubes connecting the testes to the penis did not form correctly. This condition, called congenital bilateral absence of the vas deferens (CBAVD), can be

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bypassed by aspirating sperm directly from the testicles or epididymis, and using them in IVF with ICSI to achieve fertilization. However, men with CBAVD are affected with a mild form of cystic fibrosis (CF), and this gene will be passed on to their offspring. All men with CVABD, 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 men have no sperm in their ejaculate because their testes do not produce adequate quantities (non-obstructive azoospermia). This can be due to a number of reasons such as prior radiation, chemotherapy or undescended testicles. In some men, small deletions on their Y chromosome lead to extremely low or absent sperm counts. Viable sperm can be found in testicular biopsy in some of these men. These sperm can then be used to fertilize eggs with ICSI. However, any sperm containing a Y chromosomal microdeletion will be transmitted to the offspring. Thus, the risk that male offspring might later manifest disorders including infertility is very real. However, men without a detectable deletion by blood testing can generate offspring having a Y chromosome microdeletion, because the chromosomal abnormality in a sperm may not be the same as those seen when tested by a blood test.

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b. Number of eggs to be fertilize

The probability of a successful IVF is to a large extent proportionate to the number of fertilized eggs. It is generally recommended to fertilize all the eggs retrieved with conventional IVF or to fertilize all the mature eggs with ICSI. However, some couples/individuals may wish to limit fertilization to a pre-determined number of eggs because of concern regarding the disposition of extra embryos.

_____ (name(s) of intended parent(s) named in Section 1.B.e) decide to (check only **ONE** of the following choices and sign below the election)

i. **Fertilize all the eggs retrieved.**

Signature of partner/individual _____ Date _____

Signature of partner _____ Date _____

ii. **Fertilize some (please specify a number) _____ of the eggs retrieved and discard all the unfertilized eggs.**

Signature of partner/individual _____ Date _____

Signature of partner _____ Date _____

iii. **Fertilize some (please specify a number) _____ of the eggs retrieved and freeze all the unfertilized mature eggs. (A separate consent to freeze the remaining unfertilized mature eggs is required.)**

Signature of partner/individual _____ Date _____

Signature of partner _____ Date _____

iv. **Fertilize some (please specify a number) _____ of the eggs retrieved and donate all the unfertilized eggs to the Family Fertility Center solely for the purpose of laboratory quality control. No embryo will be created with any of the unfertilized eggs.**

Signature of partner/individual _____ Date _____

Signature of partner _____ Date _____

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F. Embryo culture

a. Nature of embryo culture

Eggs or fertilized eggs are kept in conditions that support their needs and growth. They are placed in small dishes containing culture medium, which is special fluid developed to support development of the embryos made to resemble that found in the fallopian tube or uterus. The dishes containing the eggs or embryos are placed inside incubators which tightly control the temperature, atmospheric gases, pH (acidity) and humidity the embryos experience.

b. Embryo development

Microscopic examination of the eggs and embryos are carried out at specific time after insemination or ICSI to determine whether the eggs are fertilized normally and the fertilized eggs or embryos are developed normally.

The day after the eggs have been inseminated or injected with a single sperm, they are examined under the microscope for signs that the process of fertilization is underway. At this stage, normal development is evident by the still single cell having two nuclei; this stage is called a zygote. Two days after insemination or ICSI, normal embryos have divided into 2 to 4 cells. Three days after insemination or ICSI, normally developing embryos contain about 6 to 8 cells. Five to six days after insemination or ICSI, normally developing embryos have developed to the blastocyst stage, which is an embryo that has 80 or more cells, with an inner fluid-filled cavity and a small cluster of cells called the inner cell mass.

c. Limitation of microscopic examination of embryos

Microscopic examination of a fertilized egg and developing embryos is a non-invasive and the most commonly used method to select which embryo(s) to transfer. The chance that an embryo will produce a pregnancy is related to whether its development in the lab is normal, but this correlation is not perfect. This is because not all embryos developing at the normal rate do in fact have a normal set of chromosome (euploid). Conversely not all embryos developing at a less than perfect rate have an abnormal set of chromosomes (aneuploid). At the time of this writing, the only proven method to confirm whether a developing embryo has a normal set of chromosomes (euploid) is through a procedure called embryo biopsy combined with pre-implantation genetic testing (PGT).

G. Other ART procedures in conjunction with IVF treatment

a. Assisted hatching

The cells that make up the early embryo are enclosed within a flexible membrane (shell) called the zona pellucida. During normal development, a portion of this membrane opens up, allowing the embryonic cells to escape or "hatch" out of the shell. Only upon hatching can the embryonic cells implant within the wall of the uterus to form a pregnancy.

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Assisted hatching is a laboratory technique in which an embryologist makes an artificial opening in the shell of the embryo to enhance its ability to hatch and thus implant after transfer. It has been theorized that this outer shell becomes thicker and hardened with culturing in the laboratory and/or aging of the oocyte. Assisted hatching is usually performed on the day of transfer, prior to loading the embryo into the transfer catheter. The opening is usually made by laser.

Risks that may be associated with assisted hatching include damage to the embryo resulting in loss of embryonic cells, or destruction or death of the embryo. Artificial manipulation of the zygote may increase the rates of monozygotic (identical) twinning which are significantly more complicated pregnancies. There may be other risks not yet known.

Available published evidence does not support the routine or universal application of assisted hatching in all IVF cycles at this time. Family Fertility Center follows the guidelines on assisted hatching set forth by the Practice Committee of the Society for Assisted Reproductive Technology (SART) of the American Society for Reproductive Medicine (ASRM) (Fertility and Sterility Vol 90, Suppl 3, Nov 2008). Assisted hatching is offered only for patients with a poor prognosis, including those with more than two failed IVF cycles, poor embryo quality AND women older than 38 years old.

b. Embryo biopsy for pre-implantation genetic testing

See Consent to Embryo Biopsy for Pre-Implantation Genetic Testing.

c. Embryo freezing

See Consent to Cryopreservation and Storage of Human Embryos.

H. Embryo transfer

If a fresh embryo transfer is performed, after a few days of development when the requisite cell divisions have occurred, a pre-determined number of embryos will be selected for transfer into the uterus of the party named in Section 1.B.d. with a thin tube (catheter). Ultrasound guidance may be used to help guide the catheter and confirm placement of the embryos at a proper location in the uterine cavity. Although the possibility of a complication from the embryo transfer is very rare, risks include infection and loss of, or damage to the embryos.

a. Number of embryos to transfer

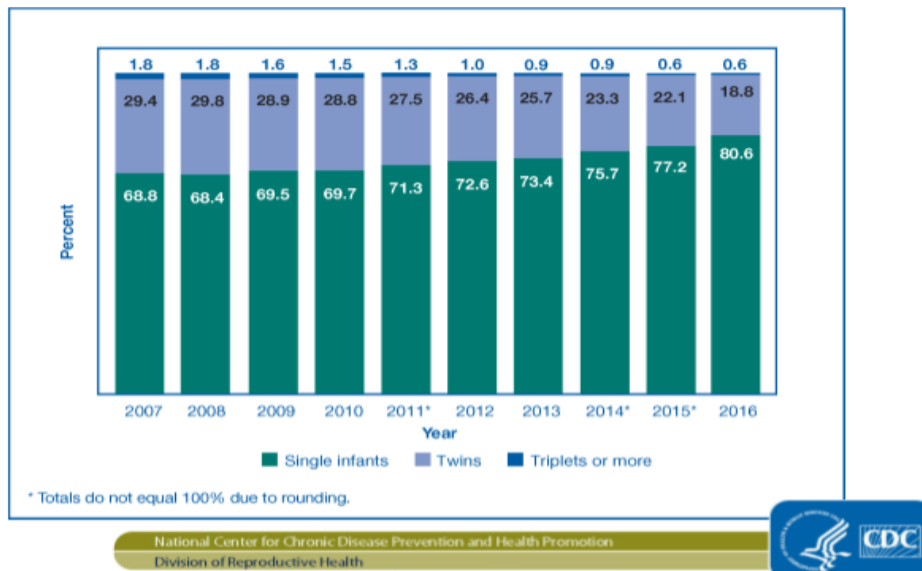
A number of factors determine the likelihood of pregnancy in IVF. Age of the woman has the greatest influence on pregnancy outcome. Increase the number of embryos transferred may increase the probability of a pregnancy per transfer, but the probability of twins and higher-order multiple pregnancy rate increases as well. Currently about 20% of all IVF pregnancies are twins or higher-order multiple gestations (triplets or greater). For comparison, spontaneously conceived dizygotic twin birthrates range from 10-40 per 1000 births in blacks, 7-10 per 1000 births in whites,

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and 3 per 1000 births in Asians. Monozygotic twin rates remain constantly worldwide at 4 per 1,000 births conceived spontaneously.

Percentages of Single Infants, Twins, and Triplets or More Among ART Transfers Using Fresh Embryos from Fresh Nondonor Eggs That Resulted in Live Births, 2007–2016



b. Twin and higher-order multiple pregnancies

The adverse consequences of preterm birth in triplet and higher-order multiple pregnancies conceived via IVF are serious and important. Almost half of triplet (and greater) pregnancies deliver before 32 weeks of gestation (7 months).

Twin gestations made up the large majority of multiple pregnancies resulting from IVF. Almost 3 out of 5 twins are born preterm (less than 37 weeks). About 1 out of 4 twins are admitted to the neonatal intensive unit. Twin babies are more than 4 times as likely to have cerebral palsy (7 in 1,000) as single babies. Twin babies are more likely to be stillborn, experience neonatal death, have birth defects of the brain, heart, face, limbs, muscles, or digestive system, and have autism than single babies.

Mothers carrying twins are twice as likely to develop pregnancy-related high blood pressure and one and a half times as likely to have gestational diabetes compared to women carrying single babies.

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c. Limits on the number of embryos to transfer

Some countries have enacted law regulating the number of embryos to transfer in an effort to prevent the adverse obstetrical and neonatal complications associated with multiple pregnancies, At the moment of this writing, no such law has been enacted in the U.S. at the federal, state or local level.

National guidelines are published by the Practice Committee of the Society in Assisted Reproductive Technologies (SART) of the American Society for Reproductive Medicine (ASRM). Following are the recommended limits on the number of embryos to transfer (see Tables below) by the ASRM as of 2017. All clinics, including the Family Fertility Center, which are members of SART are to follow these guidelines or risk losing their membership with SART. These limits differ depending on the developmental stage of the embryos and the quality of the embryos and take into account the patient’s personal history.

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

ASRM Limits on number of embryos to transfer
Fertil Steril Vol. 107 No. 4 /April 2017

| Prognosis | Age (years) of woman | | | |
|---|----------------------|-------|-------|-------|
| | <35 | 35-37 | 38-40 | 41-42 |
| Cleavage-stage embryos ^a | | | | |
| Euploid | 1 | 1 | 1 | 1 |
| Other favorable ^b | 1 | 1 | ≤3 | ≤4 |
| All others | ≤2 | ≤3 | ≤4 | ≤5 |
| Blastocysts ^a | | | | |
| Euploid | 1 | 1 | 1 | 1 |
| Other favorable ^b | 1 | 1 | ≤2 | ≤3 |
| All others | ≤2 | ≤2 | ≤3 | ≤3 |
| a. Patients with a favorable diagnosis: | | | | |
| 1. In patients of any age, transfer of a euploid embryo has the most favorable prognosis and should be limited to one. | | | | |
| 2. Patients under the age of 35 should be encouraged to receive a single-embryo transfer, regardless of the embryo stage. | | | | |
| 3. For patients between 35 to 37 years of age, strong consideration should be made for a single-embryo transfer. | | | | |
| 4. For patients between 38 and 40 years of age, no more than three cleavage-stage embryos or two blastocysts should be transferred. In cases where euploid embryos are available, a single-blastocyst embryo transfer should be the norm. | | | | |
| 5. Patients 41-42 years of age should plan to receive no more than four cleavage-stage embryos or three blastocysts. In cases where euploid embryos are available, a single-blastocyst transfer should be the norm. | | | | |
| b. Other favorable: Any ONE of these criteria: | | | | |
| 1. Fresh cycle: expectation of 1 or more high-quality embryos available for cryopreservation | | | | |
| 2. Previous live birth after an IVF cycle. | | | | |
| 3. Frozen embryo (FET) cycle: availability of vitrified day-5 or day-6 blastocysts, euploid embryos, 1 st FET cycle, or previous live birth after an IVF cycle. | | | | |

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d. Single embryo transfer

The Centers for Disease Control and Prevention of the U.S. Department of Health and Human Services, the American Society for Reproductive Medicine, and the Society for Assisted Reproductive Technologies strongly recommend single embryo transfer for women having the most favorable prognostic indicators. These include

- i. age under 35 years, first IVF cycle, good quality embryos based on morphologic criteria, and having an excess of embryos of sufficient quality to warrant cryopreservation,
- ii. previous live birth after an IVF cycle,
- iii. embryo tested euploid (having a normal set of chromosomes), and
- iv. any age, using embryos created from donor eggs.

There is no absolute guarantee to avoid multiple pregnancy. Identical (monozygotic) twinning is 3- to 10- fold more prevalent after IVF (1.5% to 4.5% vs. 0.45% in non-IVF pregnancies) and poses unique perinatal risks. Single embryo transfer (SET) is the only option to minimize the possibility of multiple pregnancy and its inherent risks to the health of mother and children. SET is the recommended choice for patients with a favorable prognosis as noted in Sections 3.H.c. and 3.H.d.

The number of embryos to be transferred must be determined and agreed upon by the physician and the parties named in Section 1.B.d and Section 1.B.e before oocyte retrieval is done.

_____ (name(s) of intended parent(s) in Section 1.B.e) decide to have (write the number of embryo(s) to be transferred, then sign below the election.)

_____ cleavage stage embryo(s) transferred, or

_____ blastocyst stage embryo(s) transferred.

Signature of partner/individual _____ Date _____

Signature of partner _____ Date _____

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e. Disposition of embryos not transferred

In cases where there is no fresh transfer, or where additional embryos remain after the transfer is completed, remaining or available embryos will be frozen (cryopreserve) for future use. Only embryos deemed suitable for freezing as determined by certain minimum morphologic criteria set by the Family Fertility Center will be frozen. Embryos that failed to meet minimum morphologic criteria will be discarded without further notice.

For all embryos that are not transferred and deemed suitable for freezing as determined by the Family Fertility Center, _____ (name(s) of intended parent(s) named in Section 1.B.e) decide to (check only ONE of the following choices and sign below the election)

i. **Freeze (cryopreserve) the excess embryos and store for later disposition.**

(Additional costs associated with freezing and future transfer of excess embryo(s) will be incurred. A separate consent to freeze and store human embryos must be signed before oocyte retrieval.)

Signature of partner/individual _____ Date _____

Signature of partner _____ Date _____

ii. **Discard all the excess embryos.**

Signature of partner/individual _____ Date _____

Signature of partner _____ Date _____

iii. **Donate all excess embryos to Family Fertility Center solely for the purpose of quality control use.**

Signature of partner/individual _____ Date _____

Signature of partner _____ Date _____

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iv. Donate all excess embryos to Family Fertility Center for reproductive purpose.

(A separate consent to donate the embryos for reproductive purpose must be signed prior to oocyte retrieval.)

Signature of partner/individual _____ Date _____

Signature of partner _____ Date _____

v. Other disposition (describe) _____

Signature of partner/individual _____ Date _____

Signature of partner _____ Date _____

I. Hormonal support of the uterine lining after embryo transfer

Successful implantation or attachment of embryos to the uterine lining (endometrium) depends on adequate hormonal support of the lining. The critical hormones for this support are progesterone and estradiol. Normally, the ovary makes sufficient amounts of both hormones. However, in IVF cycles, this support is not always adequate. Therefore, progesterone is routinely given, and sometimes estradiol may be necessary too. Progesterone is given by the intramuscular, oral or vaginal route. Estradiol is given by the oral, vaginal, dermal or intramuscular route. The duration of this support is from 2 to 10 weeks.

J. Determine if pregnancy has occurred

Following transfer of the fertilized eggs, blood samples from party named in Section I.B.d will be obtained to determine if pregnancy has occurred and if it is progressing normally.

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4. Risks of IVF

A. Failure to establish a pregnancy

The success rate of a single IVF cycle of treatment varies from less than 10% live birth per cycle start in women 42 years old or older to over 50% live birth rate per cycle start in women under 35 years old, especially among women with good quality eggs. The latest, 2017 at the time of this writing, published national average live birth rate for all women undergoing IVF in the United States is over 40% per cycle start.

Any of the following may occur during an IVF treatment which would prevent the establishment of a pregnancy:

- a) Abnormal response to fertility drug, the time of ovulation may be misjudged or it may not be predictable which would preclude the attempt to secure an egg;
- b) the attempt to recover an egg may be unsuccessful;
- c) the recovered egg may not be normal;
- d) the party named in Section I.B.b may be unable to provide a suitable sperm specimen;
- e) fertilization may not occur;
- f) cleavage or cell division of the fertilized egg may not occur;
- g) the embryo may not develop normally;
- h) implantation may not be successful;
- i) a laboratory accident may result in loss or damage to the egg, the sperm or the fertilized egg;
- j) 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 being stored there, or
- k) other unforeseen circumstances may prevent any step of the procedure to be performed or prevent the establishment of pregnancy.

B. Risks to the woman undergoing ovarian stimulation

- a. Ovarian hyperstimulation syndrome-See Section 3.A.c.i
- b. Cancer-See Section 3.A.c.ii

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- C. Risks to the woman undergoing embryo transfer
 - a. Pregnancy resulting from in-vitro fertilization (IVF)

Pregnancies that occur with IVF are associated with increased risks of certain conditions (see Table below from the Executive Summary of a National Institute of Child Health and Human Development Workshop held in September 2005, as reported in the journal *Obstetrics & Gynecology*, vol. 109, no. 4, pages 967-77, 2007). Some of these risks stem from the higher average age of women pregnant by IVF and the fact that the underlying cause of infertility may be the cause of the increased risk of pregnancy complications. There may be additional risks related to the IVF procedure per se, but it is difficult to assign the relative contributions.

Potential Risks in Singleton IVF-conceived Pregnancies

| | Absolute Risk (%) in IVF-conceived Pregnancies | Relative Risk (vs. non IVF-conceived Pregnancies) |
|----------------------|---|--|
| Pre-eclampsia | 10.3% | 1.6 (1.2--2.0) |
| Placenta previa | 2.4% | 2.9 (1.5--5.4) |
| Placental abruption | 2.2% | 2.4 (1.1--5.2) |
| Gestational diabetes | 6.8% | 2.0 (1.4--3.0) |
| Cesarean delivery * | 26.7% | 2.1 (1.7--2.6) |

In this table, the Absolute risk is the percent of IVF Pregnancies in which the risk occurred. The Relative Risk is the risk in IVF versus the risk in non-IVF pregnancies; for example, a relative risk of 2.0 indicates that twice as many IVF pregnancies experience this risk as compared to non-IVF pregnancies. The numbers in parentheses (called the “Confidence Interval”) indicate the range in which the actual Relative Risk lies. *Please note that most experts believe the rate of Cesarean delivery to be well above the 26.7% rate quoted here.

Much, but not all, of the increase in risks among pregnancies resulting from IVF relates to higher incidence of multiple births. Compared to singleton IVF pregnancies, twin pregnancies conceived via IVF are delivered on average three weeks earlier and weigh 1,000 gm less, and have a 10-fold higher risk for preterm birth (less than 37 weeks), a 7-fold increased risk for early preterm birth (less than 32 weeks), and a 2-fold higher risk for perinatal mortality.

- b. Ectopic pregnancy

While embryos are transferred directly into the uterus with IVF, ectopic (tubal, cervical and abdominal) pregnancies as well as abnormal intra-uterine pregnancies have occurred either alone or concurrently with a normal intra-uterine pregnancy. The risk of an ectopic (tubal) pregnancy with IVF is about 1% and is similar to the risk of an ectopic pregnancy among women with a history of infertility. These abnormal pregnancies often require medical treatments with methotrexate (a chemotherapy drug) or surgery to treat the abnormal pregnancy. Side effects of methotrexate

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include nausea or vomiting, diarrhea, cramping, mouth ulcers, headache, skin rash, sensitivity to the sun and temporary abnormalities in liver function tests. Risks of surgery include the risks of anesthesia, scar tissue formation inside the uterus, infection, bleeding and injury to any internal organs.

D. Risks to the child/children conceived with IVF

a. Overall risks.

Many years have elapsed since the birth of the first IVF baby in 1978, millions of children have been born worldwide following IVF treatment. Numerous studies have been conducted to assess the overall health of IVF children and the majority of studies on the safety of IVF have been reassuring. As more time has passed and the dataset has enlarged, some studies have raised doubts about the equivalence of risks for IVF babies as compared to naturally conceived babies.

A major problem in interpreting the data arises from the fact that comparing a group of infertile couples to a group of normally fertile couples is not the proper comparison to make if one wants to assess the risk that IVF technology engenders. Infertile couples, by definition, do not have normal reproductive function and might be expected to have babies with more abnormalities than a group of normally fertile couples. This said, even if the studies suggesting an increased risk to babies born after IVF prove to be true, the absolute risk of any abnormal outcome appears to be small.

Singletons conceived with IVF tend to be born slightly earlier than naturally conceived babies (39.1 weeks as compared to 39.5 weeks). The risk of a singleton IVF conceived baby being born with a birth weight under 5 pounds nine ounces (2500 grams) is 12.5% vs. 7% in naturally conceived singletons. IVF twins are not born earlier or later than naturally conceived twins.

b. Birth defects

The risk of birth defects in the general population is 2-3 %. An increased incidence of congenital malformation has been observed in infants conceived via IVF. Although most of the studies have significant methodological limitations relating to the definition of birth defects and small sample sizes for individual anomalies, the findings cannot be dismissed. A small but significant risk for major birth defects among children conceived through IVF (adjusted OR 1.3; 95% CI 1.1-1.6) was observed in very large case-control study conducted by the Finnish Registry of Congenital Malformations. Urogenital and musculoskeletal malformations in single males were the most common abnormalities. Other structural anomalies associated with IVF were neural tube, gastrointestinal, and cardiovascular defects.

c. Imprinting disorders

These are rare disorders having to do with whether a maternal or paternal gene is inappropriately expressed. The possibility of IVF-related epigenetic effects has been suggested by the increased prevalence of three rare genetic imprinting disorders. Beckwith-Wiedemann and Angelman

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Syndromes and Russell-Silver dwarfism, but the overall incidence of these disorders remain extremely low.

d. Childhood cancers

Most studies have not reported an increased risk with the exception of retinoblastoma: In one study in the Netherlands, five cases were reported after IVF treatment which is 5 to 7 times more than expected.

e. Infant development

In general, studies of long-term developmental outcomes have been reassuring so far; most children are doing well. However, these studies are difficult to do and suffer from limitations. A more recent study with better methodology reports an increased risk of cerebral palsy (3.7 fold) and developmental delay (4 fold), but most of this stemmed from the prematurity and low birth weight as a consequence of multiple pregnancy.

Potential Risks in Singleton IVF Pregnancies

| | Absolute Risk (%) in IVF Pregnancies | Relative Risk (vs. non-IVF Pregnancies) |
|--|---|--|
| Preterm birth | 11.5% | 2.0 (1.7--2.2) |
| Low birth weight (< 2500 g) | 9.5% | 1.8 (1.4--2.2) |
| Very low birth weight (< 1500 g) | 2.5% | 2.7 (2.3--3.1) |
| Small for gestational age | 14.6% | 1.6 (1.3--2.0) |
| NICU (intensive care) admission | 17.8% | 1.6 (1.3--2.0) |
| Stillbirth | 1.2% | 2.6 (1.8--3.6) |
| Neonatal mortality | 0.6% | 2.0 (1.2--3.4) |
| Cerebral palsy | 0.4% | 2.8 (1.3--5.8) |
| Genetic risks | | |
| -imprinting disorder | 0.03% | 17.8 (1.8--432.9) |
| -major birth defect | 4.3% | 1.5 (1.3--1.8) |
| -chromosomal abnormalities (after ICSI): | | |
| -of a sex chromosome | 0.6% | 3.0 |
| -of another chromosome | 0.4% | 5.7 |

In this table, the Absolute risk is the percent of IVF Pregnancies in which the risk occurred. The Relative Risk is the risk in IVF versus the risk in non-IVF pregnancies; for example, a relative risk of 2.0 indicates that twice as many IVF pregnancies experience this risk as compared to non-IVF pregnancies. The numbers in parentheses (called the “Confidence Interval”) indicate the range in which the actual Relative Risk lies.

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f. Risks of a multiple pregnancy

i. Preterm labor and delivery

The most important maternal complications associated with multiple gestation are preterm labor and delivery, pre-eclampsia, and gestational diabetes (see Section 4.C.a Risks of pregnancy). Others include gall bladder problems, skin problems, excess weight gain, anemia, excessive nausea and vomiting, and exacerbation of pregnancy-associated gastrointestinal symptoms including reflux and constipation. Chronic back pain, intermittent heartburn, postpartum laxity of the abdominal wall, and umbilical hernias also can occur. Triplets and above increase the risk to the mother of more significant complications including post-partum hemorrhage and transfusion.

ii. Prematurity

Prematurity accounts for most of the excess perinatal morbidity and mortality associated with multiple gestations. Moreover, IVF pregnancies are associated with an increased risk of prematurity, independent of maternal age and fetal numbers. Fetal growth problems and discordant growth among the fetuses also result in perinatal morbidity and mortality. Multifetal pregnancy reduction (where one or more fetuses are selectively terminated) reduces, but does not eliminate, the risk of these complications.

iii. Fetal death

Fetal death rates for singleton, twin, and triplet pregnancies are 4.3 per 1,000, 15.5 per 1,000, and 21 per 1,000, respectively. The death of one or more fetuses in a multiple gestation (vanishing twin) is more common in the first trimester and may be observed in up to 25% of pregnancies after IVF. Loss of a fetus in the first trimester is unlikely to adversely affect the surviving fetus or mother. No excess perinatal or maternal morbidity has been described resulting from a “vanishing” embryo.

Demise of a single fetus in a twin pregnancy after the first trimester is more common when they share a placenta, ranging in incidence from 0.5% to 6.8%, and may cause harm to the remaining fetus.

iv. Additional risks to multiple fetuses

Multiple fetuses (including twins) that share the same placenta have additional risks. Twin-twin transfusion syndrome in which there is an imbalance of circulation between the fetuses may occur in up to 20% of twins sharing a placenta. Excess or insufficient amniotic fluid may result from twin-to-twin transfusion syndrome. Twins sharing the same placenta have a higher frequency of birth defects compared to pregnancies having two placentas. Twins sharing the same placenta appear to occur more frequently after blastocyst transfer.

Placenta previa (placenta extends over the cervical opening) and vasa previa (where one or more of the blood vessels extends over the cervical opening) are more common complications in multiple

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gestations. Abruption placenta (premature separation of the placenta) also is more common and postpartum hemorrhage may complicate 12% of multifetal deliveries. Consequences of multiple gestations include the major sequelae of prematurity (cerebral palsy, retinopathy of prematurity, and chronic lung disease) as well as those of fetal growth restriction (polycythemia, hypoglycemia, necrotizing enterocolitis). It is unclear to what extent multiple gestations themselves affect neuro-behavioral development in the absence of these complications. Rearing of twins and high-order multiples may generate physical, emotional, and financial stresses, and the incidence of maternal depression and anxiety is increased in women raising multiples. At mid-childhood, prematurely born offspring from multiple gestations have lower IQ scores, and multiple birth children have an increase in behavioral problems compared with singletons. It is not clear to what extent these risks are affected by IVF per se.

v. Option of selective reduction

Pregnancies that have more than 2 fetuses are considered an adverse outcome of infertility treatment. The greater the number of fetuses within the uterus, the greater is the risk for adverse perinatal and maternal outcomes. Patients with more than twins are faced with the options of continuing the pregnancy with all risks previously described, terminating the entire pregnancy, or reducing the number of fetuses in an effort to decrease the risk of maternal and perinatal morbidity and mortality. Multifetal pregnancy reduction (MFPR) decreases risks associated with preterm delivery, but often creates profound ethical dilemmas. Pregnancy loss is the main risk of MFPR. However, current data suggest that such complications have decreased as experience with the procedure has grown. The risk of loss of the entire pregnancy after MFPR is approximately 1%.

In general, the risk of loss after MFPR increases if the number of fetuses at the beginning of the procedure is more than three. While there is little difference between the loss rates observed when the final number of viable fetuses is two or one, the loss rate is higher in pregnancies reduced to triplets. Pregnancies that are reduced to twins appear to do as well as spontaneously conceived twin gestations, although an increased risk of having a small for gestational age fetus is increased when the starting number is over four. The benefit of MFPR can be documented in triplet and higher-order gestations because reduction prolongs the length of gestation of the surviving fetuses. (This has been demonstrated for triplets; triplets have a 30-35% risk of birth under 32 weeks compared to twins which is 7 to 10%)

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5. Quality control in the IVF laboratory

Quality control in the IVF laboratory is extremely important to optimize the fertilization, growth and development of the embryos in an environment outside of the human body. Sometimes immature or unfertilized eggs, sperm or abnormal embryos (abnormally fertilized eggs or embryos whose lack of development indicates they are not of sufficient quality to be transferred) that would normally be discarded can be used for quality control.

You are being asked to allow the Family Fertility Center to use this material for quality control purposes before being discarded in accordance with normal laboratory procedures and applicable laws. None of this material will be utilized to establish a pregnancy or a cell line unless you sign other consent forms to allow the Family Fertility Center to use your eggs, sperm or embryos for research purposes. Please mark your choice and sign below the election:

i. I/We CONSENT to allow the clinic to utilize my/our immature or unfertilized eggs, left-over sperm or abnormal embryos for quality control and training purposes before they are discarded.

Signature of partner/individual _____ Date _____

Signature of partner _____ Date _____

ii. I/We DO NOT CONSENT to allow the clinic to utilize my/our immature or unfertilized eggs, left-over sperm or abnormal embryos for quality control and training purposes before they are discarded. All such materials will be discarded in accordance with normal laboratory procedures and applicable laws

Signature of partner/individual _____ Date _____

Signature of partner _____ Date _____

6. Ethical and religious considerations in infertility treatment

Infertility treatment can raise concerns and questions of an ethical or religious nature for some patients. The technique of in-vitro fertilization (IVF) involves the creation of human embryos outside the body and can involve the production of excess embryos and/or 'high-order' multiple pregnancy (triplets or more). You are encouraged to consult with trusted members of your religious or ethics community for guidance on your infertility treatment.

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7. Legal considerations and legal counsel

In cases when embryos are frozen for later use or when a third party is involved in the process of IVF, the law regarding parent-child status, rights of sperm or egg donors, gestational surrogate and child(ren) resulting from this treatment is, or may be, unsettled in the state in which either partner or spouse, or any donor currently or in the future lives, or in the state of Pennsylvania where Family Fertility Center is located.

Family Fertility Center has not given you legal advice, nor should you rely on the Family Fertility Center to give you any legal advice. You are strongly advised to consult a lawyer who is experienced in the areas of reproductive law if you have any questions or concerns about the present or future status of your embryos, your individual or joint access to them, your individual or joint parental status as to any resulting child(ren), or about any other aspect of this consent and agreement.

8. Psychosocial effects of infertility and its treatment

A diagnosis of infertility can be a devastating and life-altering event that impacts on many aspects of a patient’s life. Infertility and its treatment can affect an individual or couple medically, financially, socially, emotionally and psychologically. Feelings of anxiousness, depression, isolation, and helplessness are not uncommon among patients undergoing infertility treatment. Strained and stressful relations with spouses, partners and other loved ones are not uncommon as treatment gets underway and progresses.

Our health care team is available to address the emotional, as well as physical symptoms that can accompany infertility. In addition, you are encouraged to seek counseling with trained and/or licensed mental health professionals who have expertise in the area of infertility care.

While it is normal to experience emotional ups and downs when pursuing infertility treatment, it is important to recognize when these feelings are of a severe nature. If you experience any of the following symptoms over a prolonged period of time, you may benefit from working with a mental health professional:

- Loss of interest in usual activities
- Depression that doesn't lift
- Strained interpersonal relationships (with partner, family, friends and/or colleagues)
- Difficulty thinking of anything other than your infertility
- High levels of anxiety.
- Diminished ability to accomplish tasks
- Difficulty with concentration
- Change in your sleep patterns (difficulty falling asleep or staying asleep, early morning awakening, sleeping more than usual for you)
- Change in your appetite or weight (increase or decrease)
- Increased use of drugs or alcohol
- Thoughts about death or suicide

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- Social isolation
- Persistent feelings of pessimism, guilt, or worthlessness
- Persistent feelings of bitterness or anger

Our health care team can assist you to identify a local qualified mental health professional who is familiar with the emotional experience of infertility.

9. Alternatives to IVF

There are alternatives to IVF treatment including using donor sperm, donor eggs, adoption, or not pursuing any active treatment. Gametes (sperm and/or eggs) instead of embryos may be frozen for future attempts at pregnancy in an effort to avoid potential future legal or ethical issues relating to disposition of any cryopreserved embryos. Sperm freezing has been an established procedure for many decades. Egg freezing with a technique called vitrification is able to yield consistent and reliable egg survival. As of 2015, ASRM has officially recognized egg freezing is no longer an experimental procedure. Family Fertility Center offers egg freezing as one of the treatment options in the expanding field of ART.

10. Reporting IVF outcome

The 1992 Fertility Clinic Success Rate and Certification Act requires the Centers for Disease Control and Prevention (CDC) to collect cycle-specific data as well as pregnancy outcome on all assisted reproductive technology cycles performed in the United States each year and requires them to report success rates using these data. Consequently, data from your IVF procedure will be provided to the CDC, and to the Society of Assisted Reproductive Technologies (SART) of the American Society of Reproductive Medicine (ASRM). The CDC may request additional information from the Family Fertility Center or contact you directly for additional follow-up. Additionally, your information may be used and disclosed in accordance with HIPAA guidelines in order to perform research or quality control. All information used for research will be de-identified prior to publication. De-identification is a process intended to prevent the data associated with your treatment from being used to identify you as individuals.

Initials _____ / _____

CONSENT TO TREATMENT WITH ASSISTED REPRODUCTIVE TECHNOLOGIES

11. Acknowledgement

(If Section 1.B.e.ii is completed where an individual is the sole intended parent, the words we, us, our, or ours will be replaced by I, me, my and mine.)

We accept the IVF procedure as our own voluntary act and acknowledge that the child or children produced are our own legitimate children and, as our heir or heirs, with all the rights and privileges accompanying such status.

We understand that neither Dr. H. Christina Lee, nor the Family Fertility Center and its staff, can be responsible for the physical and mental characteristics of the child or children produced by this method.

We, on behalf of ourselves, on behalf of offspring born as a result of this procedure, and on behalf of their heirs, executors, administrators, successors and assigns, hereby fully release and discharge Dr. H. Christina Lee, the Family Fertility Center, and its staff from all claims and actions that we, our offspring and their above-mentioned successors now or hereafter may have arising out of the proposed IVF.

We, jointly and severally, hereby agree to indemnify and hold harmless Dr. H. Christina Lee, the Family Fertility Center, its staff, and their successor, assigns, heirs and executors and administrators from and against any and all liability, in connection with any claim brought by us, our offspring, or any other person or entity in connection with the IVF procedure.

We understand that, with any technique necessitating mechanical support systems, equipment failure can occur. Dr. H. Christina Lee, the Family Fertility Center, and its staff are not to be held liable for any loss, destruction, or damage to our sperm, egg(s) and/ or embryo(s) caused by or resulting from any malfunction of equipment, failure of utilities, fire, wind, earthquake, water, or other acts of God.

We consent to the photographing or televising of the procedures to be performed, including the eggs, the sperm, our fertilized eggs, portions of the body for medical, scientific or educational purposes, provided that our identity is not revealed by the pictures or any accompanying text.

We understand that insurance coverage for all or any part of this total procedure may not be available and acknowledge, jointly and severally, our personal responsibility for payment of all costs of this treatment, including hospital charges, laboratory charges and physician's professional fees, as well as costs incurred as a result of any complication which may occur.

We have had the opportunity to read and ask questions about the contents of this document and all the components of IVF treatment. We understand the information provided and our questions have been answered to our satisfaction. We execute this consent form freely and voluntarily. We have not relied on any inducements, promises, or representations made by Dr. H. Christina Lee, the Family Fertility Center or its staff.

Initials _____ / _____

FAMILY FERTILITY CENTER

www.familyfertility.com

H. Christina Lee, M.D., J.D., H.C.L.D., F.A.C.O.G.

Medical and Laboratory Director

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CONSENT TO TREATMENT WITH ASSISTED REPRODUCTIVE TECHNOLOGIES

The foregoing was read, discussed, and signed in my presence, and in my opinion the person(s) signing did so freely, and with full knowledge and understanding.

Print Name of Witness

Signature of Witness

Date

I have explained to the above couple/individual the nature and purpose of the procedure; the potential benefits, and possible risks associated with participation in this procedure. I have answered all questions that have been raised by the above couple/individual.

H. Christina Lee, M.D., J.D., H.C.L.D.

Date

Initials _____ / _____