

In-Vitro Fertilization Program South Jersey Fertility Center Consent

I/we _____ (patient) (s) of South Jersey Fertility Center, am/are willing to undergo treatment by In-Vitro Fertilization (IVF), Gamete Intrafallopian Transfer (GIFT) or Zygote Intrafallopian Transfer (ZIFT). Each of these treatments require an ovarian stimulation procedure to retrieve eggs from the ovaries, embryo transfer, zygote (pre-embryo) transfer or gamete (sperm and egg) transfer. The following will outline each of the steps involved in my/our treatment.

Ovarian Stimulation

The purpose of ovarian stimulation is to yield multiple, healthy, fertilizable oocytes (eggs). The transfer of multiple embryos significantly improves the pregnancy rate over single embryo transfer. Excess embryos can also be cryopreserved for future transfer. At the South Jersey Fertility Center, ovarian stimulation is individualized to meet the patient's needs, based on age, prior IVF attempts and cycle day 3 levels of FSH, LH and E2. We do not have a "universal" protocol for all patients, but rather individualize the protocol and the dosage of medications based on the individual patient.

Some of the most commonly used hormone(s) include:

1. Leuprolide acetate (Lupron): This is a gonadotropin-releasing hormone agonist (GnRH analog) that is administered subcutaneously, daily. Most commonly, this hormone is started at mid-luteal phase (day 20-23) of the cycle preceding the IVF attempt and continued until the day of human chorionic gonadotropin (hCG) administration. We advise you not to attempt pregnancy during the cycle when Lupron therapy is used. In some patients, this hormone is started on cycle day one and continued until the day hCG is given. The main advantage of this hormone is to suppress the level of FSH and LH, thus preventing premature LH surge and avoiding ovulation prior to egg retrieval. This will allow better control of the stimulation process and will improve the number and quality of eggs obtained. In some patients (age >40 and/or poor ovarian reserve with high cycle day 3 FSH levels), the use of this hormone may not be desirable, as it may have a negative effect on the progress of stimulation. Possible side effects include local redness at the site of the injection and a brief (few days) period of Estrogen deprivation symptoms, which may include sweating, hot flashes and headaches.

2. Human Menopausal Gonadotropins (hMG) – Pergonal, Humegon, Repronex Follicle Stimulating Hormones (FSH) – Metrodin, Fertinex, Gonal-F, Follistim

These are natural hormones extracted from the urine of post menopausal females or via recombinant DNA process. Pergonal, Humegon and Repronex are preparations which contain equal amounts of FSH and LH. Usually the ampule contains 75 International Units (IU) each of FSH and LH. Fertinex and Metrodin are preparations which predominantly contain FSH. Follistim and Gonal-F are recombinant FSH product (non-urinary based). FSH and LH are hormones that will stimulate multiple eggs in a given cycle, when given in supra-physiologic doses. The dose of hMG and/or FSH can vary from two to ten ampules daily, depending on the individual patient. In general, older patients and those with poor ovarian reserve require higher amounts. The major side effects include risk of ovarian hyperstimulation and multiple pregnancies, which will be addressed in further detail below. Although these preparations are considered generally safe, the long-term effects, if any, from their use are currently unknown.

3. Human Chorionic Gonadotropin (hCG): This hormone is given intramuscularly 34-36 hours prior to the egg retrieval. This hormone induces final egg maturity and is essential to retrieving mature, fertilizable eggs. The hormone may be withheld and the cycle cancelled, if the risk of ovarian hyperstimulation is high (see below).

Cancellation

A cycle may be cancelled prior to the egg retrieval for any of the following reasons:

1. If after five days, there is no response to gonadotropin (FSH/hMG) stimulation.
2. If the serum Estradiol level is low and if there are less than 3 mature size follicles formed on the day hCG is to be given, or if there is a drop in the Estradiol level.
3. High serum Estradiol level > 6,000 pg/ml on the day hCG, as the risk of ovarian hyperstimulation may be unacceptably high.
4. Medical illness during the course of treatment.
5. If there is an LH surge or evidence that ovulation has already occurred or may occur too early.

If the patient is cancelled prior to the egg retrieval, she will be required to pay only the fee of administrative service including office visits, ultrasound examinations, blood assay, and the cost of hormonal injections provided by the office.

Ovarian Hyperstimulation

This is a major, potential complication of treatment with gonadotropins (FSH/hMG and HCG). Mild to moderate hyperstimulation consists of a mild to moderate degree of ovarian enlargement and abdominal discomfort. Ovarian hyperstimulation is not uncommon with gonadotropin therapy, usually occurs on week after the hCG injection, and is usually self-limiting with gradual improvement of symptoms. Limited activity and mild analgesics are normally all that are needed to alleviate symptoms. Severe ovarian hyperstimulation syndrome is more rare and the incidence is usually less than 3%. Severe ovarian hyperstimulation syndrome involves massive ovarian enlargement due to multiple ovarian cysts, severe stromal edema, hemoconcentration, hypovolemia associated with electrolyte imbalances, ascites (accumulation of fluid in the peritoneal cavity) and hydrothorax (accumulation of fluid in the plural cavity). In severe but extremely rare circumstances, thromboembolism and death may occur. The incidence is higher in patients who produce a large number of follicles (>20) and in whom the Estradiol level on the day of hCG is extremely high (>5,000 pg/ml). Severe ovarian hyperstimulation is best managed by prevention; some preventive measures includes:

1. Decreasing the dosage of FSH/hMG in patients who show signs of higher magnitudes of increasing serum Estradiol during the course of treatment.
2. Withholding the hCG injection and canceling the egg retrieval in patients with serum Estradiol levels of >6,000 pg/ml on the day of hCG administration. In such cases, the risk of severe ovarian hyperstimulation syndrome will be completely eliminated.
3. Performing egg retrieval without transferring any embryos, thus all embryos will be cryopreserved for transfer in a frozen cycle. The patient needs to be monitored carefully for up to one week following the retrieval. Such patients usually have extremely favorable chances of getting pregnant from the cryopreserved embryos. It is well known that hyperstimulation in severe form is more common in a cycle resulting in a pregnancy. Therefore, by not transferring the embryos, the risk is minimized, but still exists.

Signs that should alert the patient to the development of this syndrome include severe abdominal distention (bloating) and pain, abrupt weight gain of more than three pounds in one day and difficulty taking a deep breath. When diagnosed, hospitalization to control the fluid imbalance, maintenance of vital organs and perfusion, prevention of hypercoagulation (blood clotting) and relief of symptoms by aspiration of the ascites fluid from the abdomen may be indicated. In stable patients, aspiration of the ascites fluid through the vagina with ultrasound guidance or through the abdominal wall may be attempted in the office or in the hospital with general improvement of the situation.

Multiple Pregnancy

Multiple pregnancies, the majority of which are twins, account for approximately 25-50% of all pregnancies. In order to reduce the incidence of triplets and quadruplets, voluntary guidelines have been established in our clinic. The maximum number of embryos to be transferred is based on the patient's age. The maximum number of embryos transferred to a patient aged 35 years or less is 2. In patients between the ages of 36 and 39, a maximum of 2-3 embryos can be transferred. In patients who are forty years of age and over, the maximum number of embryos transferred is variable. With this policy, the incidence of triplet should be decreased and the incidence of higher numbers of multiples should be decreased. We encourage you to discuss this issue with your physician and arrive at a decision on the maximum number of embryos to be transferred, prior to the egg retrieval. Embryos will be transferred Day 3 to day 5 depending on the number of embryos and embryo quality.

Ectopic Pregnancy

It should be noted that 3-5% of all pregnancies are ectopic gestations (pregnancy in the fallopian tubes). The vast majority of this occurs in women with distal tubal obstruction or with tubal and peritoneal factors accounting for their infertility. Heterotopic pregnancies (intrauterine and extrauterine) may also occur, but are extremely rare. The management of ectopic pregnancy can be surgical or medical.

Egg Retrieval

In the vast majority of cases, egg retrieval is performed transvaginally with ultrasound guidance. This procedure is usually performed under IV sedation; however, general anesthesia can also be given. Laparoscopy is usually performed for Gamete Intrafallopian Transfer (GIFT) and Zygote Intrafallopian Transfer (ZIFT) procedures. These are performed under general anesthesia. The risk of anesthesia should be discussed with the anesthesiologist at the Healthsouth Surgical Center of South Jersey prior to the retrieval.

The risks of transvaginal aspiration of follicles include infection, bleeding (which may require transfusion and laparoscopy and/or laparotomy to correct the problem), and infection (which may require hospitalization for intravenous antibiotic therapy). Deaths have been reported (not from our Center) following transvaginal follicular aspiration.

Major complications are extremely rare, but do occur, as with any minor operative procedure. It is also conceivable, as with operative procedures, that there are other risks, which cannot be specifically identified.

Laparoscopic egg retrievals (GIFT and ZIFT) are elective procedures and are performed Monday through Friday only. On rare occasions, a GIFT procedure may not be possible if retrieval must occur on a weekend. In such cases, an IVF or ZIFT might be recommended.

Embryo Transfer

This procedure is usually performed without the use of anesthesia and lasts for only a few minutes. The transfer is usually performed easily, the same way as inseminations are done. The transfer catheter is loaded with the embryos and is passed through the cervix into the uterus. On occasion, dilatation of the cervical canal may be required at the time of the transfer in order to facilitate the procedure. Side effects of the procedure include mild cramping and minimal bleeding (mostly from the use of a cervical tenaculum to straighten the cervical canal). In rare cases, infection or perforation of the uterus could occur.

Luteal Phase Support

Preparation of the endometrial lining is essential so that the embryo(s) can be successfully implanted. In order to prepare the endometrium in an IVF, GIFT or ZIFT or cryopreserved embryo transfer, we start the patient on progesterone in the form of Crinone 8% Vaginal Progesterone Gel. Usually this medication is started the day after the egg retrieval (3-5 days prior to the transfer) and the dosage is one applicator twice daily. Progesterone may also be given in the form of progesterone in oil, IM injection. The dosage is 50 mg in a single daily dose.

Progesterone treatment continues until the date of the pregnancy test or, if the pregnancy should occur, treatment will continue through 12 weeks of gestation. Progesterone can delay menses, so it is not known until the date of pregnancy test, if I am pregnant. If bleeding occurs before the date of the pregnancy test, I should continue progesterone and consult my doctor for advice. The Crinone 8% Vaginal Progesterone Gel and the Progesterone in Oil are natural hormones identical to those made in the body and therefore, are unlikely to cause any bad effect to yourself or your baby, if you should become pregnant while using this medication.

The potential side effects of progesterone medication are an allergic reaction, infection, and cellulitis from the IM injection site and vaginal irritation or infection from the vaginal preparation. There may be other minor side effects associated with hormone treatment. I further understand the Food and Drug Administration has advised that medication of this type should not be given to women who may be pregnant, since there is evidence that it may cause abnormalities in the baby. It has been explained to me that the drugs which cause abnormalities are synthetic (man-made) whereas the Crinone and Progesterone injections are made from natural progesterone and therefore, are no different from the hormone produced in my body and are unlikely to cause or increase the chances of birth defects in the baby if I get pregnant during its use. I understand that it has not been proven that progesterone is safe and that birth defects may occur if I become pregnant while using this medication.

Laboratory Procedure

The embryology laboratory defines its quality assurance policy as continuous improvement on a daily basis in every aspect of laboratory management and care. Given the nature of the material handled in the laboratory, working under optimal conditions is essential. Constant quality controls to maintain optimum conditions are of the utmost importance.

The In-Vitro Fertilization Center of South Jersey Embryology Laboratory oversees the following:

- Sterility and purity of the working environment, supplies and solutions
- Toxicity testing of all laboratory material
- Optimal preventative maintenance of all laboratory equipment
- Daily function test on all equipment
- Back-up system in the event of equipment malfunction
- Utilization of proven and reliable techniques
- Continual consideration of laboratory safety and security.

It is always possible that unforeseen conditions can occur within the laboratory environment, such as fire, unexpected devastating weather conditions, theft or accident. Hazard plans are in effect and most potential problems have been anticipated and prepared for. Therefore, unrestricted guarantee of gamete/embryo safety cannot be stated.

It should also be emphasized that occasionally unexpected lack of fertilization may occur. In such rare circumstances, your physician will discuss the matter with you and an appropriate diagnosis and/or therapeutic option will be offered.

Embryo Cryopreservation

The advantage of embryo cryopreservation is to limit the number of embryos transferred to reduce the incidence of multiple pregnancy and to give the patients an added chance of achieving pregnancy without having to undergo a complete stimulation IVF cycle. In the long run, embryo cryopreservation positively affects the success rate and offers decreased cost and time advantage.

A minimum of two, good quality embryos are required to consider cryopreservation. It is our recommendation not to freeze one, if there is only one available embryo. After consent is obtained from both partners, embryos in excess of the desired number for fresh transfer will be cryopreserved. Cryopreservation is performed on fertilized zygotes, embryos or blastocysts with a slow freezing protocol using cryoprotectant. Thawing and transfer of the embryos is performed in either a natural cycle following ovulation, or in a programmed cycle which includes administration of Lupron, Estrogen and Progesterone. From data in the literature, it seems that there is no increase in malformation of babies born from this procedure. Please refer to the cryopreservation consent form regarding rules and regulations for cryopreservation in our program.

Micromanipulation and Assisted Fertilization

Intra-Cytoplasmic Sperm Injection (ICSI)

It is estimated that approximately 30% of patients have male factor as the primary etiology of their infertility. Various procedures have been performed to enhance fertilization in patients with severe sperm abnormalities and prior failed fertilization. Procedures include Sperm Subzonal Insertion (SUZI) and Partial Zonal Dissection (PZD). The procedure that is almost exclusively applied currently is Intra-Cytoplasmic Sperm Injection (ICSI), where a single sperm is inserted directly into the cytoplasm of an egg. Manipulation of the eggs requires special equipment specifically designed to perform the very small, intricate moves utilized in this procedure.

We understand that, prior to the procedure, eggs may be treated with a solution containing an enzyme that will remove the cumulus cells surrounding the eggs and which will allow visualization of the egg itself. The egg will be held in place by an egg-holding pipette while the micro needle is introduced through the zona pellucida (or into the egg). Then the egg is manipulated, released and washed in fresh culture medium. All subsequent treatment will be the same as for non-manipulated eggs. Any embryos developing normally after this procedure will be transferred to the uterus; cryopreserved, if the patient requests cryopreservation; or disposed of. During normal fertilization, only one sperm reaches the egg and fertilizes. However, fertilization by more than one sperm is called polyspermy. Polyspermy occurs during routine IVF at a rate of 7% of all mature eggs inseminated. If polyspermy occurs during routine IVF or after micromanipulation, those embryos are considered abnormal and will not be transferred to the uterus. We also understand that some of the oocytes may be damaged during the sperm injection. Damaged oocytes do not fertilize and we do not transfer them back into the uterus. Participation in IVF with the ICSI procedure may necessitate taking medication, such as a steroid. The available data in the literature indicates that the incidence of major or minor malformation of babies born are at the usual rate as that of routine IVF pregnancies or spontaneous pregnancies. We cannot be certain at this time that manipulation of the eggs will not increase the risk of obstetrical complications or fetal abnormalities. Additionally, there is evidence that genetic abnormalities causing male factor infertility can be passed on to offspring via the ICSI procedure. This occurs in approximately 10% of cases with male factor infertility. It can be determined via blood testing if genetic abnormality causing male infertility exists. In some cases this testing may be recommended.

Assisted Hatching

Assisted Hatching is intended to benefit us by creating additional opportunity for the initiation of pregnancy by enhancing the ability of the fertilized egg to attach to the lining of the uterus. This procedure is performed by creating a small opening in the zona pellucida (egg shell) with the aid of a

micro needle. This technique is performed after the sperm has been in contact with and has fertilized the oocyte. The zona pellucida is opened in order to facilitate the normal hatching process, which must take place before the embryo is capable of implantation. Manipulation of the embryo requires specialized equipment, specifically designed to perform the very small intricate movements utilized during this procedure. The embryo will be held in place by a holding pipette while a micro needle is introduced through the zona pellucida to inject a small amount of acid solution to dissolve the opening. After the embryo is manipulated, it is released and washed in fresh culture medium. All subsequent treatment will be the same as for non-manipulated embryos. The Assisted Hatching technique is usually performed on a fresh embryo or after thawing of embryos. These embryos will be transferred to the uterine cavity. We also understand that we may need to take a regime of steroids to suppress inflammatory response. The risk involved with Assisted Hatching is that it is possible that the micromanipulation process may damage the fertilized embryo. The incidence of damage during this procedure is usually less than 5%. We also understand that the ability of the manipulated embryo to establish pregnancy after transfer in the human has not been fully determined. It is unknown if manipulation of the embryo will increase the risk of obstetrical complications or fetal abnormalities.

As with routine IVF pregnancies, pregnancy rate for the ICSI procedure and Assisted Hatching seem to be largely dependent upon the age of the patient. The rate of fertilization with ICSI is largely dependent upon the sperm and/or egg quality.

We understand that smoking in either the male or female partner can have a negative effect on embryo quality and pregnancy rates. We have been counseled regarding the importance of stopping smoking prior to proceeding with IVF/GIFT/ZIFT.

Data from your ART procedure will also be provided to the Center for Disease Control and Prevention (CDC). The 1992 Fertility Clinic Success Rate and Certification Act requires that the CDC collect data on all assisted reproductive technology cycles performed in the United States annually and report success rates using these data. Because sensitive information will be collected on you, DCD applied for an received an "assurance of confidentiality" for this project under the provision of the Public Health Service Act, Section 308(d). This means that any information that the CDC has that identifies you will not be disclosed to anyone else without your consent.

All cycles must be report and patient may not opt out of having their information included. We encourage you to discuss your case and the different options with physicians at the South Jersey Fertility Center.

I have read the above and am willing to undergo treatment at the South Jersey Fertility Center/In-Vitro Fertilization Center of South Jersey/Healthsouth Surgical Center of South Jersey by either In-Vitro Fertilization (IVF), Gamete Intra-fallopian Transfer (GIFT) or Zygote Intra-fallopian Transfer (ZIFT).

_____(Patient)

_____(Partner)

_____(Witness)

_____(Date)