

**ASSISTED REPRODUCTIVE
TECHNOLOGIES**

PATIENT INFORMATION DOCUMENT
Education Booklet - Version L

New Leaders In Fertility & Endocrinology, LLC
Reproductive Endocrinology & Infertility

Table of Contents

1)	GETTING STARTED	3
	<ul style="list-style-type: none">• Learning What You Need to Know• Giving Informed Consent & How to Use this Booklet• General Office Issues and Patient Concerns• Financial Responsibility, Insurance Coverage and Resources to help fund ART• Confidentiality: Communications with Outside Physicians & SART Audit	
2)	ASSISTED REPRODUCTIVE TECHNOLOGIES (ART)	6
	<ul style="list-style-type: none">• In Vitro Fertilization (IVF)• Stimulated Cycle Oocyte (Egg) Development• Cycle Monitoring and Cancellation of Treatment• Ovarian Hyper Stimulation Syndrome (OHSS)• Cycle Conversion to Intrauterine Insemination (IUI)	
3)	EGG RETRIEVAL, FERTILIZATION AND EMBRYO TRANSFER	8
	Egg Retrieval <ul style="list-style-type: none">• Transvaginal Oocyte (Egg) Retrieval• Egg Retrieval by Laparoscopy• Insemination, Fertilization and Culture of the Oocyte (Egg), Embryos• Intracytoplasmic Sperm Injection (ICSI)• Embryo Assessment• Blastocyst Culture• Assisted Hatching Sperm Retrieval <ul style="list-style-type: none">• Procedures and cryopreservation Embryo Transfer <ul style="list-style-type: none">• Technique and Trial (Practice) Transfers• Number of Oocytes (Eggs) or Embryos for Transfer	
4)	TREATMENT-RELATED ISSUES & SPECIAL PROCEDURES	12
	<ul style="list-style-type: none">• Cryopreservation (Freezing and Storage) of Embryos and Vitriification• Legal Concerns Regarding Cryopreservation and Long-term Storage• Frozen Embryo Transfer (FET): Natural and Synthetic Hormone Preparation• Uterine Abnormalities and ART Outcomes• Infectious Diseases and HIV (Human Immunodeficiency Virus) Antibody Tests• Pregnancy and Birth Outcome in ART• Congenital Malformations in ART• Multiple Pregnancy in ART• Pre-Implantation Genetic Screening (PGS) and Diagnosis (PGD)	
5)	THIRD PARTY AND DONOR REPRODUCTIVE PROCEDURES	19
	<ul style="list-style-type: none">• Oocyte (Egg) Donation - Categories and Preparation for Oocyte (Egg) Recipients• Sperm Donation - Selecting a Sperm Bank and a Donor for Insemination• Embryo Donation - Categories and Preparation for Embryo Recipients• Gestational Carrier Service - Reasons for Participation, legal issues and management	
6)	PATIENT NOTES AND QUESTIONS	23

GETTING STARTED

Learning What You Need to Know

The aim of assisted reproductive technologies (ART) is to help achieve a healthy pregnancy and child. In general, ART is considered when reproductive problems affecting the female, male or both, make it unlikely or impossible to achieve a pregnancy through natural intercourse. An extensive evaluation will aid in directing your team of fertility specialists to recommend an optimal course of treatment including ART.

There are a number of variations of assisted reproduction, but all involve working with oocytes (eggs), sperm and/or embryos in the fresh or frozen condition outside of the body. Since the introduction of in vitro fertilization in the late 1970's there has been an on-going increase in the number and availability of related procedures. ART includes various processes such as in vitro fertilization (IVF) is the mixing of sperm and eggs (gametes) to allow fertilization outside of the body. Intra-Cytoplasmic Sperm Injection (ICSI) is a procedure to assist fertilization in vitro.

You should have received two Patient Education Booklets: 1) General Infertility Patient Education, and this, 2) ART Patient Education Document. The purposes of these documents are to give you an overview of the many procedures available, their implementation, alternatives, risks and outcomes and terminology. This overview is supplemented by discussions with various clinicians that are all crucial in providing you with a clear and realistic picture of your own clinical situation.

Informed Consent and How to Use this Document

We are committed to providing prospective ART patients with accurate and comprehensive information about the services and medical treatments offered. This educational process includes written materials and, most importantly, consultation with your physicians and other professionals, where general information is put in the context of your individual medical circumstances. It is important that you familiarize yourself with **all information** provided to you so that you can understand treatments, potential side effects, and risks associated with the various parts of your treatment, and any available alternative treatments with their risks and benefits. Specific focus may be needed and will vary patient to patient. This Booklet is a form of legal document. Please make notes and write any questions as you read this entire Booklet, as questions can be answered at the next office visit. Certain topics and headings that may not initially apply should be read in any case, as they may become important at a later time in your treatment. Please review this Booklet in its entirety and if, after consultation you decide to proceed with ART treatment, you will be asked to provide your written consent. Unless treatment decisions change, the signed consent forms will be considered valid for ONE YEAR. Your signature on a Consent Form will verify that:

- information was made available to you through this Booklet, other educational materials, and through consultation with medical personnel and physician(s) specializing in treatment of infertility. These efforts are to assist you in making an informed decision concerning your treatment; and that
- you have reviewed these materials, understand their contents to your satisfaction, have had your questions addressed to your satisfaction and that you are voluntarily consenting to proceed with desired treatments.

GENERAL OFFICE ISSUES AND PATIENT CONCERNS

Please Read Carefully

The following describes several very important topics and concerns that patients commonly voice. Please read each carefully and adhere to the recommendations provided.

1) Patient Responsibilities: Contrary to popular belief, physicians alone rarely cure illnesses but often attempt to aid a patient's own healing process. Nowhere is this more evident than in the treatment of infertility. It requires a "TEAM EFFORT". Physicians and nurses will provide the necessary information, training, counseling and guidance but this is ineffective without a patient's dedication to become educated, compliant and knowledgeable about fertility treatment. It becomes your responsibility to read and understand written educational materials, asking questions when needed. Because of the time limitations and volume of patients involved, these written materials should be your FIRST reference. It is difficult, if not hazardous, to offer complex treatment-related information to patients by telephone, fax, email or recorded messages.

2) Communication with the office: During treatment it is vitally important that the office have an effective way to contact and provide instructions and updates to you. An active cell phone number with voice messaging and one back up number with an answering device (home, work) are required. Unless informed otherwise, the office will attempt to contact the female first, using any or all of the numbers provided, or, if necessary, may leave instructions on an answering device/voice mail. Because email is unsecured, we do not use it for important medical communication and do not check email continuously. If you have pressing questions please call the LOCAL office and always leave detailed messages with that office. Messages will be assessed and answered in an order based on the information provided. Lab results are rarely given by telephone and cannot be interpreted by routine office personnel. Effective fertility treatment relies on patient communication and we rely on you to notify the office during business hours of the onset of menstrual periods, and other developments. It is crucial that you keep us informed of your status and concerns.

Please keep numbers handy for our offices in:

Pensacola, Panama City, Tallahassee, Florida, and Mobile and Dothan Alabama, and Biloxi Mississippi

For urgent matters after office hours, scheduling or instructions call the Directory: (850) 438-9622 and a text message will be sent to the on-call medical personnel at your location. NOTE: non-urgent calls made after-hours may generate a professional fee. For true emergencies, call 911. (Do not call an office, as this delays getting help)

3) Stress and Anxiety: Regardless of one's emotional strength, the treatment of infertility may become a significant stress for couples. It is common for patients to need extra support during this time. Access to professional counselors is encouraged, frequently recommended and occasionally required for some treatments. Referral to this helpful resource is usually received with a sigh of welcome relief, as many couples experience stress but are reluctant to talk about it. Stress management may have more than mental benefits, as some published reports suggest pregnancy may be more readily achieved with counseling! There are many counselors who are experienced with fertility and offer assistance to patients.

4) Primary Care Physicians and Referring Ob/Gyns: When referred for fertility specialty care, we act as a consultant, providing care for infertility ONLY. Thus, you should keep routine visits with your Ob/Gyn or primary care physician, particularly for common gynecologic conditions: suspected infections, PAP smears, mammograms, etc. When you conceive, reassuring ultrasounds are provided to you before you return to your Ob/Gyn in the first trimester.

Confidentiality: Communication with Outside Physicians & SART Audit

In keeping with established HIPAA regulation, medical ethics and general medical procedures, details of the medical care a couple receives are confidential, except when release is legally authorized or required. It is our policy to send information or copies of the medical record only with **written** authorization of the person receiving treatment and with specific instructions as to what information is to be sent. Unless notified in writing otherwise, it is assumed that BOTH members of a couple are entitled to receive Personal Health Information (PHI). In the normal course of medical practice, verbal or written communications are made from time to time with referring physician(s) and others that provide care to the couple. If the couple does not wish for this, we must be notified in writing. Upon establishment of a pregnancy, it is our policy to send basic information to the obstetrician that referred the patient or to one designated by the patient. These letters or verbal communications will include PHI, the type of therapy used and the current status of the pregnancy monitoring.

In keeping with the federal regulations, data is sent to a national registry supervised by the Center for Disease Control in Atlanta and the Society of Assisted Reproduction Technology (SART), a part of the American Society for Reproductive Medicine in Birmingham, Alabama. This data may be verified by an audit according to government regulations. It is possible that at some time in the future, information regarding the treatment of a particular couple would be part of an audit. No information would be released to outside agencies except the information required for the completion of the audit. In the event of a pregnancy, the audit process may involve verification of the pregnancy and its outcome. If a couple chooses not to be contacted in this regard, the staff must be notified upon signing of the medical consent. It is our practice to report clinical treatment and results in scientific/medical meetings and journals without identifying specific couples involved in the treatment.

Financial Responsibility and Insurance Coverage

For all services and medical treatments provided by physicians and staff, including laboratory services and hospital costs associated with medical care and complications, financial responsibility is the sole responsibility of the couple receiving these treatments. Financial responsibility for the pregnancy and any pregnancy complications are the responsibility of the patient/couple.

The clinical and financial staff members make every effort to determine the cost of services before they are rendered, but the costs may vary depending on unforeseen circumstances, insurance interpretation/denials and/or complications of the treatment. The right to change charges and fees is reserved without individual notification. The financial staff works with the couple to determine likely insurance reimbursement for care rendered. But because information is obtained from limited sources at the insurance companies, reimbursement, benefits and coverage cannot be guaranteed. Claims that are later denied for payment by the insurance company become the responsibility of the couple, not their insurance company. For additional reading see the Insurance section in the Fertility Diagnosis and Treatment Patient Information Booklet. Asking your insurance company, or employee benefits manager, or reading about them in your policy manual may answer many questions about insurance coverage.

Financial Resources to Help Fund Treatment

Today's technologically advanced medicine defines assisted reproduction as an expensive endeavor. Requirements exist for the latest advancements in equipment, materials and disposable supplies, but most importantly, it requires highly trained and skilled people to apply this technology. With so many other stresses, the financial challenge should not be a couple's largest obstacle. Consider the variety of resources:

Parents / Family - In all probability, there is no one who knows the joy of parenthood more than those who have lived it. Your parents and family would want the same wonderful experience for you. They may also have the fortitude to assist by contributing financially to the fertility quest. Asking them to pitch in may be all that is needed to start the process.

Third-party Loans – Over the years, several lending companies have offered small loans for medical expenses and medication costs. The application process involves credit rating that determines the amounts available and the interest rates. Once approved, these companies issue payment directly to the patient, who then makes payment to NewLIFE. Companies that work with NewLIFE include American Healthcare Lending and more information is available on our website, www.FertilityLeaders.com

Home Equity Loans / Borrow from yourself - Banking institutions are willing to make small loans (\$5-10,000) at current interest rates. They often recognize the immediate need for couples and locally owned banks desire goodwill from the communities they serve. Life insurance policies accumulate substantial cash value that can be borrowed at reasonable rates as can values accumulated in retirement plans such as 401(k) and pension plans.

Visa/Mastercard Accounts - Another approach that many couples find useful is opening a new credit card account that will be used for fertility services only. New cards offer low interest rates (some at 0%) that are usually fixed for the first year, allowing couples to repay over 12 months and pay little or no interest costs.

Savings Plan - If time is on your side (female <35 years), starting a monthly savings plan is a great option. Interest bearing accounts at banks can be set up to automatically deduct an amount from your paycheck(s) and will thus accumulate steadily. Many couples like this approach, thinking of it as a car payment with the advantage of interest compounding in their favor.

Fertility Grants based on Financial Need - FertilityFoundation.org is a tax-exempt corporation that collects donations and distributes grants to couples based on financial need, diagnosis and proposed therapy. This is worth a try when appropriate for your income level. You may access other such foundations by Internet searches.

Crowd Funding – We live in a great and generous society in America. Couples who genuinely wish to become families will find a country full of people willing to offer financial support, if only they were aware of the honest need. Imagine three thousand people learn of a need and two thousand willingly donate five dollars each. That is enough to make a dream come true. To learn more about the various resources, please visit our website www.FertilityLeaders.com

Programs for Discounted Medication Costs – Several pharmaceutical manufacturers offer discounts variably based on income, military service and volume or packaged medication orders. We attempt to utilize these whenever possible but offers vary by company and over time, so please inquire when receiving your medication schedule and prescriptions.

ASSISTED REPRODUCTIVE TECHNOLOGIES (ART)

In Vitro Fertilization (IVF)

IVF is the oldest ART procedure and still the most frequently used. The term “in vitro” refers to fertilization outside the body. Originally designed to bypass damaged fallopian tubes, new applications for IVF quickly developed for male factor infertility, endometriosis, unexplained infertility, recurrent miscarriage and other conditions. Variations of IVF include donor egg, donor embryo, “natural cycle” or “low-stim” IVF and gestational surrogacy. Because of consistently low pregnancy rates the claims of lower costs for natural cycle IVF have mostly been declined in favor of stimulated IVF cycles with higher chances of pregnancy.

Stimulated Cycle Oocyte (Egg) Development and Monitoring

A woman’s body will naturally release a single egg for possible fertilization each month. IVF increases the chance for pregnancy by producing many eggs in one month. To accomplish this, patients will be given fertility medications to help the body grow more than one egg from a pool of eggs that are available each month. It is now known that many, if not most, eggs produced are abnormal, thus having more eggs improves the chance that one will be of good quality. Most IVF cycles in the U.S. and elsewhere are performed using one or more fertility drugs to increase egg number because the advantages of having more than one embryo generally outweigh the disadvantages. Some couples however wish to limit the number of eggs retrieved or fertilized and this can be accommodated in most cases. The purpose of this section is to explain how drugs may be used and their advantages, disadvantages, side effects and risks.

Recombinant technology (lab manufactured) Follicle Stimulating Hormone (FSH) is commercially available as Gonaf® or Follistim® and is a subcutaneous injection and approved by the Food and Drug Administration for use in IVF. Human Menopausal Gonadotropins (hMG) namely, Repronex®, Menopur® are purified urinary or manufactured products that usually contain FSH and some LH hormone. Human Chorionic Gonadotropin (hCG) (Novarel®, Ovidrel®) is used to stimulate the final steps of egg maturation before egg retrieval. hCG and clomiphene citrate (Clomid®, Serophene®) are FDA approved for ovulation induction in women who do not ovulate. Letrozole (Femara) is another type of oral medication used induce ovulation, though not specifically approved by the FDA for such. Their usage for ART is a natural extension.

Lupron® (leuprolide acetate) is a “GnRH agonist,” approved for pituitary regulation, but not specifically approved for ART. Additionally, Lupron is used as an ovulation trigger, when hCG is to be avoided. GnRH antagonists (ganirelix, cetrorelix) are medications approved for use in ART and both “agonists” and “antagonists” are used to prevent premature ovulation that would lead to a cancelled cycle. Other medicines that may be utilized for ART include fertility pills (clomiphene, letrozole, etc) and patches (androgen, estrogen, etc). All of these medications are used extensively in the U.S. and abroad for assisted reproduction. Additional medications may include supplemental estrogen, progesterone, aspirin, antibiotics, prednisone and others.

You will be given a DAILY SCHEDULE of when and how much medicine to take. It is important that you carefully follow these instructions. Please be sure that you take the prescribed dosage at the prescribed time. If in doubt, please call to ask questions. We will teach you and your partner or another person how to administer IM (intramuscular - in the muscle) and SQ (subcutaneous - beneath the skin) injections. Instructional videos are available online to aid in this step. Because medications are given by injection, bruising, pain or swelling at the injection site is fairly common. Allergy to the medications resulting in a rash or hives occurs rarely. Most of the side effects of these drugs are minor, involving discomfort, but not usually requiring medical intervention. Symptoms of generalized rash, swelling or difficulty breathing should be reported to your doctor.

Serious complications of these medications are rare with the exception of multiple birth [See Pregnancy and Birth Outcome in ART]. The drug manufacturers are required to acknowledge that serious pulmonary conditions and thromboembolic (blood clotting) events have been reported in conjunction with the use of ovarian stimulation medication. The risk for these complications is increased for some patients who over-respond or have drug hypersensitivity. Ovulation induction drugs are occasionally associated with the risk of ovarian hyperstimulation syndrome (painful enlargement of the ovaries, See OHSS below).

In addition to follicles containing eggs, these drugs may occasionally cause the development of ovarian cysts (non-cancerous, fluid-filled structures in the ovaries); in rare instances these may need to be removed surgically, possibly requiring short hospitalization. Though rare, the removal of an ovarian cyst can result in the loss of an ovary. It is also possible for an ovarian cyst to rupture, causing episodes of pain and be associated with sudden bleeding and require surgery and/or blood transfusion(s). Such acute bleeding is very unusual.

It is inadvisable for such fertility medications to be used during pregnancy (except progesterone and estrogen), but it is sometimes difficult to rule out a pregnancy even when it seems that normal menstruation has occurred. For this reason, women may be asked to have a pregnancy test prior to initiating a treatment cycle even after experiencing bleeding. Additionally, couples may be asked to refrain from intercourse, or use hormonal contraceptives or barrier protection at certain times during a treatment cycle.

In November of 1992, a published study addressed a potential risk of ovarian cancer associated with the use of certain medications for ovarian stimulation. Since that time, the consensus of medical opinion on the issue, as

voiced by the Society of Assisted Reproductive Technology (SART) and the American Society for Reproductive Medicine (formerly the American Fertility Society), is that there is no conclusive evidence of this risk. As part of your patient counseling, you may wish to discuss this issue with your physician.

Cycle Monitoring and Cancellation

Monitoring of ovarian stimulation involves blood tests and/or ultrasound examination and is vital to proper fertility management. Inability to comply with scheduled office visits may necessitate rescheduling or cancellation of a cycle. Transvaginal Ultrasound examinations are used to visualize the ovaries and the uterus and to help predict the timing of ovulation. Occasionally there may be some discomfort; however, generally ultrasounds are considered harmless and painless. The effects of repeated ultrasound examinations on developing eggs are not known. There are no other known risks associated with ultrasound. The taking of blood samples allows the measurement of estrogen, the main product of follicles and may cause discomfort and/or bruising, infection and/or scarring at the needle site. Rarely it may also be associated with nerve damage or infection.

Various problems may arise which may prevent the completion of an ART cycle, resulting in a cancellation, or delayed embryo transfer. A physician may stop treatment prior to the retrieval of eggs at his/her discretion, for any reason that is believed to be medically appropriate. Cancellation and cryopreservation of embryos for delayed embryo transfers will result additional expenses.

The most common reason for such a cancellation is a low response with few follicles and/or low estrogen levels. Such cancellations occur in about 15-20% of attempted cycles but are significantly more likely as a woman's age increases. It is important to understand that for any one woman, there is variability between responses month to month, and that variability increases with maternal age. It is often best to take a perspective of trial and repeat, usually addressing the low response by changing the dosage or type of medication in a later cycle.

Other responses and conditions may lower the chance of successful implantation by impairing the endometrial lining. Overstimulation, a premature rise in progesterone, or a rise in estrogen that is too rapid, or retrieval of many more eggs than expected will sometimes require cancellation, the addition of other medications and/or delayed embryo transfer to a later month. Medications used to prevent premature (spontaneous) ovulation are adjusted cautiously, and are generally started as late as possible to avoid over-suppression and low response, but occasionally, a patient will break-through prior to or after starting this suppression causing a cycle cancellation.

Ovarian Hyper-Stimulation Syndrome (OHSS)

The process of in vitro fertilization (IVF) involves the intentional, but controlled stimulation of the ovaries in order to obtain an optimal number of eggs. Mild symptoms related to the enlargement of the ovaries usually begin 5 to 7 days after ovulation (or egg retrieval) but may also occur after embryo transfer and pregnancy. Mild symptoms are fairly common and are usually managed by bed rest at home. Mild symptoms typically include: mild abdominal discomfort or distension (resulting from enlarged ovaries), mild nausea, and diarrhea. Rarely, this may progress, resulting in a dramatic increase in the size of the ovaries, causing a number of symptoms collectively referred to as Ovarian Hyper Stimulation Syndrome. OHSS can become more severe if associated with a pregnancy and may require daily assessments, lab tests, ultrasound and sometimes removal of abdominal or pelvic fluid that accumulates and causes symptoms. To manage the fluid imbalances, hospitalization will sometimes be necessary. In rare instances, removal of the ovaries may be required and other major complications such as internal bleeding, stroke and kidney failure are possible. It is impossible to reliably predict who will develop OHSS but it seems to be unique to some women but not others. If OHSS development is a concern based on prior stimulated cycles, some additional preventive and alternate medications may be prescribed. A patient who exhibits signs or symptoms that suggest increased risk of severe OHSS during ART stimulation may be canceled or have the embryo transfer postponed to months later by freezing all viable embryos. If canceled, it is usually possible to attempt another cycle with adjusted levels of medication.

Warning signs of OHSS include the following:

- persistent nausea, vomiting or diarrhea
- persistent or constant pelvic pain
- severe abdominal bloating
- weight gain of 2+ pounds/day for 2 days or more
- difficulty breathing, especially reclined
- decreased urine volume despite usual fluid intake

If you experience any one or combination of these symptoms, contact the office immediately. Most likely you will need to be seen for ultrasound and lab work to determine management. Regular communication is critical here.

Cycle Conversion to Intrauterine Insemination (IUI)

IUI may be performed instead of IVF when the ovarian response has been inadequate to proceed with egg retrieval, if a woman's fallopian tubes are open and there is adequate sperm function. IUI is reasonable if the woman's ovarian response is low and it is believed that more eggs could be obtained in a subsequent cycle. Notably however, the evidence suggests that the overall chance of pregnancy remains lower for IUI than for proceeding to egg retrieval and IVF with a few eggs. IUI allows the introduction of specially prepared sperm into the uterus through the cervix using a plastic catheter. IUI may be performed 1 to 2 days after the ovulation triggering injection (hCG). Possible side effects of intrauterine insemination (IUI) include pelvic infection, uterine cramping, bleeding, mild discomfort, and perforation of the uterus (rare).

EGG RETRIEVAL, FERTILIZATION AND EMBRYO TRANSFER

Transvaginal Oocyte (Egg) Retrieval or Ovum Pick Up (OPU)

Retrieval of eggs is critically timed to about 35 hours after the ovulation trigger. Too early and the eggs may not be mature; too late and the eggs may have been released. You will be specifically instructed on when to administer this ovulation trigger injection (either hCG or Lupron). Eggs are retrieved under sedation or other forms of anesthesia. A special needle is guided by ultrasound through the right and the left corners of the vagina to enter the ovaries and follicles (egg sac). The needle is sequentially passed into each visible and accessible follicle. Fluid suctioned from within the follicles usually contains one egg per mature follicle. The actual eggs are too small to be seen by ultrasound and notably, not all visualized egg sacs (follicles) will yield an egg. Occasionally, particularly with age >35, retrieval may not yield any eggs preventing the completion of a cycle. This ultrasound-guided procedure usually takes 5-10 minutes and has been in widespread use in the United States since 1986.

Potential Risks and Complications

During or after this procedure a woman may experience mild to moderate discomfort. Complications of this egg retrieval are uncommon. They include but are not limited to, internal bleeding and/or puncture of blood vessels, injury to bowel, bladder, uterus, ovaries and/or any other abdominal organ. These are potentially serious and even life-threatening complications that may require immediate surgery and/or blood transfusion. If a serious injury is recognized during the retrieval, repair will usually be attempted immediately and will ordinarily require major surgery and subsequent hospitalization. Rare but serious pelvic infections (including Pelvic Inflammatory Disease also known as PID) may arise days after the procedure, possibly requiring antibiotics and/or hospitalization and in rare instances, removal of fallopian tube(s), ovary(ies), uterus (hysterectomy) or colostomy. Pelvic infection or surgery may cause formation of scar tissue, decreasing a woman's chance of conventional conception through intercourse. As with any procedure, transvaginal oocyte retrieval may present other risks that have not yet been identified.

Anesthesia for transvaginal oocyte retrieval routinely involves intravenous medications for sedation but may involve tranquilizers, light general anesthesia in alternative facilities. The type of technique used and the risks of anesthesia will be discussed prior to the procedure. Sedation may be provided by a qualified iv sedation nurse or anesthetist. Any physician anesthesiologist, who may provide treatment, is not an agent or employee, but rather an independent physician providing services to patients. Complications of sedation and anesthesia are uncommon. They include, but are not limited to, allergic reactions to drugs and breathing problems. Cardiac arrhythmia / arrest and death are exceedingly rare complications.

Impaired Egg Retrieval and Laparoscopy

One or both ovaries may sometimes be completely or partially inaccessible through the transvaginal route, resulting in no eggs or a lower number than expected. This problem is occasionally suspected prior to attempted retrieval, but may only become apparent at the time of the attempted ultrasound guided procedure. While surgery has been advocated in the past, the logistics preclude scheduling and completing a laparoscopic egg retrieval with general anesthesia in the same treatment cycle. Thus, a patient may have to return in a later month with a planned surgery for egg retrieval. In most cases, retrieval of eggs that are accessible is preferable, even if limited, as laparoscopy will have significant out of pocket additional costs (hospital, anesthesia, facility fees), time delay and risks of surgery. On occasion, even laparoscopy is not successful for egg retrieval.

Potential Risks and Complications

Laparoscopy may lead to discomfort following the procedure. Surgical complications, though uncommon, include but are not limited to, internal bleeding and/or puncture of blood vessels, injury to bowel, bladder, uterus, ovaries and/or any other abdominal organ. These are potentially serious and even life-threatening complications that may require immediate surgery and/or blood transfusion. If a serious injury is recognized during the retrieval, repair will usually be attempted immediately and will ordinarily require major surgery and subsequent hospitalization. Rare but serious pelvic infections (including Pelvic Inflammatory Disease also known as PID) may arise days after the procedure, possibly requiring antibiotics and/or hospitalization and in rare instances, removal of fallopian tube(s), ovary(ies), uterus (hysterectomy) or colostomy. Pelvic infection or surgery may cause formation of scar tissue, decreasing women's chances of conventional conception through intercourse. The chance of these complications is probably greater than that with ultrasound guided aspiration, and ranges from 1 in 100 to 1 in 10,000. As with any procedure, laparoscopic oocyte retrieval may present other risks that have not yet been identified. In addition, this procedure may not result in the successful recovery of eggs.

Whenever anesthesia is required (as for example, for laparoscopy), there are anesthesia risks involved, some of which may be serious. Information about these should always be discussed with the anesthesiologist involved. The anesthesiologist should address any questions that you may have in this regard before consent to anesthesia is given. Any anesthesiologist, who may provide treatment, is not an agent or employee, but rather an independent physician providing services to patients.

Insemination, Fertilization and Culture of the Oocytes & Embryos

Immediately after retrieval, cumulus cells surrounding the eggs obscure the assessment of egg maturity by microscopy. Maturity can only be assessed after the cumulus cells are removed. Maturity is confirmed when eggs have expelled half the DNA in a “polar body,” make room for the sperm DNA. It is common and expected that 10-30% of eggs will be immature and are not likely to fertilize. If routine In Vitro Fertilization is planned, 2 - 6 hours later, sperm will be added to the dish containing all of the eggs for insemination and allow fertilization. If insemination by sperm injection is planned (see ICSI below) the cumulus cells are removed to prepare for ICSI.

NOTE: Some couples may NOT wish to use cryopreservation (freezing) of extra embryos and therefore may consider limiting the number of eggs inseminated, or the couple and physician must agree to discard extra embryos. Couples should discuss this topic and preferences noted on the Consent Form.

Assessment of fertilization is performed the next day, “Day 1” after egg retrieval and insemination. Under normal conditions, fertilization should have occurred in the majority of mature eggs. Fertilization is usually reported to patients on “Day 1.” Problems with either egg or sperm quality may lead to a decreased number of eggs being fertilized. In some instances, no fertilization of oocyte (egg) will occur. This will obviously limit success of the cycle. When normal fertilization is noted, the fertilized eggs (zygotes) are maintained in culture in the incubator for additional days. Some eggs will fertilize abnormally, with the most common being fertilization with more than one sperm. Such “polyspermic” fertilization cannot lead to normal embryos, and therefore these fertilized eggs are discarded. The majority of fertilized eggs should divide (cleave) into 2, 4, then 6-8 cells by “Day 3.” Occasionally, none of the fertilized eggs will cleave even after apparently normal fertilization. Patients will often receive a report on “Day 3.” (See section on Embryo Assessment)

Intra-Cytoplasmic Sperm Injection (ICSI)

Intra-cytoplasmic sperm injection (ICSI) is a specialized, microsurgical form of insemination, first developed in 1993 to help couples overcome male infertility problems due to an inability of sperm to fertilize an egg. With routine IVF, it was not uncommon to see very low fertilization rates for men with low numbers or abnormal sperm or semen. Even now, failed or low fertilization can be an unexpected finding with normal semen testing. As its use evolved, ICSI has become common for most ART cycles to avoid the unpredictable and detrimental fertilization problem. ICSI is used to place a single sperm into an individual egg and fertilization rates are generally good for cases of normal and impaired sperm function. In some cases, ICSI allows fertilization by sperm that are not motile but, contain normal DNA. ICSI is recommended for sperm retrieved directly from the testicle (vasectomy) and required for cases where genetic testing is planned for the resulting embryos.

Description of the Technique

For ICSI, the cumulus cells are removed from the eggs after retrieval, allowing maturity to be confirmed. Only mature eggs will be inseminated by ICSI. Using a microscope, an embryologist gently draws one sperm into a glass pipette. The tip of the pipette is then guided into an egg held steady at the end of another glass pipette. With a steady, measured forward motion, the sharpened tip of the sperm-containing pipette is inserted into the egg. The embryologist expels the sperm into the egg and the empty pipette is removed.

Potential Risks and Benefits of ICSI

ICSI involves direct handling of eggs/sperm and therefore adds to the chance that an egg may be damaged in the laboratory. Experience of the embryologist serves to reduce that risk to a minimum (1-5% of eggs). Despite general medical acceptance by fertility centers, ICSI is still a relatively new procedure. Children born as the result of ICSI may not have reached an age to reproduce in numbers to address concerns. Some studies have suggested an increased chance for certain birth defects when ICSI is used. Not all studies agree. Hypospadias (lowered opening of the penile urethra) and propagation of male infertility remain specific concerns. Experts agree that despite its apparent simplicity, ICSI bypasses important natural selection processes such as the cervical mucus, penetration of the cells around the egg and the egg’s shell. This may permit the transfer of certain male infertility conditions that have a genetic basis. Some known inherited or new DNA mutations can be associated with male infertility. There may be many that are unknown with current testing methods. Testing is recommended for men with severely abnormal semen quality. Where a genetic basis to male infertility is suspected or known (such as Cystic Fibrosis), the couple may also find it helpful or recommended to speak with a genetic counselor before choosing to use ICSI. For some males, ICSI is the only method to achieve fertilization and a chance for biologic children. (See section on Congenital Anomalies)

Embryo Grading and Assessment

Embryos are observed very carefully while in culture. A gradual attrition (reduction in number) of viable embryos is expected during the time from egg retrieval to embryo transfer. For example: 11 eggs may be retrieved, 9 may be mature of which 6 fertilize and 5 cleave. And by “Day 5” perhaps only 2 may have developed adequately to consider for transfer. While the visible appearance of an embryo prior to transfer to the uterus is an important observation, ultimately, the quality of each embryo is most accurately reflected by the “invisible” structure of the chromosomes (DNA) which control every aspect of late embryonic development. A complete set of normal chromosomes is essential for establishment and maintenance of a healthy pregnancy (see Preimplantation Genetic Screening, PGS). Sophisticated genetic testing has revealed that many, if not most, eggs and early embryos do not have normal chromosomes.

The visible appearance of embryos under the microscope is measured by the rate of cell division, shape of individual cells and the overall appearance of the embryo. The embryo evaluation process takes several characteristics into consideration. To help you better understand the grading process some terminology is explained below. **Note:** Despite these efforts, grading of an embryo is not an absolute predictor of probability of pregnancy, so that very “poor looking” embryos will sometimes make “beautiful babies.”

Cell Number – A single-cell egg divides steadily to form many cells after fertilization. The expected cell number depends on the age of the embryo (i.e., the number of hours since insemination). For example, healthy embryos reach the 6 or 8-cell stage by the 3rd day after insemination. A “Day 3” embryo that is only at the two or 4-cell stage is progressing more slowly than is desirable. These facts in combination with information from the other areas of evaluation help in determining which embryos will be chosen for transfer.

Fragmentation - When the cells of an embryo divide, it is normal for small portions of the cell to separate from the rest and remain inside the zona, the shell of the egg that keeps all the cells of the embryo together. These portions are called "fragments or fragmentation". Degree of fragmentation is scored from no fragmentation or very little to highly fragmented embryos. Less fragmentation is better.

Cell Uniformity, Shape, Clarity of Outline, and Arrangement - It is expected that cells of the embryo should be of approximately the same size and shape. If cell size is highly irregular, the embryo will be labeled as being of poor quality. Clarity of outline and cell arrangement are also evaluated. Embryos in which cells are well defined, light colored and clear, and are symmetrically arranged will be considered to be of better quality. Cells with dark, grainy appearance will not score as well. Embryos may be labeled as GOOD, FAIR, or POOR according to these criteria. At the time of embryo transfer, your physician or clinician will discuss with you the quality of your embryos as assessed by the embryologist.

Blastocyst Culture

A desirable approach to reducing high order multiple pregnancies (≥ 3) with ART has been to culture embryos longer, with the knowledge that healthy embryos continue to develop appropriately. Embryos successfully reaching the blastocyst stage (“Day 5”) may be transferred in fewer numbers with less chance of multiple implantations while achieving an equal chance of pregnancy as shown in most studies. A healthy blastocyst may contain 70-100 cells and are thus graded differently than Day 3 embryos. Blastocyst grading is scored and is usually limited to “good,” “fair,” or “poor.” Because of these advantages, culture to the blastocyst stage before embryo transfer on Day 5 is now routinely performed for NewLIFE patients. The rate of development (growing on schedule) and proper appearance of embryos have been associated with a higher proportion of embryos with normal DNA. In other words, embryos that fail to grow will not result in pregnancy. Embryos that grow appropriately have the best chance of making a healthy pregnancy. Similarly, transfer of only blastocysts may also reduce the chance of miscarriage.

Description of the Technique

The process requires special culture conditions that allow embryos to continue cell division for a total of approximately 5-6 days in culture. At this stage embryos contain hundreds of cells that begin to differentiate into future placental and fetal cell types.

Potential Benefits and Risks

By reducing the total number of embryos remaining after a cycle of IVF, fewer embryos require cryopreservation and this results in less cost to couples. A theoretical advantage of this technique is that embryo transfer is more closely timed to the appropriate stage of endometrial (uterine lining) development. In natural conception, a blastocyst would arrive in the uterus 5 to 6 days after fertilization, not as a 6-8 cell embryo (Day 3). A potential outcome with this technique is the possibility that none of the embryos will grow appropriately, leaving none to transfer and denying the chance for pregnancy in that cycle. This is a particular concern for cases with fewer eggs to work with. Although uncommon, blastocysts may split to produce identical twins, possibly at a higher rate than with Day 3 transfers. The benefits of blastocyst transfer are lower chance of triplet and greater pregnancy, higher chance of a genetically normal embryo transferred and possibly lower risk of miscarriage. This technique helps to avoid “false hopes” while waiting for a pregnancy test and is thus suitable for all ART patients and will be recommended unless circumstances indicate otherwise.

Assisted Hatching

Human eggs are surrounded by a 'shell' (zona pellucida or simply “zona”) composed of a soft gel-like substance. Sperm must pass through this layer in order to fertilize the egg and the embryo must break out of this shell so that implantation and pregnancy can result. In this way, only the most active sperm fertilize each egg and the embryo is held together during the first several days of growth. To break out of the shell and implant in the lining of the uterus, the embryo must weaken and then push through the surrounding shell - an event similar to the hatching of a chicken from its egg. An unusually thick shell may reduce the likelihood of timely hatching, implantation and pregnancy. Thinning or perforating the shell surrounding embryos immediately prior to transfer has been proposed

to increase implantation in certain cases. Because of the earlier analogy to “hatching”, this procedure is referred to as assisted hatching. The evidence does NOT consistently suggest a benefit in all cases, deferring its use in individual cases. **NOTE:** The need and recommendation for assisted hatching may not become apparent until embryos are examined in the laboratory following insemination and fertilization. Assisted hatching is performed as part of all procedures for genetic testing of embryos. Assisted hatching is not performed on Day 5 blastocysts.

Description of the Assisted Hatching Technique

Assisted hatching is performed under a microscope and involves opening the shell using one of several techniques; mechanically using a fine glass fiber; cutting the shell with laser energy or applying a weak acid solution to a single region of the shell. The embryo is held in place on a glass holding pipette by gentle vacuum while the opening is made. This small perforation weakens the shell theoretically assisting the embryo to exit the shell during the hatching process that normally takes place within the uterus and allows the embryo to establish direct contact with the lining of the uterus. Embryos are transferred to the uterus using standard techniques.

Potential Risks and Benefits

Each step of an ART process that involves direct handling of embryos is associated with a risk of damage; the more times an embryo is handled in the laboratory, the higher the likelihood that some damage might occur. Assisted hatching involves direct handling of embryos and therefore adds to the risk that an embryo will be damaged in the laboratory. Experience of the embryologist serves to reduce the risks to their minimum (1-2% of embryos). There are no published data to suggest that use of assisted hatching has any detrimental effect on the potential of the embryo to implant. For certain couples, the benefits of assisted hatching (potentially raising the chance of a successful pregnancy) will outweigh any negative effects.

SPERM RETRIEVAL FROM THE MALE

Although ICSI has improved the outcomes for men with low semen quality, for some males healthy sperm cannot be obtained from the semen, or semen cannot be produced. For example the cause of some male infertility is an absence of the vas deferens, the duct bringing sperm from the testicle into the body. Other men will have blockage (obstruction) of the vas due to infection or surgery, ie vasectomy. Further, in severe cases, healthy sperm may only be found within the testicle(s). Various techniques can, in most cases, successfully locate and obtain sperm for reproduction avoiding the alternative of using donor sperm for reproduction.

Description of the Technique

In the most simple cases, sperm may be aspirated from the epididymis located adjacent to the testicle, called Percutaneous Epididymal Sperm Aspiration, PESA. Sperm may also be aspirated with a needle directly from within the testicle called Testicular Sperm Aspiration, TESA. In the most difficult cases, a needle is not adequate and a urologist must make a surgical incision and biopsy on the testicle(s) to locate and remove sperm producing tissue, called Testicular Sperm Extraction, TESE. These approaches have offered great hope to infertile men and allowed them to defer use of donated sperm. Sperm obtained with these methods are usually few in numbers and may lack adequate motility as well. For this reason, microsurgical insemination (see section on ICSI) is required to optimize the possibility and percentage of fertilization. Sperm are usually retrieved in advance and either cryopreserved for later use or kept fresh, incubating until the female has produced eggs. In general, it is desirable to use freshly retrieved sperm. If sperm were confirmed on a previous testicular biopsy and frozen, a fresh sample may be preferred, keeping the frozen sample as a “back up”. Couples may elect to order donor sperm as an alternative so that if sperm are not retrieved, the female’s egg retrieval and ART cycle will not have to be cancelled.

Potential Risks and Complications

Anesthesia for sperm retrieval routinely involves intravenous sedation with locally injected anesthetics (ie lidocaine). The type of technique used and the risks of anesthesia will be discussed prior to the procedure. Sedation may be provided by a qualified nurse or anesthetist trained in intravenous sedation. Complications of sedation and anesthesia are uncommon but include allergic reactions to drugs and breathing problems. Cardiac arrhythmia, arrest and/or death are rare complications. Complications of injected local anesthetics can cause reaction and local bleeding. Major surgical complications with these techniques are uncommon but include but are not limited to, bleeding, infection, scar formation, pain or discomfort or injury to the testicle(s) or other organ. The risks and benefits of these therapies will be discussed with your physician prior to consents and initiation of treatment.

EMBRYO TRANSFER: Technique and Trial (Practice) Embryo Transfer

The transfer of embryos into the uterus is a final step in the ART process and it is desirable that it be accomplished with great ease. To help ensure this in some patients with cervical issues, the ease of transfer may be determined prior to the actual ART cycle by a (“trial transfer” or “catheter check”), using a plastic catheter (tubing) similar to the one that will be used for the actual embryo transfer. A trial transfer is not needed in every case. If there is any concerns or prior difficulty, plans are made to optimize the actual transfer, by using special catheters, ultrasound guidance or other instruments and occasionally dilating the cervix. In all but a few cases, the trial transfer and actual embryo transfer are easy and virtually pain free. On occasion, a woman may experience moderate to severe discomfort, cramping or significant bleeding. Embryo transfer, like any manipulation of the uterus involves a small risk of infection, which may require antibiotics, hospitalization or surgical removal of the tubes, ovaries and/or the

uterus (hysterectomy). If the catheter perforates the uterus, antibiotics, hospitalization or surgery may be required. It is almost always possible to transfer embryos into the uterus but the technique is not flawless. Other medical circumstances may preclude embryo transfer. In these cases, the option of cryopreservation with a postponed transfer is available.

Number of Oocytes (Eggs) or Embryos to Transfer

Not every embryo transferred during ART will implant, and not every embryo that implants will result in a clinical pregnancy or a live born infant. The chance of implantation varies with each individual patient/couple, although statistical averages demonstrate that the age of the woman is a key factor, possibly the most important factor. As implantation is a necessary first step to achieve a clinical pregnancy, or a live birth, pregnancy rates generally decrease with age as well. In general, more embryos can be safely transferred as maternal age increases. Most commonly, patients wait to make the decision when more information is available on the day of transfer.

The chance of multiple births (twins, triplets, etc.) and the risk of premature birth and complications from multiple pregnancy, increases with an increased number of embryos transferred. The routine use of blastocyst culture (see above) has helped significantly. In addition to maternal age transfer number may be determined for your individual case based on your diagnosis, number/quality of embryos, your physician’s judgment, your prior attempts and comfort level. NewLIFE adheres to the guidelines published by the American Society for Reproductive Medicine (ASRM) and will deviate from these when medically indicated.

ASRM Criteria for Number of Embryos to Transfer, 2016				
Cleavage-Stage Embryos				
Prognosis	Age <35	Age 35-37	Age 38-40	Age 41-42
Favorable*	1	1	2-3	3-4
All others	2	2-3	3-4	4-5
Blastocysts				
Prognosis	Age <35	Age 35-37	Age 38-40	Age 41-42
Favorable*	1	1	1-2	1-3
All others	2	2	2-3	3
*Favorable = Any ONE of these criteria: Fresh cycle: euploid embryos, expectation of 1 or more high-quality embryos available for cryopreservation, or previous live birth after an IVF cycle. FET cycle: availability of vitrified Day-5,6 blastocysts, euploid embryos, first FET cycle, or previous live birth after an IVF cycle.				
Justification for transferring additional embryos beyond recommendations should be clearly documented in the patient’s medical record.				

An additional influence in the decision should be the couple's attitude regarding fetal reduction. “Selective reduction” is a procedure employed in early pregnancy to reduce the risk of a pregnancy with quadruplets, triplets or higher, down to twins or a singleton pregnancy. If a woman has a quadruplet or higher pregnancy, the general medical recommendation may be to perform a fetal reduction procedure because of the higher risk for premature delivery, infant death and lifelong disabilities. There are several publications suggesting that fetal reduction is safe and effective for even triplet pregnancies. **NOTE:** A couple having serious emotional, ethical, or religious reservations regarding the selective reduction procedure and or cryopreservation, may wish to limit the number of eggs inseminated or embryos transferred to a number acceptable to them. Please discuss this with your partner first and then with your physician or other medical personnel **BEFORE** the ART Consent Session, in order to note your preferences before treatment begins. While the quality of the embryos on the day of transfer will also influence the decision of how many to transfer, modern ART practices have limited embryo transfer numbers to 1 or 2 in the majority of cases.

TREATMENT-RELATED ISSUES & SPECIAL PROCEDURES

Cryopreservation (Freezing and Storage) of Embryos and Vitrification

Freezing (Cryopreservation or “Cryo”) of living cells has been successfully used in research laboratories for many years, and increasingly, in veterinary and human reproductive medicine. The first birth results after the freezing and thawing of a human embryo occurred in Australia in 1985. In 1998 in the United States, there were 1,941 reported deliveries from transfer of previously cryopreserved embryos. The best available data from the U.S. and abroad suggest that the chance of birth defects in children born following the cryopreservation of embryos is the same as the rate observed in an age-matched group of pregnant women. There is no further evidence of an increased risk of birth defects or obstetrical problems in these pregnancies compared to fresh, non-frozen embryos.

The purpose of cryopreservation with ART is to optimize the stimulation to obtain good quality eggs without the obligation to transfer too many embryos at one time if several good quality embryos develop. Also, a deferred

embryo transfer is sometimes desirable or required if an impairment of implantation is suspected for a fresh transfer. Since the majority of risk, inconvenience and expense of ART associated with the oocyte stimulation and retrieval, it is desirable to gain as much benefit from these steps without increasing the rate of multiple births. In the situation where more normally dividing embryos result than the couple desires to transfer, the couple is given the choice before starting the cycle to cryopreserve any excess embryos for later attempts. Recent research is suggesting that delaying the embryo transfer allows optimization of the egg stimulation without regard for effect on the endometrial lining. In some cases, it may be preferred to “freeze all” embryos and schedule the embryo transfer in a non-stimulated menstrual cycle.

Embryos are routinely frozen using a process called “vitrification”. With this process, healthy embryos are expected to survive the cryopreservation and thaw at a high rate, approaching 80-90%. Embryos are usually thawed one at a time and after an initial thaw, poor quality or survival may suggest the need to thaw one or more additional embryos, if available.

The chance of pregnancy and birth resulting from the transfer of cryopreserved embryos depends on a number of factors specific to the patient, most importantly the woman’s age when the embryos were generated. Pregnancy rates with frozen embryos, in general, remain slightly less than that with fresh embryo transfer. Blastocyst culture (“Day 5”) and cryopreservation at the blastocyst stage appears to have improved the pregnancy rate with “frozen-thawed embryo transfers” or FET because better quality embryos are being stored. Toward advancing this benefit, cryopreservation is routinely reserved for only those embryos that reach the blastocyst stage by the fifth or sixth day of extended culture. Embryos that fail to develop are more likely to be genetically abnormal.

The number of cryopreserved embryos available will be important in determining the best way to proceed with a subsequent ART cycle. When there are only one or two frozen embryos available, the physician may suggest a new stimulation and retrieval cycle, prior to using the cryopreserved embryos. Alternatively, the physician may recommend a transfer of one or two cryopreserved embryos together with an embryo(s) obtained from another cycle. With excess cryopreserved embryos, the physician will routinely recommend FET prior to attempting another stimulation and retrieval cycle.

Legal Concerns Regarding Cryopreservation

The law regarding cryopreservation and the ownership, control and disposition of cryopreserved embryos is not completely developed or proven. In some instances, there have been conflicting legal decisions in different jurisdictions. It is our policy that embryos produced by the joining of eggs and sperm will be treated in a manner mutually agreed upon by both partners while in our possession. Where donor eggs or sperm are being used, the embryos are treated in a manner mutually agreed upon by the receiving couple at the site where they receive ART services. A gamete donor who provides egg or sperm, relinquishes rights and responsibilities toward the gametes or resulting embryos and children. Except where applicable law requires otherwise or where a court has acquired jurisdiction over the embryos, any decision regarding the embryos shall be the **joint decision** of the partners receiving ART services (the responsible parents). And this decision shall be contingent upon their mutual consent or upon a legally binding and enforceable agreement, in writing, signed by both of them. If such embryos are legally determined to be property, the couple shall hold them jointly with all rights in the survivor.

Note: In the event that a member of the couple should die, the remaining partner shall have sole right to make all decisions regarding the disposition of the embryos that remain. In the event that both members of the couple die, remaining embryos cannot be donated and will therefore be discarded unless the couple consented and was properly screened prior to their deaths.

Embryos cannot be donated unless the donating couple has fully assumed the responsibility of being screened for genetic or infectious diseases. This would allow the embryos to be donated anonymously to another infertile couple. These screening tests need to be obtained at least 6 months after the cryopreservation of the embryos. If the embryo(s) is/are donated, the donating couple, their successors and heirs, waive any and all rights that they may have in the donated embryos and in any child born as a result of their transfer. If a donation program has not been established, or if such is prohibited by law or hospital policy or otherwise deemed inadvisable, the couple authorizes and instructs the disposal of the embryo(s) in an appropriate manner.

The couple understands and must agree that if any dispute arises between the two partners regarding disposition of the embryos, the physician or practice is authorized, in its sole discretion, to refrain from taking any action unless and until otherwise directed by a final judgment of a court of competent jurisdiction. The physician or practice may rely and act on an agreement, in writing, signed by both partners, with no obligation to inquire into its validity or enforceability. The partners understand and agree that the physician or practice, in its sole discretion, may institute legal proceedings of any kind regarding the disposition of the embryos, including but not limited to a legal proceeding in any court of competent jurisdiction.

NewLIFE insists that each partner agrees, for himself and for herself and for his or her successors and heirs, to reimburse and indemnify the physician(s) or practice and its affiliates and subsidiary companies, their employees and independent contractors, for any loss, expense, cost or damage (including reasonable attorney’s fees) that may be incurred by reason of any dispute regarding the disposition of the embryos, other than a dispute initiated by persons to whom the embryo(s) have been donated.

It is the policy of this practice not to maintain storage of cryopreserved tissue indefinitely. When the use of stored embryos is not eminent, the practice will routinely transfer to a “long-term storage facility” (LTS). Therefore it is inherent that couples recognize the right of this practice to transfer cryopreserved embryos to LTS after which maintenance and costs remain with the couple. Arrangement for disposition of the embryos must then be made with the LTS facility. Options for disposition of cryopreserved embryo(s), include transfer to the uterus of the woman to attempt pregnancy, transfer to another ART program or to another LTS facility, physical delivery of the embryo(s) to the couple, disposal of the embryo(s) in an appropriate manner, or, with appropriate testing, donation to another couple. Currently, couples do not have the option of offering embryos for research, but may have in the future.

Couples will be informed from time to time of the fact that they have embryo(s) in storage. Storage fees will be charged regularly with the right to change fees being reserved. If the couple fails to maintain current records or provide notification of a change of address and is unable to be located by phone or certified letter to their last known address, the embryos will be disposed of in an appropriate manner. The couple agrees after failure to reply to such notice within 30 days of the day it was sent, embryos may be disposed of at the sole discretion of the practice.

In requesting cryopreservation services, the couple understands that: 1) their right to terminate cryopreservation services at any time is reserved but requires a current written request, 2) upon terminating those services, the couple will be asked for instructions regarding what they wish to do with any embryo(s) then cryopreserved. Notification may then be provided to the couple when the disposition is completed.

Although appropriate surveillance (quality assurance) for a variety of conditions affecting stored embryo(s) is maintained, keeping the embryos(s) at the very low temperatures necessary to safely sustain their viability for long period of time is fraught with many opportunities for failure beyond human control. In agreeing to utilize embryo cryopreservation, the partners, their heirs and successors agree to release the physician(s) and practice from any and all liability for any and all loss, damage, cost or expense that may accrue due to damage to the cryopreserved embryos, power failure of the cryopreservation containers, loss of liquid nitrogen supplies, governmental interference or regulation, or any other cause not within the direct and immediate control of personnel and practice.

Frozen-Thawed Embryo Transfer (FET): Natural and Synthetic Hormone Preparation

During a normal ovarian cycle ("menstrual cycle"), the two major events that occur are the production of an egg/oocyte and the preparation of the uterus for the implantation of the embryo. When production of oocytes is not necessary (as in frozen/thawed embryo transfer or with donated oocytes and embryos), the uterine lining (endometrium) must still be prepared for the transfer of embryos. Transfer of frozen/thawed embryos may be performed in a natural cycle or in a synthetically prepared cycle. Because regularly cycling women will, without notice, have an occasional abnormal cycle, synthetic cycles have provided increased reliability. For women who do not ovulate, those without ovaries, or those trying to synchronize with another woman, use of the synthetic cycle is required. Leuprolide injections (Lupron®) are used to suppress the ovaries and the uterine lining is prepared with estrogen and progesterone, the two major hormones produced by the ovary. Various preparations of the hormones can be used including possible injections, transdermal patches, pills and vaginal inserts, creams or suppositories.

In the case of pregnancy occurring in a synthetic cycle, there is a need to supplement the growing pregnancy with estrogen and progesterone that would normally be produced by the ovaries. Blood hormone levels may be checked and hormone therapy is withdrawn when appropriate. Vaginal progesterone will not produce high levels in the blood, but act directly on the uterine lining. Because women vary in the absorption and metabolism of estrogen and progesterone preparations, it may be desirable to check the response in advance of the actual procedure or to change the medications once a woman is cycling or is pregnant. Occasionally, two different preparations may be recommended.

Uterine Abnormalities and ART Outcomes

Obstetrical complications may occur more frequently in ART pregnancies and particularly if uterine abnormalities exist. It is routine to assess the uterine cavity within one year of ART by saline-infused ultrasound, office hysteroscopy or less reliably, hysterosalpingogram, the “dye test”. Examples of uterine abnormalities include women exposed to diethylstilbestrol (DES) exposure during fetal life, uterine polyps, fibroids and congenital uterine defects such as a septum or double cavity. Acquired uterine abnormalities may arise as scars from a D&C, myomectomy, C-sections and other uterine surgeries. Women with these types of abnormalities appear to be at greater risk for miscarriage, premature delivery and other pregnancy complications such as breech presentation and placental abnormalities. Ectopic pregnancies occur more frequently in ART pregnancies possibly due to uterine or tubal factors. The chance of multiple pregnancy is increased with ART and it is well recognized that multiple pregnancy (twins, triplets, etc.), whether occurring naturally or through medical intervention, increases the risk of complications and birth defects. Careful counseling prior to conception will help a woman to understand what these risks might be and to modify the number of embryos transferred to optimize outcomes.

If not available within the past 12 months, an evaluation of the uterine cavity by hysteroscopy or saline-enhanced ultrasound will be requested. If a woman declines to undergo the recommended testing to determine the shape of her uterine cavity, the possibility of uterine abnormalities may not be known. In that event, the best decisions regarding clinical care may not be made, and there may be an increased risk of undesirable outcomes such as miscarriages or premature birth.

Infectious Diseases and HIV (Human Immunodeficiency Virus) Antibody Tests

HIV is the virus that causes AIDS. Tests for previous exposure to the HIV virus are routinely performed on blood samples obtained from both male and female undergoing ART. A positive test indicates that you have been infected with the HIV virus and are able to infect others.

It has been the policy of the American Society for Reproductive Medicine (ASRM) to require that couples be tested for the presence of HIV and other infectious diseases. The purpose of this testing is to prevent the occurrence of AIDS (acquired immuno-deficiency syndrome) in a possible offspring. Women who harbor the virus, but have no symptoms of AIDS, may pass this serious disease to their offspring. The rate of fetal transmission may be reduced with treatment of an infected woman during her pregnancy. Men and women, whether or not they are symptomatic, may pass the virus to their sexual partners. Needle sharing with infected persons and blood products used medically are another means of transmission of the AIDS virus.

Infected people may harbor the virus for many years (up to ten years has been reported in some cases) without manifesting any symptoms of AIDS. The fact that a person harbors the virus and is potentially contagious may be determined by a blood test. The blood test may not be accurate in the first weeks or even months after contracting the viral infection, since the test measures the individual's immune (antibody) response to the virus, and this response takes time to fully develop. It is not clear whether all persons with HIV will ultimately develop AIDS, but careful medical follow-up is required.

Each state regulates the performance of the test; most states mandate that individuals being tested be educated/counseled about AIDS and about the implication of positive and negative test results. You may be asked to sign an additional consent for this test but provision of this education material to you acknowledges consent if ART is elected. In consenting to having testing for HIV, each member of the couple agrees to inform the other partner about the results of the test. In the protection of confidentiality, copies of HIV test results are not sent out without the written permission of the individuals.

Additional diseases have the potential to infect others through body tissues including sperm, eggs and embryos. Therefore, in accordance with the policies of the ASRM and American Association of Tissue Banks, individuals contributing sperm, eggs or embryos for ART, are tested for these diseases (e.g. HIV/AIDS, hepatitis B, C, cytomegalovirus (CMV), syphilis, and possibly chlamydia and gonorrhea). Blood typing is commonly added for donors and couples who are using donor sperm, donor egg or gestational carrier should be aware that the donor and/or carrier are tested for these infections. Unfortunately, the costs of these screening tests are not always covered by insurance. **NOTE:** In light of the limitations of this testing, there can be no guarantee that there will not be the transmission of HIV, or any other virus or illness.

Pregnancy and Birth Outcome in ART

Infertility is a recognized medical condition and as such it reflects inherent or genetic risk for abnormalities that pose risks to a couple's reproduction and to their children. Problems of fetal development and obstetrical complications may thus be more likely for infertile couples. This section addresses what is known and some of what is not known about pregnancy outcomes after conception with ART.

The chance that an ART procedure will result in a clinical pregnancy or a live birth depends on many factors unique to the couple. These are primarily the age of the woman, the quality of the eggs, the quality of the sperm, the number of eggs/embryos retrieved/transferred and the condition of the uterus. There are, and can be, no guarantees of success at this, or at any other ART program. There are many steps, or phases, to a cycle of ART, and the achievement of a live birth requires that each phase be successfully completed. Some patients will complete all phases of treatment, and others will not respond well enough to proceed to the next phase. It is realistic to consider that multiple attempts may ultimately be needed or that none of the treatment may be successful.

Whatever the course of treatment, the response of any individual patient cannot be predicted with certainty. Many patients are interested in the rates of pregnancy or birth achieved at this site. You are encouraged to discuss the methods utilized for calculating average clinical pregnancy or live birth rates with your physician. This information, together with a full discussion of your individual circumstances and history, is part of the process of gaining knowledge as to your own medical condition, and arriving at a reasonable understanding of your chances of pregnancy or birth following one or more treatment cycles. However, no matter how favorable the rate that may be projected for a given couple with a certain procedure, there are no guarantees of outcome.

For many reasons, ART may not result in a normal pregnancy, even though a full ART cycle is successfully completed. The principal reasons for this are the following:

- A majority of attempted ART cycles result in the transfer of at least one egg or embryo. However, only a small percentage of embryos will implant in the woman's uterus or continue development.
- Even after a missed menstrual period and a positive pregnancy test, early embryos may fail to progress.
- Embryos may not develop normally and may be spontaneously aborted (miscarriage). Miscarriage rates increase with a woman's age. ART pregnancies miscarry at similar rates to non-assisted pregnancies in women at the same age. The patients using IVF is generally older than the fertile population and would be

expected to miscarry more often. Other factors include the higher rate of multiple pregnancy in ART and earlier testing for and recognition of the pregnancy and of spontaneous miscarriage when it occurs.

- Ectopic or tubal pregnancies (where the embryo begins to develop outside the uterus) occur in a small percentage of pregnancies following ART. However, it occurs with greater frequency in infertile couples than the general population. Tubal pregnancies may be treated medically or surgically. Surgery may result in the loss of a fallopian tube, which, in turn, can further impair fertility. In rare instances, a tubal pregnancy may present a medical emergency in which the patient may go into shock as a result of blood loss and/or require transfusions and other treatment. Early diagnosis is essential for safe management.

The discovery of abnormal development, through ultrasound, amniocentesis or otherwise, might lead the couple to decide on a medical termination of pregnancy. Because infertile couples have risks above that of fertile couples, genetic screening by maternal blood (Non-Invasive Prenatal Testing, NIPT) and/or testing by chorionic villus sampling (CVS) or amniocentesis is recommended for all ART pregnancies and for women ≥ 35 years of age. Even an apparently normal ongoing pregnancy presents risks to both the mother and the baby, and does not guarantee a normal delivery at term of a normal infant. In ART pregnancies, as in pregnancies resulting from intercourse, serious unforeseen obstetrical complications occur. Such complications may result in miscarriage, the loss of the child in advanced pregnancy (stillbirth) or delivery of a baby too premature to survive. A prematurely born infant may experience serious or life threatening complications or permanent medical disability. The chance of premature labor and delivery is increased with multiple ART pregnancies (See section on Multiple Pregnancy in ART) and possibly for singleton pregnancies as well.

Congenital Malformations in ART

The chance of major birth defects in children born in the general, fertile population is about 3-4%. The chance that a child will be born with a major birth defect increases as the parents' ages increase, and genetic causes are responsible for approximately half of these birth defects. Congenital malformations are also more common in multiple pregnancies and possibly in couples who are infertile. Some studies that have compared malformation rates in fertile and infertile couples show an increased rate at 8 to 9%. Multiple gestation may have contributed to this difference. Examples of the types of defects include cleft lip, clubbed feet, cardiac and bowel defects, etc. Reports exist that associate hypospadias with ICSI (See section on ICSI). Beckwith-Weidemann Syndrome (obesity syndrome) has been linked with ART but as with all defects the differences in rates are small. There is no evidence to suggest that the most common genetic problems such as Down Syndrome or missing/extra chromosomes are increased in a pregnancy using ART. Screening blood tests, amniocentesis and/or chorionic villus sampling can aid in recognition of many of these defects early in pregnancy and should be discussed with your obstetrician. Some defects can be detected only by ultrasound screening. For this reason, we recommend ultrasound screening of the pregnancy especially in its early stages. However, not every type of defect can be detected with current technology.

In rare instances, pregnancy may result in serious harm or even death to the mother due to occurrences such as pulmonary embolism (blood clot to the lung), stroke or hemorrhage after delivery. There is no known increased risk for these complications in ART pregnancies. The infertility physicians will work cooperatively with the your obstetrician in early pregnancy. Details of the ART cycle, the pregnancy hormonal testing and ultrasound will be released to the obstetrician designated by the woman (and to the referring physician, unless indicated by the couple).

Multiple Pregnancy in ART

The rate of multiple pregnancy with ART has steadily declined as newer technologies allowed fewer but healthier embryos to be transferred, and in many cases, elective Single Embryo Transfer (eSET) is performed. Additionally, the rate of all types of complications greatly increases when there is a multiple pregnancy. Premature labor and delivery may occur more frequently in ART pregnancies and is expected with twins and multiple gestation. The health risks for premature infants increases the earlier they are born and the possibility exists for severe complications with potential life-long disabilities, if there is survival. Serious maternal complications increase, in general, with each additional gestation as shown in Table 1.

Table 1. Rates of Major Maternal Complications by Fetal Number

Number of Fetuses	Preterm Labor	Preterm Delivery	Gestational Diabetes	Pre-eclampsia
1	15%	10%	3%	6%
2	40%	50%	5-8%	10-12%
3	75%	92%	7%	25-60%
4	>95%	>95%	>10%	>60%

Source: American Society for Reproductive Medicine. Practice Committee Report. Nov 2000

When considering the possibility of these obstetrical and neonatal complications, couples may consider selective reduction to twins or singleton pregnancies. A couple having serious emotional, ethical, or religious reservations regarding the selective reduction procedure and or cryo-preservation, may wish to limit the number of eggs inseminated or embryos transferred to a number acceptable to them. Please discuss this with your partner first and then with your physician or other medical personnel BEFORE the ART consent session in order to note your preferences before treatment begins. Most patient will not declare a specific number to transfer, but will make the decision on the transfer day, when all information from the cycle is available.

Pre-Implantation Genetic Screening (PGS) and Diagnosis (PGD)

Normal human cells have 23 pairs of chromosomes, one of each pair came from each parent. Eggs and sperm have half of these. Abnormal chromosome number, called aneuploidy, is known to be the most common cause of miscarriages, and believed to be the most likely reason for an unsuccessful ART cycle. One example of aneuploidy is Down Syndrome (an extra chromosome 21, or trisomy). Aneuploidy most often arises from the egg and the chances of aneuploidy increase with the age of the woman's eggs. It is more common that chromosome pairs do not split evenly as eggs become older resulting in too many or too few chromosomes in the resulting egg. The goal of PGS is to select and replace embryos that are less likely to have chromosomal abnormalities, e.g. missing one chromosome (monosomy) or extra chromosome (trisomy). An abnormal number of chromosomes is usually lethal for embryos and they stop growing resulting in a miscarriage or fail to implant. Aneuploidy may also be associated with abnormal embryo development and early miscarriage.

Previous technologies did not allow for counting of all 23 pairs. Newer technologies, while expensive, aid in screening for all 24 distinct chromosomes (1-22, X, Y) contained within a normal embryo's cell(s). Genetic testing has allowed chromosomally abnormal embryos to be identified and withheld from transfer to the woman. The finding and transfer of normal embryo(s) raises the chances of successful pregnancy and reduces risk of miscarriage. In some cases, no normal embryos are found and transfer is not possible. Similarly, PGD uses genetic laboratory technologies to test cell(s) from an embryo, but for a specific genetic disease, which may be carried in some families, such as Sickle Cell, Cystic Fibrosis, Hemophilia, etc. Parents may be screened for these types of genetic disorders by doing a blood test called "Carrier Screening," that is offered (but not required) during the initial diagnostic testing. Often only the female is tested initially. Most are found to not be a carrier. If positive, the male is asked to be screened to exclude his carrier status. Therefore, PGD is particularly useful when both parents are determined to be "carriers" of the disease. PGD (single gene testing) is sometimes performed without PGS (24 chromosome test).

Pre-implantation genetic testing requires DNA from one or more of an embryo's cells, removed by making an opening in the shell (zona) surrounding the embryo (biopsy). Cell(s) is/are placed in a protective solution and sent via express mail to an outside genetic laboratory for testing. In order to complete the testing, the DNA of the cells must first be amplified many times to provide enough DNA to test. The results are usually available several days afterward and therefore not readily available prior to a fresh embryo transfer. There are two different stages of embryo development where a biopsy can be performed. A day 3 embryo biopsy (Cleavage Stage) involves removing 1-2 cells called blastomeres (from a total of 6-10 cell embryo) but this approach has been abandoned routinely as it may impair embryo development. Day 5 embryo biopsy is the preferred timing and involves removing 5-10 cells from the Trophectoderm (cells that become the placenta). The other type of cells in a day 5 embryo are called the inner cell mass (ICM) that go on to form the fetal cells, therefore these cells are avoided during the biopsy process. Embryo biopsy on Day 5 has some advantages by use of more than one cell, but requires cryopreservation of all developing embryos while awaiting the test results. Use of PGS/PGD results necessitates the thawing and transfer of embryos in a later Frozen Embryo Transfer cycle (see FET) with its additional costs. As technologies advance, a reduced turn-around time to results and lower costs may allow earlier selection and fresh transfer. While cryopreservation and later thaw/transfer is preferred. Some couples elect to transfer 1 or 2 embryos fresh (PGS unknown) and cryopreserve others while waiting on the PGS results. While the obvious concern is transfer and conception with an abnormal embryo, this has been the standard prior to the development of PGS, and fortunately, abnormal embryos rarely implant or progress to delivery.

Findings from use of PGS has been enlightening, revealing that the majority of eggs and subsequent human embryos are genetically abnormal. This is so common it may explain why humans do not conceive in every month of trying. It is expected that half or more of embryos sampled will test abnormally, and the rate will vary with maternal age. Once embryos are deemed genetically abnormal, they will not be transferred or maintained in cryopreservation. If cryopreserved before test results were available, embryos with abnormal testing will be routinely discarded.

Potential Risks and Benefits of Preimplantation Genetic Testing

Technical issues will prevent testing or reporting in some cases. For example, embryo biopsy may not be possible. One or more cells from embryos may not result in DNA amplification, preventing genetic analysis. In these instances, the genetic status may be unknown. It is assumed that DNA from the biopsied cell(s) represents the DNA of the remaining cells of the embryo. While true in theory, there are exceptions where embryos may contain a mixture of cells with different DNA (mosaic). Further some chromosome abnormalities can be missed with current technology. Thus, embryos with "normal" test results may still contain other abnormal chromosomes that were in cells not tested. Therefore, when a couple conceives after PGS, direct chromosome analysis by chorionic villus sampling (CVS) or amniocentesis remains recommended as standard of care, particularly for women ≥ 35 year of age. This is particularly true when an embryo with "unknown status" or embryos of mixed genetic status are transferred. In addition to the gold standard tests that involve invasive procedures, there is also a relatively new test called Non-Invasive Prenatal Testing (NIPT). This test is performed at 8 weeks or more of gestation and requires only a maternal blood draw. These pieces of fetal DNA found in the mother's blood can be tested for a subset of chromosome abnormalities (ONLY tests for chromosomes X, Y, 21, 18 and 13). The risks to offspring resulting from microsurgical biopsy of embryos are not fully known, but are believed to be acceptably low as the world-wide experience with PGD/PGS has not suggested significant detrimental effects to date. The genetic testing does not expose the patient to any greater risks of physical injury than already associated with ART procedures. There is no

guarantee or promise of a successful pregnancy, of the reliability of testing, or the genetic outcome as not all genetic disorders cannot be identified. In addition and summary:

Potential benefits from the use of PGS/PGD are:

- Decreasing the number of embryos transferred thereby reducing the chance of high multiple pregnancy,
- Increasing the chance of a normal pregnancy,
- Reducing the chance of miscarriage,
- Gaining information that may be applicable to your future care and fertility treatments and decisions.

Potential risks of PGS/PGD include but are not limited to:

- Recognized and unknown detriment to embryos,
- A decreased number of excess embryos that may otherwise be cryopreserved and stored,
- An error in diagnosis due to biological and laboratory technology issues,
- A missed genetic abnormality due to limitations of technology,
- Assignment of a genetically normal embryo as “abnormal”

As the use of PGS/PGD is voluntary, provision of your consent is required. Similar genetic information may be obtained after 8 weeks of pregnancy by NIPT, or with CVS or amniocentesis, as discussed above. Your decision whether to use PGS/PGD will not affect your current or future care at NewLIFE. Consent to use PGD may be cancelled at any time prior to embryo biopsy. By providing your signed consent, you have not waived any other legal rights as a patient.

The fees for PGS/PGD are additional expenses to ART treatment and you and/or your insurance company are responsible for payment. As genetic testing is relatively new, insurance rarely provides payment and you may be asked to make a deposit in advance. Information obtained during testing for aneuploidy will be recorded in your medical records. The U.S. Food and Drug Administration (FDA) and other licensed state/federal regulatory agencies may currently or in the future have the authority to verify the records.

DONOR SERVICES

OOCYTE (EGG) DONATION

Oocyte (egg) donation, available since the mid 1980's, involves harvesting one or more oocytes from the ovaries of a woman with normal ovaries ("egg donor"), inseminating it/them with the sperm of the intended father and transferring a number of any resulting embryos to the uterus of the intended mother. If pregnancy is established, the mother then becomes the "gestational" mother and experiences the pregnancy and birth, although she is not the genetic mother. Her partner providing the sperm is the genetic father. More recently, donated eggs can be cryopreserved (egg freezing) and stored until needed, making selection and use of donor eggs quite similar to the decades of using of sperm banks.

Working with national egg banks, NewLIFE has made available an oocyte (egg) donation service to treat infertility arising from the absence of ovaries or the inability of ovaries to produce healthy eggs. The service can also be used to help couples with potential genetic abnormalities. These services involve Assisted Reproductive Technologies, IVF, ICSI etc. Therefore, prospective users of donor eggs should read the ART sections of this document.

The participants, both the donor and the recipients, will be subjected to preliminary screening procedures, including review of medical records, physical examination, blood testing, screening for familial genetic and infectious disease, and psychological evaluation. On May 25, 2005 the FDA imposed specific and extensive regulations upon programs offering fresh donated eggs or tissues. The increased costs of screening and maintaining records have precluded access for some couples, but egg freezing has made the process easier and more accessible for patients.

Further, custody rights and other legal issues are less rigorous with the use of banked donor eggs or sperm. Legal disputes have arisen and demonstrated the complexity involved with fresh and known donor services. Further, state laws may vary. If concern exists, consultation with an attorney is recommended.

Oocyte (Egg) Donor Categories

Egg donors are usually healthy women between the ages of 21 - 28. The following are general categories of potential egg donors.

- Anonymous Donors - Many women opt to undergo the egg donation process as anonymous donors. These individuals donate eggs to infertile couples whose identities also remain anonymous.
- Known Donors - Due to the relative scarcity of egg donors, sisters, friends or others close to the recipient, frequently donate eggs. In addition, recipients sometimes opt to recruit an egg donor on their own. NewLIFE does not offer known donor egg services.

The primary benefit to every woman who donates eggs is the altruistic aspect of helping another person or couple to achieve pregnancy and motherhood. In addition, anonymous donors receive remuneration for their time, effort, inconvenience and discomfort and in some cases this provides some financial benefits to a donor.

Through the egg banking services, anonymous donors will be matched, as closely as possible, to prospective recipients according to the recipients' priorities as to ethnic background and physical characteristics. All donors are required to comply with FDA regulations for donated tissues, and for purposes of improved outcome they are usually non-smokers. Questionnaires about known familial and genetic diseases are used to identify potential risks, as extensively as may be possible, for at least two generations. Both the donor and her partner (if applicable) will be screened for genetic and sexually transmitted diseases such as Cystic Fibrosis, AIDS, hepatitis and syphilis, according to American Society for Reproductive Medicine and FDA guidelines.

Participants in the oocyte donation service must understand that there are limitations to relying on medical and family history in an attempt to exclude the possibility of genetic disease in a potential offspring. It is virtually certain that all human beings harbor genes that can, under certain conditions, lead to serious illnesses. It is likely that it will never be possible to test for all of these genes in either the egg donor or the genetic father. There are certain diseases with a strong genetic component, however, that would cause a donor to be excluded from participation in the service. Similarly, most of us have some genetic predispositions in our family for such things as mild high blood pressure, heart disease or cancer. Unless close relatives of the donor show tendencies for early onset of serious diseases, she will be allowed to donate.

It is not possible or reasonable to notify donors and recipients of a genetic disease in either the donor or the offspring developed or recognized in the future. There is no requirement for donors to notify the Egg Bank of their whereabouts or subsequent medical history. When offspring from donated eggs are noted to have a genetic disease, the Egg Banking service will provide notice to the practice and patient who received that donor's eggs. The long term emotional and psychological consequences of this form of family building are not known, especially when sisters or other close relations have ongoing involvement in the life of the child/children.

Selection of an Egg Donor and Preparation for Recipients of Donated Oocytes (Eggs)

Women electing to use donated eggs will work with the egg banking services, to identify the donor and to arrange for purchase and delivery of the eggs. Most donor banks provide 6-8 eggs per cycle. The banks have determined that the quality of these donor eggs is adequate to assure a high success rate (survival of the eggs after thaw, fertilization, development to the blastocyst stage, implantation and pregnancy). Because these young donors have high fertility, the current requirements are to transfer a SINGLE embryo, unless findings suggest otherwise. It is usually unnecessary to screen embryos for aneuploidy (PGS) because of the low risk in younger women.

The woman using donated eggs must prepare her uterine lining (endometrium) to be synchronized with the embryo in order for pregnancy to be possible. The woman's cycle may be manipulated with birth control pills and Lupron®. Once suppressed, the woman is instructed to initiate estrogen (oral and transdermal patches), followed by progesterone (vaginal and intramuscular preparations) to prepare the uterine lining for transfer of the embryos. To simplify this and to avoid errors, a daily schedule of medications is provided.

Once the timing of the Donor Egg/Embryo Transfer (DEET) cycle is set, the cryopreserved eggs are ordered for delivery just prior to that cycle. The husband's semen sample or other sperm source will be required on the day that the eggs will be thawed. Sperm are injected (See ICSI above) to increase fertilization rates assessed the next day, "Day 1." Embryos are kept in culture (see above ART sections) and reassessed on Day 3 and cultured until "Day 5" when embryos should have reached the blastocyst stage. A single embryo is typically transferred into the woman's uterus under ultrasound guidance (see Embryo Transfer, ET). Pregnancy testing is arranged in approximately 7-12 days after ET, and followed by ultrasound confirmation when visualization of heart activity is expected.

This entire process requires one menstrual month of management and has provided so many women with the experience of motherhood, when nature could no longer provide such an outcome. Patients are given ample time to ask questions of both the egg banking facilities and fertility team members. Paperwork to provide patient consent is required and provided prior to scheduling the DEET cycle.

USE OF DONOR SPERM FOR CONCEPTION

When there is a reduction in the number or quality or absence of available sperm, or if you are a single female or in a same sex relationship, it is especially important to consult with the physicians and other professionals in order to make decisions about treatment. One option to build families is the use of donor sperm. Increasingly, medical technology has allowed the use of a male partner's semen sample, even when the number of sperm and/or motility is extremely low. In some cases, fertilization may be achieved with "conventional" in vitro fertilization. Increasing the number of motile sperm placed with each oocyte may be sufficient to achieve fertilization in some or most oocytes. If fewer motile sperm are available, or if this approach does not succeed, microsurgical insemination of the oocyte may be the only feasible approach (see Intracytoplasmic sperm injection).

Using donor sperm for artificial insemination or with ART may be advisable when both the male and female partners have fertility problems, such as absent fallopian tubes with absent or poor sperm quality. In other cases, a woman may have no obvious fertility problems but a course of donor intrauterine insemination (IUI) for male factor infertility has not resulted in a pregnancy. Although the success of intracervical and intrauterine insemination (IUI) with frozen - thawed donor sperm appears to be lower than the chance of conceiving with fresh sperm, with ART the chance of fertilization is about the same as with fresh normal sperm. However, as with fresh sperm, occasionally fertilization may not take place. A separate CONSENT FORM is required for use of donor sperm samples.

Several national sperm banks (see list below) recruit and screen donors (anonymous donors) according to standards established by the American Society for Reproductive Medicine, Federal Drug Administration (FDA) and the American Association of Tissue Banks. These standards have been established to reduce the risk of transmission of genetic disease and of infectious disease, including HIV (the virus that causes AIDS). However, in spite of these precautions it is possible for donated sperm to harbor genetic abnormalities that may be passed on to the embryo and resulting child. Infected sperm or embryos may pass on a disease to the woman attempting pregnancy and/or the resulting child.

The sperm banks make every effort to assure the quality of the sperm samples they provide. Occasionally, the number of motile sperm may be lower than the acceptable guidelines at the time of thawing of the specimen. If so, the alternative is to use the sub-optimal sample, or forego treatment altogether for that cycle.

Occasionally, patients will choose to use donated sperm from brothers, friends or others known to the recipients. The sperm from such "known" donors must be screened in the same manner as anonymous donors and may not be readily available in local services.

Prior to initiation of a treatment protocol with donor sperm, a patient will be asked to select a sperm bank, obtain a current donor catalog and to provide a list of their choices in descending order. (see Selecting a Sperm Bank below) This is necessary because sometimes a first or second choice is unavailable at the time the order is placed. The patient will place the order with sufficient notice to have the sperm sample on hand prior to the ART procedure. If

the patient does not give sufficient time, the cycle may need to be delayed, postponed or canceled at the discretion of the physicians and other staff.

The risk of major birth defects following use of donor sperm appears to be the same as the general population. Similarly, there is no apparent increase in the risk of pregnancy complications.

Selecting a Sperm Bank and Donor for Insemination

Today, most patients needing such treatment choose anonymous donation from reliable, FDA-approved sperm banking facilities. The following will assist you in that selection process. **RESOLVE** is a national consumer organization serving the unique needs of those striving to build a family. Because choosing a sperm bank can be difficult and confusing, RESOLVE developed the following questions to guide members through their search for a sperm bank.

1. Do you keep a medical history on the donor?
2. How long do you keep these records?
3. Do you offer a service where adult children conceived through donor insemination can have access to the donor's medical records if necessary?
4. How much non-identifying information about the donor do you provide to the consumer?
5. Do you keep track of the number of pregnancies achieved per donor?
6. Do you require the donor to stay in your program for a specific time or provide a minimum number of donations in a six month period?
7. Can a consumer purchase and store sperm so that they can use the same donor for a second child?
8. What are the costs to store pre-purchased, reserved specimens?
9. If the specimen received is inadequate (poor motility, abnormal morphology or low count), what is the sperm bank's responsibility? (The American Society for Reproductive Medicine recommends at least 20 million sperm with 3+ forward motility per vial used.)
10. Does your information on each donor include:
 - Religious Background
 - Race
 - Physical Characteristics
 - Ethnic/Cultural Background
 - Educational Background
 - Career/Professional Role
11. Do you screen for: and
12. How often are the tests repeated:
 - Sickle Cell Anemia
 - Genital Warts
 - Chlamydia
 - Gonorrhea
 - Mycoplasma hominis
 - Hepatitis B
 - Hepatitis C
 - HIV (AIDS)
 - Syphilis
 - Tay-Sachs
 - CMV
13. Do you check and report the donor's blood type?
14. Do you test the donor for HIV (AIDS)? Do you use a donor's sperm before he tests negative for HIV (AIDS)?
15. Do you follow the recommendation of the American Society for Reproductive Medicine (ASRM) for holding specimens for 180 days before retesting for HIV and only then using the specimen?
16. Do you do genetic testing on donors?
17. What is the minimum age of your donors?

Additional/Optional Questions

18. Have you met and passed the accreditation process of the American Association of Tissue Banks (AATB)?
19. Do you offer a sufficiently varied donor selection to satisfy the needs of a diverse patient population?
20. What quality control measures do you take to ensure that the client is receiving the correct semen specimen?
21. Do you have a technical support staff such as a medical geneticist and cryobiologist? Is there a qualified medical director available for consultation? Can these resources be used in the event a patient requires genetic counseling, custom donor selection or adverse reaction management?

Some list those attributes to be considered in a donor such as race and/or ethnic group, height, build, eye color, hair color and texture, blood type and Rh if indicate. Other considerations may include: level of education, languages spoken, talents and hobbies, IQ and/or SAT scores.

Patients may open an account with most established sperm banks. However, a patient must be under a physician's care and usually produce an "Authorization for Release of Semen" signed by the physician. The patient may then have to file a request to establish an account with the pertinent personal and credit information. Payment for an order is usually required within 30 days of purchase. Shipment will be made directly to the physician in small liquid nitrogen containers that can store samples from 1 - 2 weeks. Samples will be shipped by one of any commercial shipping agents including FedEx, UPS, Delta Dash, or US Postal Service.

A limited non-selected list of commercial semen donor companies, addresses and web sites.

California Cryobank, Inc.
1019 Gayley Avenue
Los Angeles, CA 90024
866-9-CRYOBANK
(866-927-9622)
www.cryobank.com

Genetics and IVF Institute
3015 Williams Drive, Suite 108
Fairfax, VA 22031
800-552-4363 or 703-698-7355
Email: FamilyS@givf.com
www.givf.com

Biogenetics Corporation
187 Mill Lane
Mountainside, NJ 07092
800-637-7776 or 908-654-8836
Email: director@sperml.com

Cryogenic Laboratories, Inc.
1944 Lexington Avenue North
Roseville, MN 55113
651.489.8000 or 800.466.2796
E-Mail: info@cryolab.com
www.cryolab.com

Xytex Corporation
1776 Peachtree Street, Suite 175
Atlanta, GA 30309
706-733-0130 or 800-277-3210
E-mail: xytex@xytex.com
www.xytex.com

NW Andrology & Cryobank
508 West 6th, Suite #610
Spokane, WA 99204
1-800-786-5251
E-MAIL:
info@nwcryobank.com
www.NWcryobank.com

EMBRYO DONATION

A Donor Embryo Service is designed to address infertility arising from conditions which limit a couple's ability to produce healthy embryo(s) of their own. These include advanced maternal age and premature ovarian failure. It involves the timed transfer of donated embryo(s), which have been cryopreserved, to a uterus made receptive by a the administration of hormones.

Embryo Donation Categories

Potential Embryo donors fall into two categories:

- (1) In the case of **non-anonymous donors**, the donors selected agree to transfer their embryo(s) to a recipient previously known to them, as with a relative or friend. The donors and recipients may enter into their own agreements, independent of a standard consent form. NewLIFE does not offer "known" or non-anonymous sperm donation services.
- (2) **Anonymous donors** use the service to donate their Embryo(s) to unknown recipients. One can find more information on this topic through the National Embryo Donation Center. Phone 866-585-8549. They also have a website at: www.embryodonation.org

Preparation of Embryo Recipients

The participants in this service, both donors and recipients, will undergo preliminary screening procedures, including review of medical records, physical examination, blood testing, screening for familial genetic and infectious disease including sexually transmitted disease such as HIV (the virus that causes AIDS), hepatitis, syphilis and psychological evaluation. As these tests, specifically the testing for HIV, do not always detect antibodies at the time of testing, there remains a chance, although small, that the embryo resulting from the donor service may be infected. This could then infect the embryo recipient; conversely, an infected recipient could transmit an infection to an embryo or resulting child. Partners of donors and recipients will undergo screening and psychological evaluation of a more limited nature.

The endometrium must be synchronized with the embryo in order for pregnancy to be possible. For cryopreserved donor embryos and patients with ovarian failure, the cycle will be stimulated with sequential estrogen and progesterone. The estrogen is given orally or (through a patch) while the progesterone is administered vaginally, orally or by injection. Endometrial biopsy in a prior cycle may be necessary to assess the response to this synthetic cycle. For patients whose ovaries are functioning, even intermittently, it may be desirable to suppress ovarian function before synchronizing the cycle with the donor using oral contraceptive pills and/or leuprolide acetate (Lupron®).

Most embryos survive the freezing and thawing cryopreservation process to apparent viability. Because viability cannot be assessed until the thawing process is complete, the exact number of embryos available for transfer will not be known until the time of transfer. The clinical pregnancy and livebirth rates for cycles with cryopreserved embryos are generally lower than the corresponding rates when fresh embryos are used.

Because this type of assisted reproductive technology is relatively new, there may not be legislation, either at the federal or state law, which specifically addresses the issues surrounding the embryo donation process. Thus, the legal rights and obligations of the parties involved including the rights of the embryo(s) and the infant(s) born as a result of the donor embryo service, and the ramifications of the embryo transfer procedure, are not free from doubt. It is therefore strongly recommended that you consult **your own legal counsel** (even if you do not believe that you have any unanswered questions) so that you may be properly advised with respect to your rights and obligations as they relate to the donor embryo service.

While some physical attributes may be available from the donating couple, there can be no assurance that any particular set of physical characteristic will be achieved in any resulting children. All embryo donors should have completed a general questionnaire about known familial genetic diseases. This information may be made available to the recipients. There is not any procedure in place to enable couples to obtain and/or search for available information about the personal or medical conditions of their donors or their families subsequent to the embryo transfer process.

Before the commencement of the donor embryo procedure, prospective participants will be supplied with consent forms concerning the donor embryo service and will be required to give detailed written consents with respect to the procedure and its potential ramifications.

Gestational Carrier Services (NOTE: NewLIFE does not provide gestational carrier screening services)

A Gestational Carrier Service may address infertility arising from conditions that limit a woman's ability to carry embryo(s) to successful completion of pregnancy on her own. Gestational carrier involves the timed transfer of embryos to the uterus of the Embryo Recipient, another woman with demonstrated or presumed ability to sustain growth of the embryos. The participants in a Gestational Carrier Service, both genetic parents and embryos recipients, will undergo preliminary screening procedures, including review of medical records, physical examination, blood testing, screening for familial genetic and infectious disease, and psychological evaluation. Genetic fathers and recipient's partners undergo screening and psychological evaluation of a more limited nature.

Because this type of assisted reproductive technology is relatively new, there may not be legislation, either at the federal or state level, which specifically addresses the issues surrounding the gestational carrier process. Thus, the legal rights and obligations of the parties involved, including the rights for the embryo(s) and any infant(s) born as a result of the Gestational Carrier Service, and the ramifications of the embryo transfer procedure are not free from doubt. Therefore, it is strongly recommended that you consult **your own legal counsel** (even if you do not believe that you have any unanswered questions) so that you may be properly advised with respect to your rights and obligations as they relate to the Gestational Carrier Service. It is imperative, to protect the integrity of the process, that the embryo recipient avoid unprotected intercourse at various times during the treatment cycle. Since the response of both the ovaries and the endometrium is slightly unpredictable, in some cases the synchronization will not be possible and the embryos will be cryopreserved for transfer in a subsequent cycle, either using a natural or synthetic cycle.

Reasons for Participation in Gestational Carrier Service

In most cases, the genetic mother has had a hysterectomy, or has abnormalities of the uterus, such as fibroid or DES changes or other medical conditions, which restrict her ability to successfully sustain embryo growth. The genetic mother needs to have normally functioning ovaries that can produce healthy eggs, leading to healthy embryos, and tests are performed to determine this to the extent possible.

Potential Pregnancy Outcomes and Long Term Effects

All of the participants in the Gestational Carrier Service must realize that the establishment of a pregnancy cannot be predicted or controlled. In fact, pregnancy occurs in less than half of cycles in both natural and assisted reproduction. Furthermore, pregnancy entails risks to both the mother and baby. Even pregnancies that are progressing normally may encounter complications, some of them annoying or inconvenient, such as the need for bed rest, others serious or even life threatening. A woman who has had one or more uncomplicated births may not necessarily experience an easy uncomplicated pregnancy in later births.

Cesarean section (surgery to deliver the baby) may be required for the health of the mother or the baby and is almost customary for twins and triplets. It may be necessary to avoid intercourse during early or late pregnancy to protect the health of the mother or baby. Since the ability to transfer an embryo into the uterus of an unrelated mother is relatively new in human experience, there is very little information about the psychological consequences of gestational carrying. While it would seem desirable for the genetic parents to have a baby that is a product of their genetic heritage, there is little information on the consequences of using a surrogate on the genetic parents emotionally, or on their relationship with the child subsequently.

Similarly, the embryo recipient has no genetic relationship to the child, but has the most intimate kind of biological connection in other respects. The gestational carrier may not believe that it will be emotionally difficult to relinquish the child to the genetic parents after birth, but there have already been legal actions which allege that it has been difficult for certain women to sever their connection to the baby in that way. Since the embryo recipient can be a close friend or relation of one or both of the genetic parents, in some cases there may be an ongoing social connection between the carrier, her male partner, the genetic parents and the child. The impact of this arrangement on any or all participants in the Gestational Carrier Service has not been established.

The embryo recipient, her partner (if applicable) and the genetic parents will be screened for sexually transmitted diseases such as HIV (the virus that causes AIDS), hepatitis and syphilis. Because these tests (the HIV testing in particular) are not always accurate and reliable in detecting the presence of these diseases, there remains a chance that an embryo resulting from the Gestational Carrier Service will be infected despite contrary test results. This in turn could cause the recipient to become infected as well. Conversely, an infected recipient could transmit the infection to the embryo or any resulting child.

