

CONSENT FORM FOR RECIPIENTS OF EGG DONATION

INSTRUCTIONS:

This consent form provides a description of the treatment that you are undertaking.

- Read the consent completely. If you have any questions please speak with your doctor.
- Do not make any additions or deletions to the consent.
- Treatment **cannot** be started until all consents are signed.
- Consents must be signed in front of your nurse or physician.

INTRODUCTION

In Vitro Fertilization (IVF) is a treatment that helps an infertile woman achieve a pregnancy. The technique involves four main steps: 1) the development of eggs in the woman's ovaries; 2) the removal of eggs from her ovaries; 3) the placement of the eggs and sperm together in the laboratory to allow fertilization to occur, and; 4) the transfer of fertilized eggs (embryos) into the woman's uterus for the establishment of pregnancy.

The reproductive potential of some women is compromised because they do not produce eggs, produce defective eggs and/or embryos, or are carriers of a genetic condition. An option for these women is to undergo egg donation, which is done in conjunction with IVF treatment. Treatment with egg donation involves a woman who serves as an egg donor and a woman who serves as the recipient. It is a process whereby the egg donor has eggs removed from her ovaries. The eggs are then fertilized with sperm in the laboratory. The fertilized eggs (embryos) are then transferred into the uterine cavity of the recipient woman for implantation and the establishment of pregnancy. Following the delivery, the intention is that the recipient couple will be the rearing parents of the offspring. Boston IVF has established age criteria for recipients: recipients must not have reached their 50th birthday on the day of fresh embryo transfer or their 52nd birthday for frozen embryo transfers.

This consent explains the treatment and describes the major risks. In addition, the responsibilities of those who participate in this treatment are discussed. This consent is valid for a period of one calendar year after it has been signed. Please make a copy for your records. It is recommended that you review the consent prior to each treatment cycle. If you have any questions about your treatment then it is your responsibility to speak with your physician.

Pre-treatment Recommendations

During treatment a woman should avoid any activity, behavior and medications that could reduce her chance of conceiving and having a healthy baby. In addition, the recommendations listed below should be followed.

1. A prenatal vitamin should be taken on a daily basis before the treatment is begun. This will reduce the chance that a baby will be born with a neural tube defect (e.g. spina bifida), which is a birth defect that affects the development of the spine.
2. Smoking must be avoided before and during treatment. It is also contraindicated during pregnancy.
3. Recreational drugs are absolutely contraindicated.
4. Ingestion of aspirin or aspirin-like products (e.g. Motrin[®], Advil[®], Anaprox[®], Naprosyn[®], Aleve[®], etc.) should be avoided during treatment. However, in certain circumstances your doctor may prescribe low dose aspirin (baby aspirin, 81 mg). Tylenol[®] is safe to take before and during pregnancy.
5. The use of alcohol should be avoided during treatment and after pregnancy is established.
6. The use of all prescription and over-the-counter medications (including herbal remedies) should be discussed with a physician before starting a treatment cycle.
7. Ingestion of some fish, which contain higher amounts of mercury, can affect the development of the nervous system of a fetus. During the treatment and after pregnancy is established you should avoid eating these fish-shark, swordfish, king mackerel, tilefish and canned tuna fish. You should limit the intake of all other fish to 12 oz. per week.

DESCRIPTION OF EGG DONATION TREATMENT

Egg donation treatment is done in conjunction with IVF, which involves several steps. Success cannot be guaranteed at any or all of these steps. If optimal results are not appreciated at any step, it may be recommended that the treatment be stopped and the cycle cancelled. The steps of the treatment are discussed below.

- I. **Ovulation Induction:** The egg donor will take medications to stimulate the development of multiple ovarian follicles (the fluid-filled cysts in the ovary that contain eggs).
- II. **Egg Retrieval:** The egg donor will have the eggs removed from her ovaries.
- III. **Preparation of the Endometrium:** The uterine cavity of the recipient woman will be hormonally prepared to allow implantation of the embryos to occur.
- IV. **Insemination of the Eggs:** Following the egg retrieval the eggs and sperm will be placed together in the laboratory and incubated in an effort to achieve fertilization and support growth of the embryos.
- V. **Embryo Transfer:** One or more embryos will be transferred into the uterus of the recipient woman.
- VI. **Embryo Freezing:** Following the embryo transfer, any remaining embryos of suitable quality may be frozen (cryopreserved) and stored for future use.

The egg donor will undergo steps I-II. The recipient will undergo steps III- VI that are described below.

Preparation of the Endometrium

Within the ovaries the eggs are present in cysts called follicles. During a woman's menstrual cycle, usually one mature follicle develops within the ovary, which results in the ovulation of a single egg. The developing follicle up to ovulation predominantly produces estrogen which stimulates the growth of the lining of the uterine cavity, called the endometrium. After the egg is released at the time of ovulation the collapsed follicle (now called a corpus luteum) continues to produce

estrogen but now begins to produce progesterone. Progesterone matures the endometrium and prepares it for implantation of an embryo. The timing of estrogen and progesterone stimulation of the endometrium relative to the arrival of the embryo is important.

Since the recipient's endometrium must be properly prepared to receive donated eggs, the menstrual cycles of the donor and recipient must be synchronized. Synchronization of the menstrual cycles of the donor and recipient is accomplished with the use of medications that are discussed below. These medications have not been approved by the FDA for this purpose.

The medications that will be administered to the recipient to prepare the endometrium are as follows:

Estrogen (Estrace[®], Vivelle[®], Estraderm[®]) - As is a natural menstrual cycle, you will receive a form of natural estrogen to thicken and prepare your uterine lining. The route of estrogen administration may be oral, vaginal or through a patch placed on the skin.

Progesterone (Progesterone, Prometrium[®], Crinone[®]) - As is a natural menstrual cycle, you will receive a form of natural progesterone to help prepare your uterine lining. The route of progesterone administration may be vaginal, oral or through an intramuscular injection.

Progesterone supplements are not FDA-labeled for use during pregnancy. It should be noted, however, that studies have shown that there is no increased risk of congenital birth defects developing in an unborn child or health risks to a woman who takes forms of natural progesterone supplements during pregnancy.

Some oocyte recipients do not have menstrual cycles. Women without menstrual cycles often use birth control pills or other forms of hormone replacement therapy. When preparing to receive donated eggs, the recipient will receive instructions when to discontinue the birth control pills or hormone replacement therapy. She will then be instructed to take estrogen and progesterone according to a specific treatment regimen.

Some oocyte recipients have normal menstrual cycles. Recipient women with menstrual cycles will take a medication, GnRH Agonist (Lupron[®]) or GnRH Antagonist (Cetrotide[®], Antagon[®]) to suppress the natural menstrual cycle. Usually the GnRH agonist or antagonist may be used in conjunction with or following the use of a birth control pill. Then, she will be instructed to take estrogen and progesterone according to a specific treatment regimen.

GnRH Agonist (Lupron[®])

GnRH Agonist (Lupron[®]) – This synthetic hormone is administered by subcutaneous injection. The administration of a GnRH agonist initially causes release of FSH and LH from the pituitary gland. However, with continued administration there is a temporary depletion of FSH and LH, which suppresses a LH surge thereby preventing ovulation. On occasion, the GnRH agonists may be used in conjunction with or following the use of a birth control pill.

Side Effects

The use of these medications (Oral contraceptives, GnRH agonist, GnRH antagonist, estrogen, and progesterone) can cause side effects such as nausea, vomiting, hot flashes, headaches, mood swings, joint pains and visual symptoms. Some women may have an allergic reaction to the drugs. A rare risk of estrogen administration is the formation of blood clots, which can compromise the blood supply to vital organs, causing serious problems. Problems described with estrogen usage include breast cancer, stroke, or heart attack. Any of these conditions may cause death or serious long-term disability. Most studies of low-dose, short-term estrogen usage by women do not show an increased risk of these complications.

Insemination of the Eggs

On the day of the egg retrieval, a sperm sample is obtained. Under some circumstances, sperm can be frozen prior to the day of egg retrieval for use on the day of egg retrieval. Reasons to consider sperm freezing would be if the male partner may not be available on the day of the egg retrieval or there has been difficulty in the past with the production of a semen sample. You are responsible for making arrangements to freeze sperm prior to the start of treatment if this applies to you. The source of the sperm can be from the male partner or in some situations the couple (patient) may choose to use donor sperm. The biologist processes the sperm sample and then the eggs are inseminated. There are two approaches to the insemination of the eggs that are discussed below:

1. **Standard Insemination**- If the sperm sample is adequate then a standard insemination of the eggs can be performed. After the sperm sample has been processed, a mixture of the sperm and eggs is placed in a plastic dish containing a nutrient culture media and then placed in an incubator in the laboratory to allow fertilization to occur. The nutrient culture media contains a serum additive, which is a blood product, and there is a rare chance of transmission of a viral infection. The morning after the egg retrieval, the eggs are examined to see if fertilization has occurred.
2. **Intracytoplasmic sperm injection (ICSI)** - ICSI is a laboratory procedure performed to increase the chances of fertilization.

The ICSI procedure is a process, whereby, with the aid of a microscope and fine instruments, a single sperm is injected directly into the egg. Indications for ICSI include- a previous IVF cycle with poor fertilization, a previous semen analysis demonstrating significant abnormalities and in situations where surgical aspiration of sperm from the vas deferens or testicle is required. In most cases it is known at the start of the IVF cycle that ICSI will be performed. However, in other cases the sperm sample on the day of the egg retrieval may be unexpectedly inadequate for standard insemination and the ICSI procedure may be performed.

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 (X and Y) 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 is increased with ICSI. The prevalence of de novo (not inherited) balanced translocations in offspring derived from ICSI is increased. The prevalence of these combined (0.36%) 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 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 CBAVD, as well as their partners, should be tested for CF gene mutations prior to treatment, so that the risk of their offspring having CF can be estimated and appropriate testing performed. It is important to understand that there may be CF gene mutations that are not detectable by current testing and parents who test negative for CF mutations can still have children affected with CF.

Some 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 (mutations) on their Y chromosomes lead to extremely low or absent sperm counts. Testicular biopsy and successful retrieval of viable sperm can 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 also generate offspring having a Y chromosome microdeletion, because the chromosomes in the sperm may not be the same as those seen when tested by a blood test. If you would like additional information about the genetic issues surrounding IVF and the ICSI procedure talk to your physician about a referral to a genetics counselor.

The following additional risks are associated with the performance of the ICSI procedure:

1. The eggs may fail to become fertilized or may be damaged precluding their ability to be fertilized.
2. ICSI may yield presently unknown risks to the baby and/or mother.
3. Studies have shown that some cases of male infertility may be genetic. Therefore there is the possibility that infertility may be passed on to the offspring as stated above. Some studies show an increased risk of chromosomal and other abnormalities in babies born as a result of the ICSI procedure. If pregnancy is achieved testing can be performed to determine the chromosomal makeup of the fetus. If you would like additional information concerning genetics and inheritance, you should ask your physician to refer you to a genetic counselor prior to the start of your treatment cycle.
4. ICSI may compromise the protective effect of the membrane that surrounds the embryo, which may result in bacterial contamination and infection in the embryo that would render it non-viable.

On average, 60-70% of eggs will fertilize following the standard insemination or the ICSI procedure but in some cases none of the eggs fertilize. If fertilization is confirmed, plans are then made for the embryo transfer. In some cases of documented fertilization the embryos stop their development and the embryo transfer is cancelled.

Embryo Transfer

After fertilization has been confirmed, the development of the embryos is monitored in the laboratory. If the embryos continue their development then plans are made for the embryo transfer. The embryo transfer is performed 3 to 6 days following the egg retrieval. Embryos transferred 3 days after the egg retrieval are generally at the 4 to 8 cell stage. Embryos transferred on day 5 or 6 are at a more advanced stage and may have developed into a blastocyst, which is made up of over 50 cells. Your physician will discuss with you the optimal time of the transfer. In the event that the embryos stop their development the embryo transfer is not performed.

At the time of the embryo transfer, a physician will review the fertilization results and the development of the embryos. A decision will be made regarding the number of embryos that will be transferred. Increasing the number of embryos transferred will increase the chances of pregnancy, but will also increase the risk of a multiple pregnancy (e.g., twins, triplets, etc). Remaining embryos that are not transferred will be examined and, if they are of suitable quality, may be frozen, stored and transferred at a later date. Alternatively, these "extra" embryos can be discarded.

Embryos which result from abnormal fertilization (i.e., polyspermy -when more than one sperm fertilizes an egg) will be discarded because they have no chance of developing normally. In addition, embryos that fail to develop properly (e.g., fail to divide, demonstrate other significant abnormalities of development) will also be discarded. Eggs and/or embryos, which have failed to develop (not viable), will not be transferred and will be discarded.

In order to perform the embryo transfer the woman is placed in the same position for a pelvic exam. A speculum is placed into the vagina and the cervix is visualized. The vagina and cervix are rinsed with a solution. In some cases an abdominal ultrasound is performed to help visualize the passage of the catheter. The biologist loads the embryos into a catheter, which the physician inserts through the cervical canal and into the uterine cavity. After placement of the catheter the embryos are injected into the uterine cavity. The catheter is examined by the biologist to confirm that the embryos have been discharged. Following the procedure the woman will be sent home. Activity should be limited on the day of the embryo transfer. Thereafter, normal activity should be resumed.

Very rarely, a uterine infection may occur after embryo transfer. The most common symptoms associated with infection are pain and fever. If fever, vomiting, abdominal pain or any other symptoms develop following embryo transfer, you should contact your physician.

Assisted Embryo Hatching

Your physician may recommend that assisted hatching be performed on the embryos just prior to the transfer. The zona pellucida is the outer protective membrane that surrounds the egg. After the sperm has penetrated the egg and fertilization has occurred, the embryo develops within the confines of the zona pellucida for a period of 5-7 days. Thereafter, an area of the zona pellucida thins out and the embryo "hatches" or is expelled out of the confines of the zona pellucida. It is only then that the embryo has the opportunity to implant into the uterine wall for the establishment of a pregnancy. It is possible that some embryos do not undergo this "hatching" process normally. A laboratory technique has been developed to facilitate the embryo with this "hatching" process and is referred to as *assisted hatching*. There is controversy as to whether the performance of assisted hatching increases the chance of a successful pregnancy following IVF treatment.

The assisted embryo hatching procedure- With the aid of a microscope and fine instruments, the zona pellucida (the outer membrane surrounding the embryo) is thinned by either the application of a dilute acidic solution or a laser. The embryos are then transferred back into the incubator until the embryo transfer is performed. Your physician may prescribe an antibiotic and a corticosteroid (methylprednisolone), which will be started on the day of the egg retrieval and continued for a period of four days.

The following risks are associated with the assisted hatching procedure.

1. The embryos may be destroyed or injured precluding their ability to implant.
2. There is an increased chance that an embryo splits and leads to a set of identical twins. This type of a multiple pregnancy is referred to as monozygotic twinning (MZT). The risks associated with MZT are described later in the consent. .
3. The procedure may yield presently unknown risks to the baby and/or mother.
4. Assisted hatching may not improve your chances of establishing a pregnancy.
5. There are risks associate with medications that may be prescribed
 - a. Methylprednisolone- This medication has an anti-inflammatory action and modifies the immune response. The following side effects may occur but are more common when this drug is administered for a longer duration or at higher doses: mood swings, insomnia, depression, psychotic manifestations, muscle weakness, permanent hip replacement, impaired wound healing, increase sweating, headaches, vertigo, allergic reaction, loss of muscle mass, osteoporosis and abdominal distention. Other side effects include an increase in blood pressure, salt and water retention, increase excretion of potassium and calcium may occur. The use of methylprednisolone may mask the signs of an infection, make one susceptible to a new infection, and make it difficult to localize the source of an infection.
 - b. The use of antibiotics may result in the following side effects which are dose-related: nausea, vomiting, diarrhea, loss of appetite, rashes, sensitivity to the sun, rare hypersensitivity reaction which may cause shock, blood diseases including reduced platelets or fractured blood cells which could result in anemia and/or bleeding.

Embryo Cryopreservation of viable, high quality embryos (if any) not transferred:

I/We understand that to date, there are no known effects from long-term storage of cryopreserved (frozen) embryos. Although there are theoretical risks of congenital malformations, I/we understand that the best available research suggests that the rate of birth defects in children born following the cryopreservation of embryos is the same as the rate observed in an age-matched group of pregnant women who conceived without assisted reproduction:

1. _____ Patient initials _____ Partner initials I/We AGREE to embryo cryopreservation
(if applicable)

OR

2. _____ Patient initials _____ Partner initials I/We DO NOT AGREE to embryo cryopreservation
(if applicable)

Disposition of Cryopreserved Embryos:

Any disposition of embryos requires the written authorization of both partners. If your embryos were formed using eggs/sperm from a third party donor, your instructions to donate these embryos must be in accordance with prior agreements with the egg/sperm donor or applicable law. Your instructions to donate the embryos may require separate consent from the egg/sperm donor.

I/We understand and agree that in the event of death or incapacitation of one partner, the embryo(s) will become the sole and exclusive property of the surviving partner, unless otherwise directed by law, a court order or as designated in my/our will. If the surviving partner, friends or family members wish to conceive with these embryos after your death, a legal document indicating this intent will be required.

I/We understand that the cryopreserved embryos will incur a charge according to the Fees for Embryo Cryopreservation and Storage policy of Boston IVF. Cryopreserved embryos will be maintained until specific directives and authorization for those directives are provided by me/us. Options for disposition are discussed in the Consent for Treatment Guideline and consent forms are required at the time of disposition. Boston IVF reserves the right at its sole discretion to make decisions regarding the final disposition of cryopreserved embryos if fee obligations are not met. In the event of divorce or dissolution of the relationship between patient and partner, embryos cannot be used, donated or discarded without the expressed, written consent of both parties or as directed by a court order, even if donor eggs/sperm were used.

Risks of Pregnancy

Pregnancies that occur with IVF are associated with increased risks of certain conditions including pre-eclampsia, placenta previa, placental abruption, gestational diabetes and cesarean section. 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.

Currently more than 30% of IVF pregnancies are twins or higher-order multiple gestations (triplets or greater). Identical twinning occurs in 1.5% to 4.5% of IVF pregnancies. IVF twins deliver on average three weeks earlier and weigh 1,000 gm (2.2 pounds) less than IVF singletons. Of note, IVF twins do as well as spontaneously conceived twins. Triplet (and greater) pregnancies deliver before 32 weeks (7 months) in almost half of cases.

Additionally, 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. These abnormal pregnancies often times require medical treatments with methotrexate (a weak

chemotherapy drug) or surgery to treat the abnormal pregnancy. Side effects of methotrexate 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.

A miscarriage is a failed intrauterine pregnancy. The risk of miscarriage in the general population is 15-20%. The risk of miscarriage increases with advancing maternal age. For women over 40 years of age, the risk may exceed 40%. Studies have shown that there is either no increase or a slight increase in the risk of miscarriage in women who conceive with IVF. Most miscarriages are associated with lower abdominal cramping and bleeding, but do not necessarily require surgical treatment. In some cases, removal of the pregnancy tissue must be accomplished by a surgical procedure called a dilatation and curettage (D&C).

Risks to Offspring

1. Overall risks:

Since the first birth of an IVF baby in 1978, more than 3 million children have been born worldwide following IVF treatments. 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). IVF twins are not born earlier or later than naturally conceived twins. 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.

2. Birth Defect:

The risk of birth defects in the normal population is 2-3 %. In IVF babies the birth defect rate may be 2.6-3.9%. Studies to date have not been large enough to prove a link between IVF treatment and specific types of birth defects.

3. Imprinting Disorders:

These are rare disorders having to do with whether a maternal or paternal gene is inappropriately expressed. Since the incidence of this syndrome in the general population is 1/15,000, even if there is a 2 to 5-fold increase to 2-5/15,000, this absolute risk is very low.

4. Childhood cancers: Most studies have not reported an increased risk with the exception of retinoblastoma:

5. Infant Development: In general, studies of long-term developmental outcomes have been reassuring so far; most children are doing well.

6. Risks of a Multiple Pregnancy: The most important maternal complications associated with multiple gestation are preterm labor and delivery, pre-eclampsia and gestational diabetes (see prior section on Risks to Woman). 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.

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.

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 (mature fetus or newborn) 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.

Monozygotic twinning (MZT) is a multiple pregnancy that results from the splitting of a single embryo, which will lead to a set of identical twins. The incidence of MZT is increased in pregnancies conceived following IVF and may occur between 1.5-5% of IVF pregnancies. In addition to the above stated complications associated with a multiple pregnancy with MZT there is a greater chance of twin-to-twin transfusion, which can affect the growth of the fetuses and increase the chance of other complications. Twins sharing the same placenta have a higher frequency of birth defects compared to pregnancies having two placentas. MZT occurs more frequently after blastocyst transfer.

Placenta previa and vasa previa are more common complications in multiple gestations. Abruption 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.

A multiple pregnancy may pose increased emotional and financial hardship for a couple. The risk of a multiple pregnancy can be reduced by decreasing the number of embryos that are transferred but this also reduces the overall chance of success. You are encouraged to have a discussion with your physician about the optimal number of embryos to transfer.

The 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 the 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%.)

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). We encourage patients and their spouses or partners who so desire to consult with trusted members of their religious or ethics community for guidance on their infertility treatment.

Psychosocial Effects of Infertility Treatment

IVF can be psychologically stressful. Anxiety and disappointment may occur at any of the phases described above. Significant commitment of time and finances may be required. Patients are encouraged to consider meeting with a counselor. If you are interested in meeting with a social worker or psychologist, please speak to your physician.

Legal Considerations and Legal Counsel

The law regarding embryo cryopreservation, subsequent thaw and use, and parent-child status of any resulting child(ren) is, or may be, unsettled in the state in which either the patient, spouse, partner, or any donor currently or in the future lives, or the state in which the ART Program is located. We acknowledge that the ART Program has not given us legal advice, that we are not relying on the ART Program to give us any legal advice, and that we have been informed that we may wish to consult a lawyer who is experienced in the areas of reproductive law and embryo cryopreservation and disposition if we have any questions or concerns about the present or future status of our embryos, our individual or joint access to them, our individual or joint parental status as to any resulting child, or about any other aspect of this consent and agreement.

Reporting Outcomes

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 my/our 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) (if my/our clinic is a member of this organization). The CDC may request additional information from the treatment center or contact me/us directly for additional follow-up. Additionally, my/our 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 my/our treatment being used to identify me/us as individuals.

There are many complex and sometimes unknown factors, which may prevent the establishment of pregnancy. Known factors, which may prevent the establishment of pregnancy, include, but are not limited to, the following:

1. The egg donor's ovaries may not respond adequately to the medications.
2. Technical problems including inadequate visualization or the position of the egg donor's ovaries may prevent the retrieval of the eggs.

3. There may be failure to recover an egg because ovulation has occurred prior to the time of the egg retrieval.
4. The eggs may not be normal.
5. The male partner may be unable to produce a semen sample or the semen sample may be of insufficient quantity or quality.
6. Fertilization of the eggs and sperm to form embryos may not occur.
7. Cell division of the embryos may not occur.
8. The embryos may not develop normally.
9. Embryo transfer into the uterus may be technically difficult or impossible.
10. If the transfer is performed, implantation may not result.
11. If implantation occurs, the embryo(s) may not grow or develop normally
12. Equipment failure, infection, technical problems, human error and/or unforeseen factors may result in loss or damage to the eggs, semen sample and/or embryos.

The foregoing general information is based upon the experience and knowledge of the Boston IVF physicians. It is based, in part, upon a review of the literature pertaining to Reproductive Medicine. This information is generally accurate and comprehensive, however, medicine is a dynamic discipline and reproductive medicine in particular is constantly evolving. Estimates of risks factors and the relative benefits of alternative treatment that have been discussed with you represent the best professional judgment of the physicians and caregivers of Boston IVF taking into account your specific needs and circumstances.

ANONYMOUS VERSUS KNOWN EGG DONATION

Egg donors can be either be anonymous donors or known to the recipient. These two categories are detailed below:

Anonymous Donors: Anonymous donors are recruited by a third party agency. Boston IVF only allows donors from approved agencies that adhere to ethical guidelines established by the American Society for Reproductive Medicine. (ASRM). Boston IVF does not allow donors that have been recruited directly by a recipient. Egg donors volunteer to participate in the egg donation with the understanding that they will not know the identity of the recipient. Likewise, the recipient or recipients will not know the identity of the egg donor. Donors recruited through a third party agency sometimes reveal identifying information to the recipient and likewise the recipient sometimes reveals identifying information to the donor. The degree of information exchange varies from agency to agency. As a recipient of donor eggs it is your responsibility to find out in advance the type and amount of personal identifying information that is available to you about the donor and what information about you the donor will receive.

Boston IVF complies with national recommendations for egg donor screening as outlined by the American Society for Reproductive Medicine and the FDA. Donors provide a comprehensive medical, social and family history. In keeping within national guidelines, donors do not provide Boston IVF with copies of medical records from treatment that they may have received during their lifetime. Therefore, an egg donor may omit important information, unintentionally or intentionally, from her history.

Donors take a written psychological test and meet with a social worker for psychological screening. Donors have a complete physical exam including a pelvic examination with tests for the sexually transmitted diseases, gonorrhea and Chlamydia. Donors are also screened for sexually transmitted diseases including HIV and the viruses that cause hepatitis B and C. In addition, donors are re-screened for sexually transmitted diseases a second time within 30 days of the egg retrieval as per FDA regulations. Unfortunately, no test or screening process in medicine is perfect or 100% accurate. This includes the unintentional transmission of a genetic characteristic, trait, disease potential or actual disease from the donor to the embryo. Furthermore, an infectious disease may escape detection during the screening process and be transmitted to the recipient. Fortunately, it is estimated that such transmission is extremely rare.

Known Donors: Donors in this category are brought to Boston IVF by a specific, designated recipient. The donor knows the identity of the recipient and the recipient knows the identity of the donor. All oocytes retrieved from the known donor are designated for the use of the known recipient. Boston IVF has established guidelines with regard to age of the donor and relationship of the donor to the recipient. Donors that do not meet these guidelines may not be permitted undergo egg donation.

RIGHTS OF THE DONOR AND RECIPIENT

The intentions of the egg donor and recipient are clear and unambiguous from the outset. When the egg donor signs her consent form she explicitly agrees that once the eggs leave her body, she waives any right and relinquishes any claim to the donated eggs as well as any embryos or offspring that might result from their use. The recipient in turn, releases the egg donor from any and all liability for any problem occurring during pregnancy and for any mental or physical disabilities, financial support, care, custody or living expenses, education, health and welfare of the child(ren) born as a result of egg donation. The recipient also accepts complete financial responsibility for the care and storage of any embryos frozen for her during treatment. The recipient has the right to determine the fate of all embryos frozen for her including but not limited to discarding them, donating them to another recipient or donating them for research. Anonymous donors also expect the right to privacy following egg donation. The recipient clearly and unambiguously agrees not to seek the identity of the donor now or in the future.

UNANTICIPATED CHANGES IN THE LAW

State or Federal laws may change in the future that permit the donor and/or recipient to locate one another. There is no way to predict when or if such a change will ever occur. We recommend that you speak with a lawyer about the implications of this possibility.

FINANCIAL RESPONSIBILITIES

I/We understand that insurance coverage for any or all of the above procedures may not be available and that we will be personally responsible for the expenses of this treatment. In particular we understand that we are responsible for all costs, for both the recipient and the donor, related to the ovum donation and subsequent fertilization and transfer including medications, blood tests, medical evaluations, social services screenings, psychological evaluations, and surgical procedures. We hereby authorize Boston IVF to release such information from our medical records as may be necessary for the settlement of all claims for payment of these charges.

ACKNOWLEDGMENT OF INFORMED CONSENT AND AUTHORIZATION

I/We acknowledge that we, the undersigned, are voluntarily participating in the Boston IVF egg donor program in order to conceive a child and that we will acknowledge our parentage of any child or children born through this technique. I/We acknowledge that we have read all pages of this consent form and all of our questions concerning the treatment have been fully answered to our satisfaction.

I/We have discussed this treatment in detail with a Boston IVF physician and caregivers in language that we understand. We understand the purpose, risks and benefit of the treatment. **I/We acknowledge that we have read all pages of this consent form and all of our questions concerning the treatment have been fully answered to our satisfaction.**

I/We are aware that there are other centers in the area that offer this treatment and we have freely chosen to have the treatment at Boston IVF.

I/We acknowledge that we have undergone medical, psychological and legal counseling that has been met with our satisfaction.

By consenting to treatment at Boston IVF we accept the responsibilities, conditions and risks involved as set out in this document and as explained by the staff of Boston IVF. In addition, we consent to the techniques and procedures used to accomplish this treatment described in this document and as explained by the physicians and staff of Boston IVF.

I/We understand and acknowledge that medicine is not an exact science and that in cases of doubt Boston IVF physicians and caregivers will exercise their best professional judgment.

I/We acknowledge and agree that acceptance into treatment and our continued participation is within the sole discretion of Boston IVF. We understand that should this cycle be unsuccessful, it may be determined that further treatment may not be indicated.

I/We acknowledge that it is our responsibility to notify Boston IVF in writing if we become aware of any information that Boston IVF should have in order to discharge its obligations under this agreement.

I/We agree to notify BIVF immediately in writing of any change in our marital status including separation or divorce.

I/We also understand that we are financially responsible for any medical expenses that are not covered by our insurance policy.

I/We understand that medical information concerning our treatment may be analyzed and could be used in a publication. In accordance with federal law, identifying information and information concerning our treatment will be submitted to a national data registry that publishes statistics on treatment outcomes. In order to obtain this information we give Boston IVF consent to contact any physicians who provided care during and after a pregnancy. I/We understand that no publication resulting from these or other scientific studies will contain our name or other information that would allow us to be identified.

I/We understand that Boston IVF complies with national recommendations for egg donor screening as outlined by the American Society for Reproductive Medicine. I/We understand that no test or screening process in medicine is perfect or 100% accurate. This includes the unintentional transmission of a genetic characteristic, trait, disease potential or actual disease from donor to embryo. Furthermore, some infectious diseases of the donor, depending on the incubation period, may escape detection during the screening process and be transmitted to the recipient. We accept the risks associated with receiving a donated egg.

I/We have read and understand the section in this consent form describing the rights of the donor and recipient.

I/We accept all responsibility and release the egg donor from any and all liability for any problem occurring during pregnancy and for any mental or physical disabilities, financial support, care, custody or living expenses, education, health and welfare of the child(ren) born as a result of egg donation. I/We accept complete financial responsibility for the care and storage of any embryos frozen. I/We understand that anonymous donors expect the right to privacy following egg donation. If I/we are using an anonymous egg donor, we clearly and unambiguously agree not to seek the identity of the anonymous egg donor now or in the future unless otherwise agreed between the recipient (couple) and the donor not through or involving Boston IVF.

By signing this document, I/we acknowledge that we have had a thorough discussion with our Boston IVF physician and caregivers. This discussion included information on the risks, benefits, side effects and complications of the treatment. Furthermore, I/we acknowledge that the discussion with our Boston IVF physician provided sufficient information to allow us to make an informed decision whether or not to proceed with treatment. The discussion with our Boston IVF physician included alternatives including the option of having no treatment.

