



BRIGHAM AND
WOMEN'S HOSPITAL
A Teaching Affiliate of Harvard Medical School

Education Booklet for Informed Consent for Assisted Reproduction:

In Vitro Fertilization
Intracytoplasmic Sperm Injection
Assisted Hatching
Preimplantation Genetic Diagnosis
Embryo Freezing
Egg Freezing
Frozen Embryo/Egg Transfer
Donor Egg/Gestational Carrier

The Center for Infertility and Reproductive Surgery
The Center for Assisted Reproductive Technology
Brigham and Women's Hospital
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Dear Patients,

Welcome to the Brigham and Women's Hospital Center for Assisted Reproductive Technology (ART).

You may have come to our program having only recently discovered that you need ART to have a child or this may be a later step in a series of treatments. You may have decided to freeze eggs due to age or medical reasons. We understand that having to undergo these treatments in order to have a child now or in the future is probably not what you envisioned for yourself when you first thought about having a family. Our physicians, nurses, embryologists, and social workers have extensive experience treating people using ART. We are dedicated to helping you through this process by making sure you understand it and have the emotional support you need every step of the way.

The emotional aspects of treatments can sometimes become more stressful than the physical ones. Because of this, we have two social workers who specialize in helping patients and families navigate this journey. Please let your doctor, nurse, or secretary know if you would like to receive a call from one of them.

This manual will describe the treatments you may undergo. It is meant to prepare you to sign consents for your treatments. These treatments are complicated: please feel free to call your nurse or physician with questions and/or concerns.

We wish you the very best with your upcoming treatment.

Your BWH ART team

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A. In Vitro Fertilization (IVF): A Summary

INTRODUCTION

Your doctor has recommended In Vitro Fertilization (IVF) as a way for you to become pregnant or s/he may have recommended that you freeze eggs for future use. S/he has made this decision with you after a review of your history and testing. If appropriate this includes your partner's history and testing.

This booklet will review IVF, and the other techniques that may be used with it, from beginning to end including the risks. After reading this booklet you will have time to ask questions; then you will be asked to sign the consents for IVF and other procedures as recommended. **References in red indicate the page for full descriptions.**

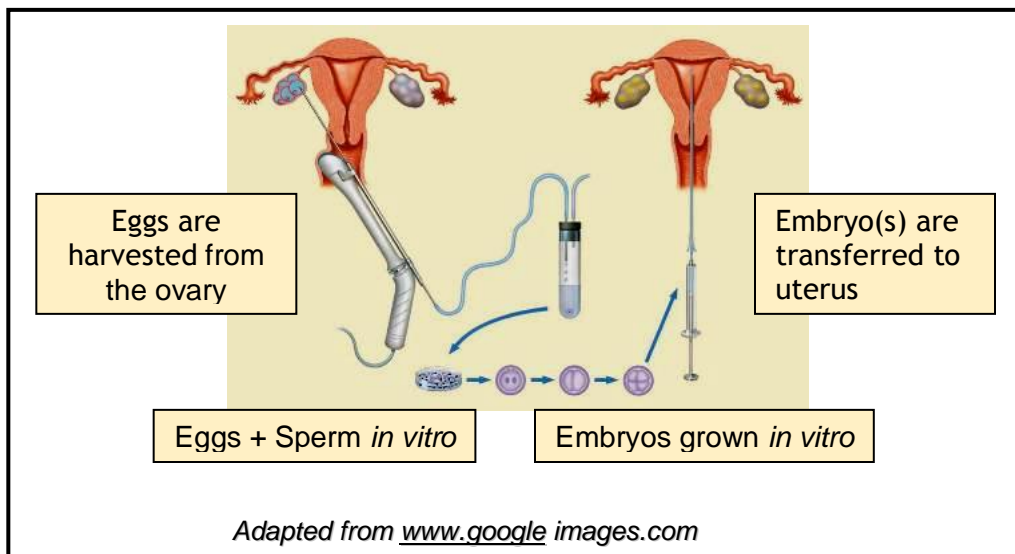
THE PROCESS

In order to become pregnant, an egg is fertilized by a sperm. During naturally occurring pregnancies the fertilized egg travels down the fallopian tube to the uterus and implants in the uterus. In IVF, eggs are removed from a woman's ovaries; the eggs and sperm are combined outside her body and allowed to grow for a few days in an incubator. The fertilized eggs are then called embryos and some are then put into the woman's uterus to hopefully implant (attach to the lining of the uterus) to create a pregnancy. Eggs or embryos may also be frozen for later use.

An IVF cycle usually includes:

- Medicine to mature many eggs in the ovaries (ovulation induction) (Page 6-8)
- Surgery to remove eggs from the ovaries (egg retrieval) (Page 9-10)
- Mixing the eggs with sperm to cause fertilization (insemination) (Page 10-12)
- Growing the fertilized eggs in an incubator for a few days (becoming embryos) (Page 10-12)
- Putting one or more embryos in the uterus (embryo transfer) (Page 12)

What is *In Vitro* Fertilization?



Before and during your IVF cycle you should:

- Tell your doctor what medicines you are already taking, including over the counter medicines, herbals, and supplements.
- Take a prenatal vitamin that contains folic acid.
- Stop smoking, drinking, and any recreational drugs.
- Avoid (unless prescribed by your IVF doctor) aspirin, Motrin, Advil, Naprosyn, Aleve, Ibuprofen.
- Limit caffeine consumption to no more than 200 mgs a day (2-8 ounce cups of regular coffee)
- You CAN take Tylenol per label instructions.

OVULATION INDUCTION AND TESTING (Page 6-9)

- You will take some of the following drugs as well as others. Some are pills, some are shots, some are vaginal inserts:
 - To prevent the ovaries from releasing eggs on their own:
 - Birth control pills, Lupron, Ganirelix, Cetrotide.
 - To stimulate the ovaries to grow many eggs at once
 - Gonal-f, Follistim, Bravelle, Menopur, Repronex, Luveris, and Clomiphene Citrate.
 - To prepare the eggs for egg retrieval
 - Human Chorionic Gonadotropin (HCG), Leuprolide acetate (Lupron), Ovidrel.
 - To help keep a lining in the uterus after the egg retrieval
 - Progesterone (shots, vaginal suppositories, Crinone gel).
 - Other drugs
 - Medrol, Estrace, Dexamethasone, Letrozole, baby aspirin.
- You will have the following tests during the cycle:
 - Blood tests: estradiol, progesterone, pregnancy (HCG)
 - Vaginal probe ultrasounds to see the ovaries and uterine lining and measure the fluid sacks that contain the eggs (follicles).

EGG RETRIEVAL (Page 9-10)

The egg retrieval will usually be performed 36 hours after you take the HCG shot. It is a day surgery procedure done under general anesthesia. Your legs will be in stirrups, your vagina will be cleaned with a sterile solution, and an ultrasound probe will be put in your vagina so that the doctor can see the follicles. A needle is used to go through the wall of the vagina and into each follicle to remove the fluid. The procedure takes 15-30 minutes. The fluid is examined by the embryologists to look for eggs.

The number of follicles will give you an idea of how many eggs will be retrieved. Not every follicle will contain an egg and not every egg retrieved will fertilize. Some eggs may have ovulated before the retrieval and some eggs may not develop properly. Sometimes some tiny follicles may grow larger and produce eggs. Rarely, no eggs are retrieved.

SPERM COLLECTION

If you have a partner who will be producing a fresh sperm specimen on the day of the egg retrieval it will usually happen during your surgery. There is a private room for this purpose. Your partner should abstain from ejaculating (producing a sperm sample) for 2 days before the egg retrieval. Some women may be using frozen sperm from a partner or a donor. Some partners may be having a sperm removal surgery on the day of or before the egg retrieval.

POST EGG RETRIEVAL RECOVERY

You will be monitored by nurses and anesthesiologists after your surgery. You may feel sleepy from the anesthesia. If you have pain you will receive pain medicine. Your recovery will likely be 1-1.5 hours. Before you leave, an embryologist will tell you how many eggs were retrieved and, if appropriate, what the sperm specimen was like.

FERTILIZATION (Page 10-12)

Eggs that are retrieved are placed in small dishes containing fluid to support their growth and development. The dishes are then put in an incubator which controls the temperature and the air content. To achieve fertilization, a few hours after the eggs are put in the dish, sperm is added to the dish; or, in the case of Intracytoplasmic Sperm Injection (ICSI) a single sperm is injected into each mature egg (Page 13-14). The eggs are checked the next day for normal fertilization. The normally fertilized eggs will be kept in the incubator until the day of the embryo transfer.

EMBRYO TRANSFER (Page 12)

After 3-5 days of growing, one or more embryos will be transferred into your uterus. The transferring doctor will recommend how many and which embryos to transfer. This is based on your age, what has happened in other IVF cycles, and the number and evaluation of the embryos. **You may choose to have fewer than the recommended number of embryos transferred but not more.** Embryos for transfer are loaded into a thin plastic tube (catheter). The catheter is then placed into the uterus through the cervix. A syringe at the outer end of the catheter is used to give pressure to empty the catheter. Ultrasound is sometimes used to help guide the catheter or verify the placement in the uterus. There is no anesthesia for the embryo transfer.



B. Details of IVF

1. Usual treatments and their risks

a. OVULATION INDUCTION AND MEDICATIONS

- The success of IVF largely depends on growing many eggs at once
- Injections of naturally occurring hormones are used for this purpose
- Other medications are used to prevent ovulation
- Doses of medication and timing of egg retrieval require monitoring of the ovarian response, by blood tests and ultrasounds.
- An overly vigorous ovarian response can occur, or conversely an inadequate response

Ovulation induction is a process in which a woman's natural hormones are suppressed and injectable medications are used to mature more than one egg.

Oral contraceptive pills: Many treatment protocols include oral contraceptive pills to be taken for 1 to 4 weeks before stimulation injections are started in order to suppress hormone production or to help schedule a cycle.

Risks, discomforts: headache, hypertension, nausea, breakthrough bleeding, weight gain, breast tenderness, blood clots.

GnRH-antagonists (Ganirelix Acetate or Cetrorelix Acetate) (Ganirelix®, Cetrotide®): The main role of this medicine is to prevent a premature LH surge, which would result in ovulation before egg retrieval and therefore would result in no eggs being obtained. They tend to be used for short periods of time in the late stages of ovarian stimulation or at the end of the prior cycle in the patch protocol. These medications are given by subcutaneous (small needle) injection.

Risks, discomforts: headache, nausea.

GnRH-agonists (Leuprolide Acetate) (Lupron®): The main role of this medicine is to prevent a premature LH surge, which would result in ovulation before the egg retrieval- which would result in no eggs being obtained. GnRH-agonists initially cause a release of FSH and LH from the pituitary, so they can also be used to start the growth of the follicles or start the final stages of egg maturation. You will give yourself this medication by subcutaneous (small needle) 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. Though Leuprolide acetate is an FDA (Federal Drug Administration) approved medication, it has not been approved for use in IVF, although it has routinely been used in this way for more than 20 years.

Risks, discomforts: hot flashes, vaginal dryness, burning on urination, difficulty sleeping bloating, headaches, hair loss, pain or numbness in extremities, local reactions at the injection site and temporary reduction in bone density.

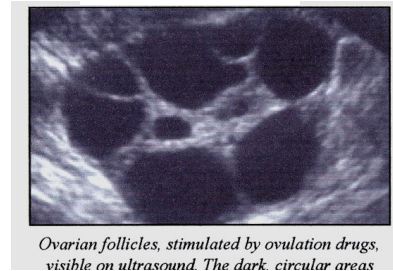
Gonadotropins or injectable "fertility drugs" (Follistim®, Gonal-F®, Bravelle®, Menopur®, Repronex®, Luveris®): These naturally occurring hormones stimulate the ovaries in hopes of maturing several oocytes (eggs) over the span of 7-14 days. They all contain follicle



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) (Menopur, Repronex). LH is a hormone that may work with FSH to increase the production of estrogen and growth of the follicles. Luveris®, which contains only LH, can also be given as a separate injection in addition to FSH. You will give yourself these injections by subcutaneous (small needle) injection.

Risks, discomforts: weight gain, mood changes, stomach pressure, headaches, nausea, vomiting, bloating.

Figure 1



Human chorionic gonadotropin (HCG) (Profasi®, Novarel®, Pregnyl®, Ovidrel®): hCG is a natural hormone used in IVF to mature eggs and make them ready to fertilize. The timing of this medication is critical to retrieve mature eggs. These medications are given by subcutaneous (small needle) or intramuscular (big needle) injection.

Risks, discomforts: headache, irritability

Progesterone (Endometrin®, Crinone®, Prochieve®, Prometrium®, or pharmacist-compounded suppositories, Progesterone in oil): This medicine is a hormone produced by the ovaries after ovulation to support the uterine lining for implantation (attachment) of the embryo. After egg retrieval, in some women, the ovaries will not produce enough of this hormone for long enough to support the uterine lining and thus the pregnancy. Progesterone is often continued for many weeks after a pregnancy has been confirmed. Progesterone has not been associated with an increase in fetal abnormalities. These medications are given by intramuscular (big needle) injection or vaginal insert.

Risks, discomforts: depression, sleepiness, bloating, weight gain, breast tenderness, headache, fatigue, allergic reaction and if given by intra-muscular injection includes the additional risk of infection or pain at the injection site.

Estradiol (Vivelle®, Estrace®): This medicine is a hormone produced by the ovaries to build and maintain a lining in the uterus in preparation for implantation. These medications can be taken by oral, trans-dermal (skin patch), or vaginal administration.

Risks, discomforts: nausea, bloating, gallbladder disease, abnormal blood clotting, migraines, darkening of the skin, growth of benign tumors, jaundice, breast tenderness, intolerance to contact lenses, increased vaginal secretions.

Other medications: Such as steroids, heparin, low molecular weight heparin or aspirin may also be included in the treatment protocol based on your medical history.

Risks, discomforts: depends on the specific medication.

RISKS of ovulation induction and the medications:

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. These medications are given to mature multiple follicles, and many women experience some bloating and minor discomfort as the follicles grow and the ovaries become temporarily enlarged. Other possible complications include the following:

- **Multiple Pregnancies:** The most important complications associated with multiple pregnancies are premature labor and delivery, pre-eclampsia (high blood pressure during pregnancy), and gestational diabetes (see following 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 relaxation of the abdominal wall, and umbilical hernias also can occur. Triplets and above increase the risk to the mother of more significant complications including severe bleeding after delivery and need for blood transfusion.

- **Ovarian Hyperstimulation (OHSS):** After the egg retrieval, the follicles, which have been drained, can fill up with fluid and form cysts. This results in ovarian enlargement and can lead to lower abdominal discomfort, bloating and distention. These symptoms occur within two weeks after the egg retrieval. The symptoms usually resolve within 1-2 weeks and treatment includes drinking electrolyte fluids such as Gatorade. Pregnancy can worsen the symptoms of ovarian hyperstimulation and make it last longer. If OHSS occurs your physician may recommend a period of reduced activity.

Severe ovarian hyperstimulation is characterized by the development of large ovarian cysts and fluid which collects in the abdomen and, sometimes, the lungs. Symptoms of severe ovarian hyperstimulation include abdominal distention and bloating along with weight gain, shortness of breath, nausea, vomiting, and decreased urine output. Approximately 2% of women will develop severe ovarian hyperstimulation and may need to be admitted to the hospital for observation and treatment. To help with the symptoms of severe ovarian hyperstimulation, an ultrasound-guided removal of fluid from the abdominal cavity (paracentesis) can be performed which results in improvement in the symptoms of bloating and distention. Rare, but serious consequences of severe ovarian hyperstimulation, include formation of blood clots that can lead to a stroke, kidney damage, and possibly death.

Every woman who takes these medications can develop ovarian hyperstimulation. In some cases when there is concern that a woman is at high risk for ovarian hyperstimulation, the cycle may be cancelled or the eggs will be retrieved and any embryos that result may be frozen.

- **Ovarian Torsion (Twisting):** In less than 1% of cases, a fluid filled cyst(s) in the ovary can cause the ovary to twist on itself. This can decrease the blood supply to the ovary and result in significant lower abdominal pain. Surgery may be required to untwist or possibly remove the ovary.
- **Ovarian Cancer:** Some research has suggested that the risk of ovarian cancer may increase in women who take any fertility drugs over a long period of time. These studies had significant flaws which limited the strength of their conclusions. More recent studies have not confirmed this risk. A major risk factor for ovarian cancer is infertility itself, suggesting that early studies may have incorrectly attributed the risk associated with infertility to the use of medications to overcome it.

b. MONITORING DURING THE CYCLE

- The progress of the cycle will be monitored by blood tests and ultrasound.
- Orders will be based on test results.

The progress of the cycle will be monitored by blood tests and vaginal probe ultrasounds. Testing is used to evaluate the estradiol level and to monitor the number and size of follicles in the ovaries. These tests will occur frequently, for 1-2 weeks, occasionally longer. The test results will guide the physician in managing the cycle.

RISKS of monitoring:

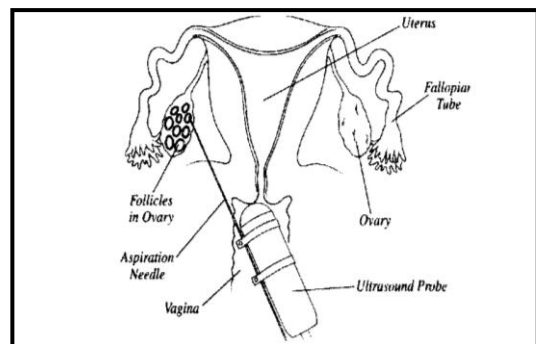
- Blood drawing may be mildly uncomfortable and produce bruising at the needle site, and rarely clot formation or infection in the vein.
- Vaginal probe ultrasound is mildly uncomfortable with no known risks.

c. EGG RETRIEVAL

- Eggs are removed from the ovary with a needle using ultrasound guidance
- Anesthesia is provided to make this comfortable
- Injury and infection are rare

Egg retrieval is the removal of eggs from the ovary. A vaginal ultrasound probe is used to see the ovaries and the follicles within the ovaries. A long needle, which is seen on ultrasound, goes into each follicle and suctions out the fluid. The fluid includes oocytes (eggs) and granulosa (egg-supporting) cells. Rarely the ovaries are not accessible by the vaginal route and laparoscopy (abdominal ultrasound-guided retrieval) is necessary (if applicable, risks of this procedure will be discussed with you by your doctor). General anesthesia is used to reduce if not eliminate discomfort. For this reason you will need a ride home after the egg retrieval.

Figure 2



(Reprinted with permission from the American Society for Reproductive Medicine)

RISKS of egg retrieval:

- **Infection:** Bacteria present in the vagina may be transferred into the abdominal cavity by the needle. This could cause an infection in the uterus, fallopian tubes, ovaries, or other abdominal organs. The chance 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 which could include the ovaries. Infections can negatively affect future fertility. Antibiotics are used before/after the egg retrieval to reduce the risk of infection. Despite the use of antibiotics, there is no way to eliminate this risk completely.

- **Bleeding:** The egg retrieval needle goes through the vaginal wall and into the ovary to get the eggs. These structures contain blood vessels and there are other blood vessels nearby. A small amount of bleeding is common during egg retrievals. The incidence of major bleeding problems is less than 0.1%. Major bleeding could require surgical repair and possible loss of the ovary, or a need for blood transfusion. Both are rare. (Although very rare, review of the world experience with IVF indicates that unrecognized bleeding has led to death.)
- **Trauma:** Even with the use of ultrasound, it is possible to damage other abdominal or pelvic organs during the egg retrieval. Reports in the medical literature have noted damage to the bowel, appendix, bladder, ureters (tubular structures which take the urine from the kidneys to the bladder), and ovaries. Damage to internal organs may result in the need for additional treatment such as surgery for repair or removal of the damaged organ. The risk of such trauma is low.
- **Anesthesia:** Anesthesia that is used during the egg retrieval can produce unintended complications such as an allergic reaction, low blood pressure, nausea or vomiting, and in rare cases death.
- **Failure:** It is possible that the egg retrieval will fail to get any eggs or the eggs may be abnormal or of poor quality and may not fertilize or produce a viable pregnancy.

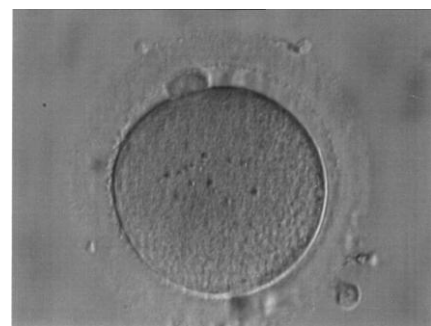
d. FERTILIZATION AND EMBRYO CULTURE

- Sperm and eggs are placed together in specialized conditions (culture media, controlled temperature, humidity and light) in hopes of fertilization occurring
- Culture medium is designed to permit normal fertilization and early embryo development, but the content of the medium is not standardized.
- Embryo development in the lab helps distinguish embryos with more potential from those with less or no potential to create a pregnancy.

After the eggs are retrieved, they are immediately carried to the embryology laboratory. The eggs are put in small dishes containing *culture medium* (a fluid that supports development of the embryos, made to resemble the fluid in the fallopian tube or uterus). The dishes are then put into incubators, which control the temperature and atmospheric gasses.

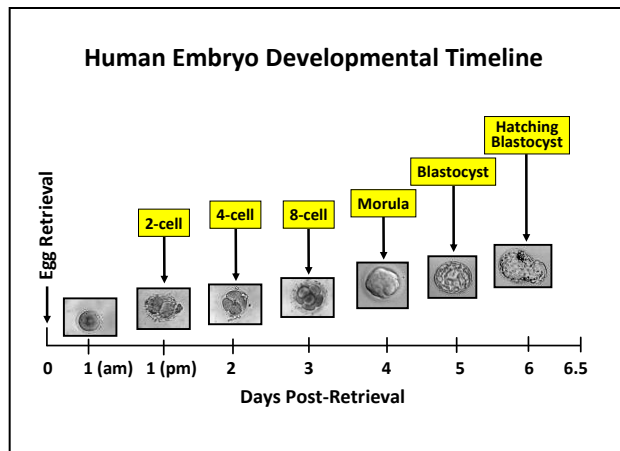
A few hours after eggs are retrieved, sperm are placed in the culture medium with the eggs, or individual sperm are injected into each mature egg using a technique called Intracytoplasmic Sperm Injection (ICSI) (see below). The dishes are then returned to the incubator. Embryos are checked for fertilization and periodically examined over the next few days to evaluate their development. (The media is changed at the fertilization check and may be changed again on day 3 if a day 5 transfer is done.)

Figure 3

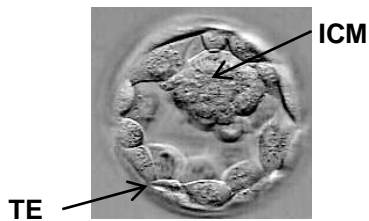


Mature egg (oocyte)

The day after the egg retrieval, the eggs are looked at for signs of fertilization. Normal development is evident by the egg having 2 nuclei; at this stage, the fertilized egg is called a zygote. A day later it has divided into about 4 cells (2-5 is common). Three days after insemination or ICSI, normally developing embryos contain about 8 cells (6-10 is common). Five days after insemination or ICSI, normally developing embryos have developed to the blastocyst stage containing about 110 cells.



The blastocyst has a fluid filled cavity and consists of about 110 cells of two distinct



Photograph of a human blastocyst (ICM=inner cell mass; TE=trophoblast)

types: the inner cell mass which is destined to become the baby, and the trophoblast cells which are destined to form the embryonic portion of the placenta.

Since many eggs and embryos are not normal, it is expected that not all eggs will fertilize and not all embryos will grow at a normal rate. The chance that a developing embryo will produce a pregnancy is related to whether its development in the lab is normal, but this relationship is not perfect. Therefore, not all embryos developing at the normal rate are chromosomally normal, and not all poorly developing embryos are abnormal. Nonetheless, an embryo's visual appearance is the most common guide in selecting the best embryo(s) to transfer.

RISKS in the embryology lab:

- **No fertilization:** Fertilization of the egg(s) may not occur.
- **Abnormal fertilization:** One or more eggs may be fertilized abnormally resulting in an abnormal number of chromosomes in the embryo; these abnormal embryos will not be transferred into the uterus.
- **Poor development:** The fertilized eggs may deteriorate before dividing into embryos, or adequate embryonic development may fail to occur, resulting in low pregnancy rates.
- **Bacterial or yeast contamination or a laboratory accident:** May result in loss or damage to some or all of the eggs or embryos.
- **Equipment failure:** Laboratory equipment may fail and/or extended power losses could occur which might lead to the destruction of eggs, sperm, and embryos.
- **Unforeseen events:** Other unforeseen circumstances may prevent any step of the procedure to be performed or prevent the establishment of a pregnancy.

- **Natural disasters:** 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.

e. EMBRYO TRANSFER

- After a few days of development, the best appearing embryo(s) is/are selected for transfer
- The number chosen influences the pregnancy rate and the multiple pregnancy rate
- A woman's age and the appearance of the developing embryo(s) have the greatest influence on the pregnancy rate and outcome
- Embryos are placed in the uterine cavity with a thin catheter (tube)
- Extra embryos of good quality that are not transferred may be frozen

After a few days of development, one or more embryos are selected for transfer to the uterus. Embryos are placed in the uterus with a thin tube (catheter). Ultrasound guidance may be used to help guide the catheter or confirm placement in the uterus.

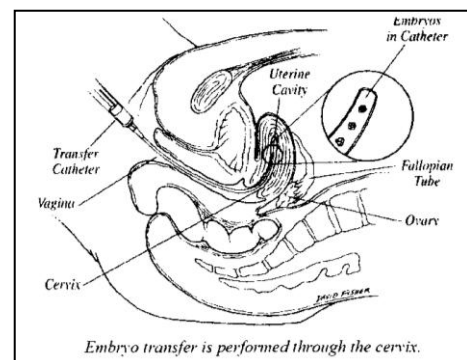
The number of embryos transferred influences the pregnancy rate and the multiple pregnancy rate. The age of the woman and the appearance of the embryo(s) have the greatest influence on pregnancy rate and the multiple pregnancy rate. While it is possible, it is unusual to develop more fetuses than the number of embryos transferred. The transferring doctor will discuss the number to be transferred before the transfer is performed.

In some cases, there will be embryos remaining in the lab after the transfer. Depending on their quality, it may be possible to freeze them for later use. (Section 2.c.).

RISK of embryo transfer (very rare):

- Infection
- Loss of or damage to the embryos

Figure 4



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2. Additional procedures some patients may have and their risks

a. INTRACYTOPLASMIC SPERM INJECTION (ICSI)

- ICSI is used to increase the chance of fertilization when fertilization rates are anticipated to be lower than normal or sperm numbers are very low
- A slight increased risk of genetic and other defects in offspring has been reported
- ICSI will not improve egg defects
- ICSI is recommended for fertilization of frozen-thawed eggs.

ICSI may be recommended for patients with severe male factor infertility (low sperm numbers, motility, or abnormally shaped sperm). It may also be recommended for patients with failed or low fertilization in prior cycles. It may also be used in some cases of preimplantation genetic diagnosis (PGD).

After eggs are retrieved they are rested for several hours in an incubator. The eggs are then examined for maturity. Usually 60-70% of the eggs are mature (the range is 0-100%), the remainder are generally discarded. Fertilization is accomplished by injecting a single sperm into the mature eggs. Usually 60-70% will fertilize (the range is 0-100%).

In addition to the usual IVF medications, a steroid (Medrol) will be ordered to decrease the theoretical possibility of the body rejecting the ICSI embryo. Steroids may decrease the body's ability to fight infection. Additional, uncommon, side effects of steroids (generally with long term use) are: cataracts, high blood pressure, psychological or emotional changes, seizures, hip or bone injury, ulcers, or high blood sugar.

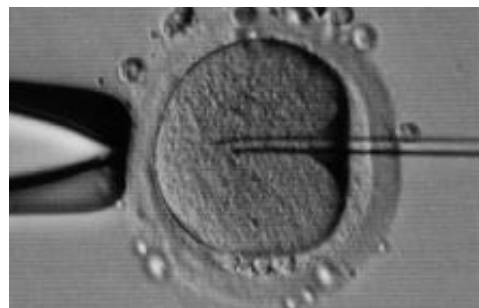
It is recommended that patients pregnant after ICSI have prenatal diagnostic testing either by chorionic villus sampling (where a biopsy of the placenta is taken) or amniocentesis (where fluid is collected from around the baby using an ultrasound-guided needle). Additionally, a careful mid-pregnancy level II ultrasound should be performed. This monitoring will not detect all fetal abnormalities.

The safety and effectiveness of ICSI has not been fully established. Selection of the most normal looking sperm does not ensure that the sperm is normal. Injection of a sperm into an egg may damage/destroy the egg.

World experience obtained from follow-up of ICSI pregnancies and offspring shows the following:

- Newborns conceived by ICSI have a very slight increase in sex chromosome abnormalities (0.8% vs. 0.4%) and non-sex chromosome abnormalities (0.8% vs. 0.3%). There may also be an increase risk of imprinting disorders which involve mental retardation (0.02% vs. 0.007%).

Figure 5



A sperm being injected into an egg; ICSI

- Men who have a normal reproductive tract and no sperm in their ejaculate may have abnormalities of the Y chromosome. Since males inherit their Y chromosome from their fathers, sons may inherit the abnormality and have infertility problems.
- The occurrence of birth defects appears to be similar between ICSI newborns and IVF and natural conception newborns. However, some studies have shown a slight increased risk of birth defects in ICSI newborns. Long term developmental effects of ICSI children are not yet known.

b. ASSISTED HATCHING (AH)

- Assisted Hatching involves making a hole in the covering (zona pellucida) that surrounds the embryo
- Hatching may make it easier for embryos to escape from the covering which surrounds them so that they can implant in the uterine lining.

It has been suggested that failure of embryos to “hatch” from the zona pellucida (the outside covering of the embryo) may be part of the reason embryos don’t implant in the uterine lining. Assisted hatching (AH), which creates a small hole in the zona pellucida, may be used to help the hatching.

The AH procedure is usually done 1-3 hours before the embryo transfer. The embryos are examined before AH is performed. The best looking embryos will be chosen for transfer. During AH a small hole is made in the embryo’s outer coating with either an acid buffer (Acid Tyrodes) or a laser beam. The embryos are then placed back in the incubator to rest before transfer into the uterus.

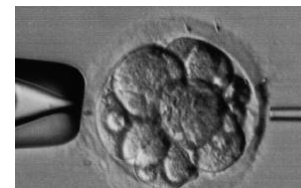


Figure 6

Photograph of a day 3 embryo undergoing Assisted Hatching

In addition to the usual IVF medications, a steroid (Medrol) will be ordered to decrease the theoretical possibility of the body rejecting the AH embryo. Steroids may decrease the body’s ability to fight infection. Additional, uncommon, side effects of steroids (generally with long term use) are: cataracts, high blood pressure, psychological or emotional changes, seizures, hip or bone injury, ulcers, or high blood sugar.

It is recommended that all patients pregnant after AH have prenatal diagnostic testing either by chorionic villus sampling (where a biopsy of the placenta is taken) or amniocentesis (where fluid is collected from around the baby with an ultrasound-guided needle). Additionally, a careful mid-pregnancy level II ultrasound should be performed. This monitoring will not detect all fetal abnormalities.

The safety and usefulness of AH has not been fully established.

- AH makes a small hole in which microorganisms (bacteria and viruses), foreign substances, and products of immune cells normally found in the uterus may reach the embryo. These might badly affect embryo growth.
- Because a hole is being made, there is a risk of damage to or destruction of the embryo.
- Because a small hole is being made, there is a risk that the embryo might get “pinched off” when hatching from the zona. This pinching off may make the embryo split, causing identical twins which share a placenta. These identical twins have a higher risk of

problems before birth including unequal growth, cesarean section, and death of one or both twins and require closer monitoring during pregnancy.

c. PREIMPLANTATION GENETIC TESTING (PGT)

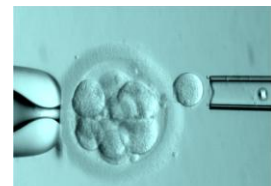
- Preimplantation genetic testing (PGT) involves removing a cell or cells from an embryo to perform genetic testing before transfer of the embryo into the uterus.
- It can be used to diagnosis specific genetic abnormalities (PGD) or to screen for general chromosomal abnormalities (PGS).

When PGT is used to test embryos for specific genetic problems, including single gene defects, it is called preimplantation genetic diagnosis (PGD). PGD makes it possible for couples or individuals who have or carry serious inherited disorders to decrease the risk of passing the disorder on to their child(ren). When PGT is used to screen embryos for general chromosomal abnormalities, it is referred to as preimplantation genetic screening (PGS). In both PGD and PGS, a hole is created in the zona pellucida (the membrane surrounding the embryo) as in assisted hatching and a cell or cells are removed from the embryo and sent for analysis to a testing lab either at Brigham and Women's Hospital or to an outside lab.

Medical insurance may not cover the costs of PGD/PGS or the IVF procedures. It may not cover the costs required by the PGD/PGS lab. You will be required to pay these fees before any procedures begin.

Person(s) desiring PGD/PGS will meet with a genetic counselor to assess their risks, sign consents, and make arrangements with which ever lab will be doing the genetic testing. The lab will sometimes require that blood samples of the person(s) be sent to the lab. There may be a waiting period until the blood sample(s) are processed.

Figure 7



Day 3 Biopsy to
remove a single cell

d. EMBRYO FREEZING

- Freezing of viable embryos not transferred after embryo transfer provides additional chances for pregnancy.
- Frozen embryos do not always survive the process of freezing and thawing.
- Ethical and legal dilemmas can arise when couples separate or divorce; disposition agreements are essential.
- It is the responsibility of each couple with frozen embryos to remain in contact with the clinic on an annual basis and to pay all required costs for maintaining the embryos in storage.

Freezing embryos (cryopreservation) is a common procedure. Since many eggs are often produced during ovulation induction, sometimes more embryos are available than are transferred. Embryos of good quality can be frozen for future use. This saves the risks, expense, and inconvenience of ovulation induction to obtain eggs in the future.

The availability of cryopreservation allows patients to transfer fewer embryos during a fresh cycle, reducing the risk of high-order multiple gestations (triplets or greater). Other possible reasons for cryopreservation of embryos include: freezing all embryos in the initial cycle to prevent severe ovarian hyperstimulation syndrome (OHSS) or to preserve for future use when

future fertility might be decreased due to necessary medical treatment (e.g., cancer therapy or surgery).

There are several techniques for embryo cryopreservation, and research is ongoing. Traditional methods include “slow,” graduated freezing in a computerized setting, and “rapid” freezing methods, called “vitrification.” Current techniques result in a high percentage of embryos surviving the thawing process after cryopreservation, but there can be no certainty that embryos will thaw normally, or be viable enough to divide and eventually implant in the uterus and create a pregnancy.

Performing Vitrification



Pregnancy success rates for transfer of cryopreserved embryos can vary from practice to practice. Overall pregnancy rates at the national level with frozen embryos are lower than with fresh embryos. This, in part, results from the routine selection of the best-looking embryos for fresh transfer, reserving the 'second-best' for freezing. There is some evidence that pregnancy rates are similar when there is no such selection.

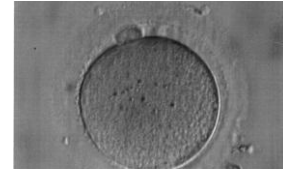
Cryopreservation techniques could theoretically damage the embryo. Extensive animal data (through several generations), and limited human data, do not indicate any likelihood that children born from embryos that have been cryopreserved and thawed will experience greater risk of abnormalities than those born of fresh embryos. However, until very large numbers of children have been born following freezing and thawing of embryos, it is not possible to be certain that the rate of abnormalities is no different from the normal rate.

e. EGG FREEZING

- All women are at risk of losing their eggs due to aging, medical problems, or treatments
- Eggs can be frozen
- Injections of naturally occurring hormones are used for this purpose
- Other medications are used to prevent ovulation
- Doses of medication and timing of egg retrieval require monitoring of the ovarian response by blood tests and ultrasounds
- An overly vigorous ovarian response can occur, or conversely an inadequate response

All women are at risk of losing their eggs due to aging, and others are at extra risk of losing eggs due to medical problems, or medical treatments that put them at risk of running out of eggs prematurely. If women freeze their eggs when they are young or before they lose them due to illness or medical or surgical treatments, they might be able to have a baby with their own eggs in the future. Studies in young women (generally less than 30 years old) show that the likelihood of pregnancy from a frozen, then thawed egg is the same as that from fresh eggs. There is less experience with freezing eggs in older women in that it is unclear if pregnancy rates are the same as or lower than that of fresh eggs. Studies to date do not show higher rates of birth defects.

Figure 8



Mature egg (oocyte)

The process to obtain mature eggs is the same as standard ovulation induction and egg retrieval for IVF (Page 6-11). We expect to get approximately the same number of eggs from the ovaries as we see while the ovaries are being checked, but in some cases the numbers may be higher or lower.

- **Use of Eggs in the Future:** We assume that you would attempt to become pregnant in the future with the eggs still in your ovaries, and would use your frozen eggs only if you have few eggs left in your ovaries (decreased ovarian reserve); no longer have eggs (menopause); or you have infertility that is not responding to fertility treatments.

Your eggs will remain frozen until you are ready to undergo uterine preparation and have them thawed, fertilized (by injection of sperm, Page 13-14), and transferred (page 20-21). In some cases the uterus is damaged or removed as part of the treatment that led you to freeze your eggs; in these cases the plan will be to have the fertilized eggs (embryos) carried in the uterus of another woman (gestational carrier) (Page 25-26).

Before this, depending on your age and medical condition, you may be required to undergo pre-pregnancy screening tests to make sure that you are healthy enough to carry a pregnancy safely. Such tests could include tests for heart and lung function, and tests for diabetes. We may require that you see a high risk obstetrician to counsel you about your risk of becoming pregnant.

Once you are ready for pregnancy, you will meet with your IVF doctor to discuss how many eggs will be thawed and injected with sperm.

- **Risks of Freezing and Thawing your Eggs:** The safety of egg freezing and storage has not been proven. There is no guarantee that any eggs harvested and frozen will survive freezing and thawing. We cannot guarantee or promise that any egg(s) we collect will be capable of being fertilized and creating a baby.

To achieve a pregnancy, you will need to use (IVF) procedures, meaning the eggs harvested would later be thawed and fertilized in a laboratory setting. At this time, research shows that the best way to fertilize eggs that have been frozen is by injecting a single sperm into each of the eggs in a procedure called intracytoplasmic sperm injection (ICSI) (Page 13-14).

Fetal abnormalities may occur with regular IVF and related procedures, this may also occur with natural pregnancies. If you do become pregnant, there is a possibility of miscarriage, tubal pregnancy (a pregnancy that occurs outside the uterus, also called ectopic pregnancy), and pregnancy with more than one baby. (See risks/complications in sections before and after this section).

- **Financial Responsibilities:** Medical insurance will not usually cover the costs of egg freezing, the IVF procedures, the monitoring needed for egg freezing, or the freezing. You will be required to cover these costs as detailed in the financial sheet you will be given and asked to sign. Plus, you will be required to purchase supplemental insurance to cover any complications from the cycles. It is possible that you will not need to use these frozen eggs in the future. Therefore it is possible that you would pay for this but not have a baby from the frozen eggs. Insurance also may not cover the costs of thawing, the procedures to fertilize, and embryo transfer cycle. Once your eggs are frozen, your financial responsibilities and disposition choices are discussed in the next section.

f. STORAGE OF FROZEN EMBRYOS AND EGGS

The Brigham and Women's Hospital (BWH) will store your frozen embryos or eggs on-site for 36 months following their freezing. After 36 months, BWH will transfer your embryos or eggs to New England Cryogenic Center, (a private cryopreservation facility located in Newton, Massachusetts) unless you make other arrangements with us before the end of the 36 month period to discard your frozen embryos or transfer them to a facility other than the New England Cryogenic Center. **In order to freeze embryos or eggs you MUST sign a Storage Services Agreement with New England Cryogenic Center at the same time as you sign the freezing consent form.** If you do not sign these documents, your unused embryos will not be frozen and will be discarded, you will not be able to start a cycle to freeze eggs.

Frozen specimen storage tanks



Financial Responsibilities

There will be no charge for storage of embryos or eggs for the first 12 months following freezing. After approximately 12 months, you will be billed \$1,150 which will be due and payable 30 days later. \$650 of this amount is advance payment for the next 12 months of storage (months 13 to 24). The remaining \$500 is a deposit toward the fee charged by the New England Cryogenic Center and will be held in escrow by BWH until your frozen embryos or eggs are transferred to the New England Cryogenic Center (at the end of the 36 month period). After approximately 24 months, you will receive a second annual storage bill for the final 12 months of storage (months 25 to 36) at BWH. Because annual storage charges are subject to change, the price will increase for the next two fiscal years. Starting October 1st 2013, the annual storage price will be \$850 and on October 1st of 2014 the annual storage price will be \$1,000. If you have embryos or eggs frozen in different fiscal years, you will see this reflected on your billing statement.

With respect to the fees for storage at BWH, the full yearly fee applies even if embryos or eggs are stored for only a portion of the year. **For this reason if you are considering using your frozen embryos or eggs, you are strongly encouraged to meet with your physician no later than 8-9 months after your cycle to make arrangements for a cryo-embryo transfer cycle before the 12-month period.** Your \$500 deposit for future storage at the New England Cryogenic Center will be refunded to you if, before the expiration of the 36 month period, you have either used all of your frozen embryos or eggs or have made arrangements with us to discard your frozen embryos or eggs or transfer them to a facility other than the New England Cryogenic Center.

You will be charged all of the above fees separately for each group of embryos frozen.

Failure to make timely payments for storage of your frozen embryos or eggs will result in the initiation of collection action and may affect your credit rating.

It is your responsibility to notify the BWH IVF Program in writing of any change of address or phone number.

You (and your partner, if applicable) may request to discard your embryos or eggs or to transfer them to another facility at any time during the 36 months following embryo or egg

freezing by providing us with a notarized letter signed by you (and your partner, if applicable) to the Brigham and Women's Hospital IVF Laboratory. **If you do this before the end of the first 12-month period, you will not be responsible for annual storage fees or the New England Cryogenic Center fees. If you do not do this before the end of the first 12-month period, you will be responsible for the annual storage fee(s) described above.** For frozen embryos or eggs that have been stored beyond the first 12-month period but used or discarded before the end of the 36 month, the New England Cryogenic Center fee of \$500 will be refunded to you. After 36 months, the embryos or eggs will be under the control of the New England Cryogenic Center, and you will need to contact them to arrange for the disposition of your embryos.

Disposition of Cryopreserved Embryos and Eggs

In the event of the death of you and/or your partner or spouse or, if applicable, in the event of either divorce, or you and your partner's separation after embryos or eggs have been produced and cryopreserved, it will be necessary for the disposition of any cryopreserved embryos or eggs that remain at BWH to be determined. (Should any of these events occur after your cryopreserved embryos or eggs have been transferred to New England Cryogenic Center, their policies and procedures will govern and BWH will have no role or responsibilities with respect to the disposition of your cryopreserved embryos.)

Possible options for disposition may include:

1. Discarding the cryopreserved embryo(s) or egg(s).
2. Donating the cryopreserved embryo(s) or egg(s) for approved research studies if available.
3. Donating the cryopreserved embryo(s) or egg(s) to another couple in order to attempt pregnancy. (In this case, you may be required to undergo additional infectious disease testing and screening due to Federal or State requirements.) **Note:** BWH does not have an embryo or frozen egg donation program. You may ship your embryos or eggs to another institution or program.
4. Use by one partner with the permission of the other for that use.
5. Transferring the cryopreserved embryo(s) or egg(s) to off-site storage at New England Cryogenic Center or another facility.

As both the legal and medical aspects of the disposition of cryopreserved embryos or eggs are rapidly evolving, the BWH IVF Program cannot promise or guarantee what the available or acceptable avenues for disposition will be at any future date.

Disposition in the Event of the Death of Patient and if applicable, Death of Spouse or Partner, or Divorce or Dissolution of Relationship

Before making any disposition of embryos or eggs under any of the circumstances described above, the BWH IVF Program will require what it deems to be appropriate documentation. In general, in the event of a separation or divorce between you and your spouse or partner, the BWH IVF Program will require a notarized statement signed by both parties, a separation agreement, or a court decree or order. In the event of the death of you or your spouse or partner, the BWH IVF Program will generally require a probated will or court order. In

addition, depending on the disposition option requested or selected, you and/or your partner may be required to sign additional consent form(s) or other documents.

[Disposition in the Event of the Simultaneous Death of Patient and Spouse or Partner](#)

If both you and your spouse or partner dies at the same time, the BWH IVF Program will discard any remaining cryopreserved embryos unless within six (6) months of your deaths, the BWH IVF Program receives a probated will or court decree with alternative disposition directives.

g. FROZEN EMBRYO TRANSFER

A cycle to transfer frozen embryos may use some of the same medications used in ovulation induction (Page 6-8). The embryo transfer is the same as that for IVF (Page 12).

Lupron®: To prevent the body from going through a regular cycle.

Estrace®, **Vivelle®**: To stimulate the uterus to grow a lining.

Progesterone (shots, vaginal suppositories, Crinone gel): To prepare the lining in the uterus to permit embryos to implant.

Monitoring will consist of blood tests and ultrasounds. An unmedicated or “natural” frozen embryo transfer cycle will have the above monitoring plus at home urine testing. In either case, if the embryos were created using ICSI, AH, and/or Pre-implantation Genetic Diagnosis (PGD), a steroid (Medrol) will be ordered to decrease the theoretical possibility of the body rejecting the embryo. Steroids may decrease the body’s ability to fight infection. Additional uncommon side effects of steroids are: cataracts, high blood pressure, psychological or emotional changes, seizures, hip or bone injury, ulcers, or high blood sugar.

It is recommended that all patients pregnant after ICSI/AH/PGD undergo prenatal diagnostic testing either by chorionic villus sample or amniocentesis. Additionally, a careful mid-pregnancy level II ultrasound should be performed. This monitoring will not detect all fetal abnormalities.

g. FROZEN OOCYTE TRANSFER

A cycle to transfer frozen oocytes (eggs) may use some of the same medications used in ovulation induction (Page 6-8). Fertilization and embryo culture is the same as that for IVF (Page 10-12). The embryo transfer is the same as that for IVF (Page 12).

Lupron®: To prevent the body from going through a regular cycle.

Estrace®, **Vivelle®**: To stimulate the uterus to grow a lining.

Progesterone (shots, vaginal suppositories, Crinone gel): To prepare the lining in the uterus to permit embryos to implant.

Monitoring will consist of blood tests and ultrasounds. ICSI (Page 13-14) will be used to fertilize the oocytes to create embryos. A steroid (Medrol) will be ordered to decrease the theoretical possibility of the body rejecting the embryo. Steroids may decrease the body’s ability to fight infection. Additional uncommon side effects of steroids are: cataracts, high

blood pressure, psychological or emotional changes, seizures, hip or bone injury, ulcers, or high blood sugar.

It is recommended that all patients pregnant after ICSI undergo prenatal diagnostic testing either by chorionic villus sample or amniocentesis. Additionally, a careful mid-pregnancy level II ultrasound should be performed. This monitoring will not detect all fetal abnormalities.

3. Overall risks of assisted reproductive treatments

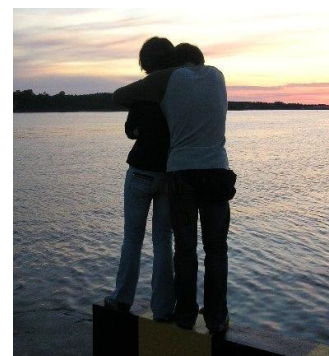
a. PSYCHOLOGICAL RISKS

A diagnosis of infertility can be a devastating and life-altering event that affects many parts of a patient's life. Infertility and its treatment can affect a patient and, if applicable, her spouse or partner medically, financially, socially, emotionally, and psychologically. Feelings of anxiety, depression, isolation, and helplessness are common among patients going through infertility treatments. Strained and stressful relations with spouses, partners, other loved ones, and friends are common as treatment gets underway and progresses.

Our team is available to address the emotional, as well as physical symptoms that can happen with infertility. Patients may also consider talking with mental health professionals who are specially trained in the area of infertility care.

While it is normal to experience emotional ups and downs when going through infertility treatments, it is important to recognize when these feelings are of a severe nature. If you experience any of the following symptoms over a long 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 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
- social isolation
- persistent feelings of pessimism, guilt, or worthlessness
- persistent feelings of bitterness or anger



b. PREGNANCY-RELATED RISKS

Failure to become pregnant - A cycle may be cancelled, there may be no eggs retrieved, there may be no sperm available, eggs may not fertilize, or embryos may not develop normally. Even if the best looking embryos are transferred into the uterus, you may not get pregnant.

Ectopic pregnancy (tubal pregnancy) - Embryos are transferred directly into the uterus with IVF; however, ectopic (tubal, cervical, or abdominal) pregnancies can occur alone or at the same time as a normal intra-uterine pregnancy (called a heterotopic pregnancy). Ectopic pregnancies can rupture the tube, causing potentially fatal bleeding and require very close monitoring and treatment. These abnormal pregnancies are often treated medically with Methotrexate injections (a weak chemotherapy drug) or surgery to remove 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. If a normal pregnancy is present in the uterus along with an ectopic pregnancy, surgery is most often performed for removal of the ectopic pregnancy and can lead to miscarriage. In some cases of unusual ectopic pregnancy location, a solution containing potassium can be injected into the ectopic pregnancy, avoiding surgery.

Abnormal intrauterine pregnancy - You will be monitored carefully for pregnancy. In some cases the blood pregnancy tests are positive, but have low numbers, showing that a pregnancy may not be growing normally. A chemical pregnancy (very early miscarriage) occurs when the pregnancy tests start positive, then go back down to negative on their own. In some cases the pregnancy tests will continue to rise, but an abnormal pregnancy occurs where a fetus doesn't develop (a blighted ovum) or a pregnancy may grow normally at first but a miscarriage or failure of the pregnancy to continue to grow may occur. In some cases abnormal pregnancies will miscarry on their own. In other cases surgery (dilatation and evacuation, or D&E) or medicine (Misoprostol) to cause the miscarriage may be necessary.

Risks of IVF pregnancy - Pregnancies that occur with IVF are associated with increased risks of certain conditions. 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 itself, but it is difficult to know if they are related to IVF or not.

Multiple pregnancy – Currently more than 30% of IVF pregnancies are twins or higher-order multiple gestations (triplets or greater), and about half of all IVF babies are a result of multiple gestations. 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 less than IVF singletons. Of note, IVF twins appear to do as well as spontaneously conceived twins. Triplet (and greater) pregnancies deliver before 32 weeks (7 months) in almost half of cases. (See complications of prematurity below).

The number of embryos transferred influences the pregnancy rate and the multiple pregnancy rates. The age of the woman and the appearance of the developing embryo(s) have the greatest influence on the pregnancy outcome and the chance of multiple pregnancies. While it is possible, it is unusual to develop more fetuses than the number of embryos transferred. (See further risks below). Placenta previa (where the placenta grows over the cervix) and

vasa previa (where the cord is over the cervix) are more common complications in multiple gestations. Abruptio placenta (where the placenta separates from the uterine wall before the baby is born) also is more common and postpartum hemorrhage may complicate 12% of multifetal deliveries.

c. RISKS TO THE OFFSPRING

Overall risks - Since the first birth of an IVF baby in 1978, more than 3 million children have been born worldwide following IVF treatments. Many studies have been done to assess the overall health of IVF children and most of the studies on the safety of IVF have been reassuring. As more time has passed and the numbers have gone up, some studies have raised doubts about the equality of risks for IVF babies 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 causes. 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 actual risk of any abnormal outcome appears to be small.

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

Patients with more than twins are faced with the options of continuing the pregnancy with all risks, terminating the entire pregnancy, or reducing the number of fetuses in an effort to decrease the risk of maternal and perinatal complications.

- **Imprinting disorders** - Rare disorders in which genes are inappropriately expressed. Two studies found that 4% of children born with Beckwith-Weidemann Syndrome were the result of IVF. Another study found no increase in imprinting disorders in children from IVF.
- **Childhood cancers** - One study found 5 cases of retinoblastoma in IVF children which is 5-7 times more than usual.
- **Infant development** - Long term studies of development have been largely reassuring.

d. ETHICAL AND RELIGIOUS CONSIDERATIONS

Infertility treatment can raise concerns and questions of an ethical or religious nature for some patients. In vitro fertilization (IVF) involves the creation of human embryos outside the body. It can produce excess embryos and/or 'high-order' multiple pregnancies (triplets or more). We encourage patients and, if applicable, their spouses or partners who so desire, to consult with trusted members of their religious or ethics community for guidance on their infertility treatment.

C. Third Party Reproduction

1. Egg Donation

Egg donation has been recommended as a way for you to have a baby. This recommendation was made after review of your history and testing. If appropriate, this included your partner's history and testing. Egg donation is done by obtaining the eggs of another woman ([Ovulation Induction and egg retrieval page 6-10](#)). The eggs will be inseminated with sperm ([Fertilization and embryo culture page 10-12](#)). If fertilization occurs the embryos will be transferred into your uterus in the hope that a pregnancy will occur ([Embryo transfer page 12](#)).



a. EGG DONOR RECIPIENT EVALUATION

You, and if applicable, your partner will be screened for communicable diseases. You may be required to have a medical evaluation to ensure you are healthy enough to carry a pregnancy.

In many cases it will be necessary to prepare the uterus to accept your embryos by the use of estrogen and progesterone ([Medications for IVF pages 6-8](#)). You may need to go through one or more practice cycles. This will require blood and ultrasound testing ([Monitoring during the cycle page 9](#)). This practice cycle ends with an endometrial biopsy to verify the uterus will be prepared for embryos to implant.

b. FINDING AN EGG DONOR AND HER EVALUATION

The patient is responsible for finding an egg donor. The donor may be a family member or acquaintance or she may be anonymous and found through an agency.

The donor will need to be approved by the BWH IVF Program. The IVF Program Staff will screen the donor before approving her as a donor. The screening will include history, physical examination, behavior, and evidence of communicable diseases per the Food and Drug Administration (FDA) guidelines. She will also be required to have additional testing, as regulated by the FDA, near the time of the egg retrieval. Despite the testing of the egg donor and if applicable, her partner prior to transfer of the embryos for the presence of infectious diseases, including HIV (the virus that causes AIDS), the Program can provide no assurance that any child conceived from donated eggs will not acquire an infectious disease in connection with services provided by the Program. The donor will be screened for familial and genetic diseases as selected by the recipient. The donor will have a social work and/or a psychological assessment. The BWH IVF Program cannot guarantee the reliability of the history the donor provides. The BWH IVF Program reserves the right to reject any donor who does not meet its screening standards.

c. FINANCIAL RESPONSIBILITIES

Because the egg donor is producing eggs on the recipient's behalf, the recipient is responsible to the Hospital for the ordinary costs of the donor's treatment by the BWH IVF Program including, but not limited to, any medical and psychological evaluations, testing, medication

and procedures. The costs of the donor's screening are not reimbursed even if she fails her screening testing.

Complications may arise in connection with the Program's treatment of the egg donor, resulting in additional medical and hospital expenses. The recipient is required to purchase supplemental insurance to cover such expenses for the donor.

d. COORDINATING AN EGG DONATION CYCLE

If donor and recipient are having periods they may be required to use birth control pills and/or Lupron to coordinate their cycles. The donor will go through an IVF stimulation cycle (Ovulation induction and egg retrieval pages 6-10). The recipient will be given estrogen and progesterone to stimulate the uterus to create a lining (Medications for IVF pages 6-8, Fertilization and embryo transfer page 10-12, Embryo transfer page 12).

The coordination may be affected by donor or recipient time constraints, failure of one or the other to respond to the medications, or errors in taking medicines.



2. Gestational Carrier

Gestational Carrier has been recommended as a way for you to have a baby. This decision has been made after a review of your history and testing. If appropriate this included your partner's history and testing. A Gestational Carrier cycle involves obtaining eggs from the patient, or the eggs of an egg donor (Ovulation Induction and egg retrieval page 6-10). The eggs will be inseminated using sperm (Fertilization and embryo culture page 10-12). If fertilization occurs the embryos will be transferred into a gestational carrier in the hope that a pregnancy will occur (Embryo transfer page 12). One partner of the intended parents must have a genetic relationship to the baby when a gestational carrier is used.

a. INTENDED PARENT EVALUATION

You, and if applicable, your partner will be screened for communicable diseases. The screening will include history, physical examination, behavior, and evidence of communicable diseases per Food and Drug Administration (FDA) guidelines. Because tissue (i.e., embryos) is being transferred into a gestational carrier, the intended parent(s) will also be required to have additional testing, as regulated by the FDA, near the time of the egg retrieval.

b. FINDING A GESTATIONAL CARRIER AND HER EVALUATION

You are responsible for finding a gestational carrier. The carrier may be a family member or acquaintance or she may be found through an agency.

The gestational carrier will need to be approved by the BWH IVF Program. The Program's Staff will screen the gestational carrier before approving her as a carrier. The screening will

include history, physical examination, behavior, and evidence of communicable diseases per FDA guidelines. Despite the testing of the carrier and if applicable, her partner prior to transfer of the embryos for the presence of infectious diseases, including HIV (the virus that causes AIDS), the Program can provide no assurance that any child delivered by the carrier donor will not acquire an infectious disease in connection with services provided by the Program. The carrier will have a social work and/or a psychological assessment. The BWH CIRS cannot guarantee the reliability of the history the carrier provides. The BWH CIRS reserves the right to reject any carrier who does not meet its screening standards.

In many cases it will be necessary to prepare the gestational carrier's uterus to accept embryos by the use of estrogen and progesterone ([Medications for IVF pages 6-8](#)). She may need to go through one or more practice cycles. This will require blood and ultrasound testing ([Monitoring your cycle page 9](#)). This practice cycle ends with an endometrial biopsy to verify that the uterus will be prepared for embryos to implant.

c. FINANCIAL RESPONSIBILITIES

Because the gestational carrier is carrying a pregnancy on the intended parent's behalf, the intended parent(s) is(are) responsible to the Hospital for the ordinary costs of the carrier's treatment by the BWH CIRS including, but not limited to, any medical and psychological evaluations, testing, medication and procedures. **The costs of the carrier's screening are not reimbursed even if she fails her screening testing.**

d. COORDINATING A GESTATIONAL CARRIER CYCLE

If intended parent and carrier are having periods they may be required to use birth control pills and/or Lupron to coordinate their cycles ([Medications for IVF pages 6-8](#)). The intended parent (or egg donor) will go through an IVF stimulation cycle ([Ovulation Induction and egg retrieval page 6-10](#)). The carrier will be given estrogen and progesterone to stimulate the uterus to create a lining ([Medications for IVF pages 6-8](#)).

The coordination may be affected by intended parent or carrier time constraints, failure of one or the other to respond to the medications, or errors in taking medicines.

Notes