ASSISTED REPRODUCTIVE TECHNOLOGIES (ART)

PATIENT EDUCATION DOCUMENT

Fertility Education Booklet - Version O

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

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GETTING STARTED

What do I need to know about ART and how to use this Document to optimize success?

The aim of assisted reproductive technologies (ART) is to help achieve a healthy pregnancy with a healthy mother and child. Every person you will meet in this practice works with you in various ways to help achieve this goal. An extensive evaluation has provided information directing your team of fertility specialists to recommend an optimal course of treatment that includes ART. To optimize ART success requires a "team effort" where patients have an important role in this effort, that can improve the chances that ART results in a successful pregnancy.

You should have received two Patient Education Booklets: 1) a General Infertility Patient Education, and this, 2) ART Patient Education Document. The purposes of these documents are to provide you an understanding of the many facets and procedures of ART, its terminology, implementation, alternatives, risks and outcomes. READ THE ENTIRE DOCUMENT and questions may arise that can be addressed and supplemented by many interactions and discussions with various clinicians throughout the process.

How to make better informed decisions about ART?

We are committed to providing our ART patients with accurate and comprehensive information about the services and medical treatments offered. This educational process includes various written materials and, most importantly, conversations and consultation with your physicians and other professionals, where general information is put into the context of your unique 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. This Booklet is a form of legal document and is a part of the process by which you provide written consent (permission) to perform various procedures. Please make notes and write questions in the space provided on the last page) as questions can be answered at the next office visit. Various topics and procedures that may not apply initially, should be read, as they may become important at a later time in your treatment. Please review these Booklets in their entirety and if, after consultation you decide to proceed with ART treatment, you will be asked to give your consent in writing. 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 these Booklets, other educational materials, and through conversations and consultation with medical personnel and that 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 voluntarily consent to the designated treatments.

How do I communicate with the office and other common 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: To be effective, patients have a responsibility to become educated, knowledgeable and compliant about fertility treatments, to read and understand written educational materials and to ask questions when needed. Because of the time limitations involved, these written materials should be your FIRST reference.

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 patient first, using any or all of the numbers provided, or, if necessary, may leave instructions on an answering device/voice mail. It is difficult, if not hazardous, to offer or manage patients in complex treatments by telephone, fax, email or recorded messages alone. As standard email is unsecured, but secured, one-way messaging by the Patient Portal is used to share documents and send specific written instructions to patients. Patient replies to the Portal and email are not useful for urgent messaging as they are not checked regularly or frequently. If you have pressing questions, please call your LOCAL OFFICE and, if necessary, leave a detailed message with that office. Messages are answered in an order based when they were received AND by the urgency of the information you provide. 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 your LOCAL OFFICES.

For URGENT matters arising AFTER OFFICE HOURS that require IMMEDIATE ATTENTION, call the **Doctor's Directory at 850-444-5507** and a message will be sent to on-call medical personnel at your LOCAL OFFICE. Menstrual starts, ovulation surges, scheduling of tests and medication refills are non-urgent matters and should wait for regular office hours. **NOTE:** non-urgent calls made after-hours may generate a professional fee. For true emergencies, call 911 (Do not call an office, as this will delay getting help).

3) Stressors and Anxiety: The entire NewLIFE Team makes efforts to reduce the common stressors while in treatment. Regardless of one's emotional strength, the "fertility journey" may become a significant stressor creating a need for 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 welcomed with a sigh relief, as many are reluctant to ask about it. Stress management may have more than mental benefits, as some published reports suggest successful pregnancy may be more likely with counseling! There are many counselors who are experienced with fertility and offer assistance to patients.

4) Primary Care and Ob/Gyn Physicians: When referred for fertility specialty care, fertility specialists act as consultants, providing care for infertility ONLY. Therefore, routine visits with your Ob/Gyn or primary care physician should be kept and scheduled, particularly for common gynecologic conditions: suspected infections, PAP smears, mammograms, etc. When you conceive, ultrasounds are provided to you for reassurance in the first trimester BEFORE you return for care with your Ob/Gyn.

Confidentiality: Communications with Other Physicians, Entities & SART Audit

In keeping with established HIPAA regulation, medical ethics and general medical procedures, details of the medical care received 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 patient/couple. If this is not desired, 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 patient/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. We routinely contact pregnant patients to follow up and confirm pregnancy success and outcomes. As to help advance this specialty, it is our practice to selectively report clinical treatment and results in scientific/medical meetings and journals without patient-identifying information.

What are possible personal financial responsibilities, insurance issues for ART?

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 patient/couple receiving these treatments. Financial responsibility for the pregnancy and any pregnancy-related 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 provided, including to determine likely insurance reimbursement. Unfortunately, payment by health insurance companies are often inconsistent, and patient costs may vary depending on unforeseen circumstances, insurance interpretation/denials and/or complications of the treatment. Insurance information obtained from limited and often ambiguous sources at insurance companies, cannot and does not

guarantee reimbursement, benefits and coverage. Claims that are later denied for payment by the insurance company become the responsibility of the patient/couple, not the insurance company. Asking your insurance company, or employee benefits manager, or reading about them in your policy manual may answer questions about insurance coverage. The right of this practice to change charges and fees is reserved without individual notification. This practice may not be contracted ("participating") with an insurance plan, but this may be irrelevant if the plan does not have fertility coverage. For more reading, see Insurance section of General Patient Information Booklet.

What financial resources might be available to help pay for ART?

While this Practice remains a national, industry leader for lower ART costs, today's technologically advanced services for assisted reproduction are inherently expensive. The latest advancements are needed for equipment, materials and disposable supplies, and importantly, the highly trained and skilled people who apply this technology. With so many other concerns, financial challenges should not be the greatest obstacle. Consider various 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. Lending companies that work with NewLIFE are 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. Home equity can be used to support these loans. Also, accumulated cash value can be borrowed from life insurance policies and retirement benefits such as 401(k) and pension plans.

Personal Credit Card 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. It's not for everyone, but it is amazingly effective for most.

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. Also, searching for alternative pharmacy options may offer lower cost medications.

BEWARE: Some companies act as "middle men", intervening between a patient's insurance company and fertility providers. These companies (e.g. ArcFertility, WinFertility, Progeny) take fees for arranging discounted ART services, but may try to limit patients' options for care, even if you are already established with your best option!

ASSISTED REPRODUTIVE TECHNOLOGIES (ART)

What are In Vitro Fertilization and Assisted Reproductive Technologies?

In general, ART includes interventions to aid in conception and pregnancy using sperm, eggs and embryos outside of the human body. In Vitro Fertilization, "IVF" literally means fertilization outside the body in a laboratory. 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 IVF cycle typically includes the following steps or procedures:

- Taking medicine to grow several eggs at once
- Removing the eggs from the ovary or ovaries
- Mixing eggs and sperm together so the eggs will be fertilized
- Growing any resulting fertilized eggs (embryos) in the lab
- Placement ("transfer") of one or more embryo(s) into the uterus
- Taking hormone medications to help you have a successful pregnancy

Sometimes, other IVF steps may be included:

- Injecting individual sperm into each egg, called intracytoplasmic sperm injection, "ICSI"
- Cryopreservation (freezing) of eggs or embryos that are not transferred to the uterus
- Genetic testing of the embryos for abnormal genes or number of chromosomes.

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How are eggs stimulated to develop?

When ovulating, a woman's body will naturally release a single egg each month. IVF increases the chance for pregnancy by producing several eggs at once. To accomplish this, patients use fertility medications consisting of oral medications and/or injections of natural hormones (Follicle Stimulating Hormone, FSH and Luteinizing Hormone, LH) to stimulate more than one egg from the pool that are available each month. As not every egg is normal, having more eggs improves the chance to obtain some of good quality. The purpose of this section is to explain how some of the medications may be used and their advantages, disadvantages, side effects and risks.

Gonadotropins, or injectable "fertility drugs" (Gonal f® or Follistim® Menopur® Bravelle®, low dose hCG (human chorionic gonadotropin) are natural hormones found in the body and are manufactured and approved by the Food and Drug Administration (FDA) for these purposes. These stimulating medications are usually given under the skin ("subcutaneously") and daily over 8 or more days. Oral medications, such as Clomid® and letrozole (Femara®) are used for ovulation induction in women who do not ovulate and may be used in ART.

Extra follicles growing may cause a woman to ovulate too early. Medications such as Lupron® (leuprolide acetate), a "GnRH agonist," and GnRH antagonists (Ganirelix®, Cetrotide®) and medroxyprogesterone acetate (Provera®) are used individually, to prevent premature ovulation that would lead to a cancelled cycle. Started too early, ovulation preventing medications may reduce the number of follicles responding, so timing is important. Lupron is FDA approved for other uses but has been used extensively for ART for over 20 years. In addition to hCG as an "ovulation trigger" to mature the eggs, Lupron® may be used before egg retrieval. Other medications that may be used include: contraceptive pills, patches, or rings; estrogen pills or patches; progesterone vaginal suppositories or injections; aspirin, heparin or Lovenox®, oral androgens, and transiently, antibiotics and steroids.

How are medications administered?

Patients are given a MEDICATION SCHEDULE for when and how much medicine to take each day. It is important that instructions are carefully followed, the prescribed dosage at the prescribed time. If in doubt, please call to ask questions during office hours. Our staff will teach you and your partner or another person how to administer subcutaneous ("SubQ") and, if needed, intramuscular ("IM") injections. Helpful instructional videos are also available online after hours. Other medications may be given by pills, skin patches, and vaginal suppositories.

What are medication risks and side effects?

Reactions to any medicine as an injection may include bruising, redness, swelling, or pain at the injection site. In rare cases, there may be an allergic reaction. Some women have bloating or minor discomfort as the ovaries briefly become enlarged. About 1% of women will develop Ovarian Hyperstimulation Syndrome (OHSS) [see section

below]. Other side effects can include headaches, weight gain, feeling tired, mood swings, nausea, or rarely, clots in blood vessels. Ovarian cysts (non-cancerous, fluid-filled structures in the ovary) may develop and in rare instances, require surgery requiring short hospitalization. Though rare, an ovarian cyst can result in the loss of an ovary due to twisting causing episodes of pain, or rupture with bleeding and blood transfusion(s).

It is inadvisable to avoid most fertility medications when pregnant, but it is sometimes possible to be pregnant even when it seems that normal menstruation has occurred. For this reason, women may be asked to have a urine or blood 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.

The Society of Assisted Reproductive Technology (SART) and the American Society for Reproductive Medicine (formerly the American Fertility Society) attempt to address concerns that using fertility drugs can cause breast, ovarian, or uterine cancer. These cancers are more common in women with infertility, so it is difficult to know whether the infertility is the reason for the cancer or the use of the medications. In current studies that take into consideration the increased risk of cancer due to infertility, there does not seem to be an increased risk of cancer due to the fertility drugs alone. More studies need be done to confirm whether there is an association of cancer with use of fertility drugs.

How will my cycle be monitored and what might cause a change or cancellation?

Vital to proper management, assessment of ovarian response to medications is accomplished with blood tests and/or ultrasound examination. Though at times uncomfortable, generally, ultrasound examinations are harmless and painless. The taking of blood samples (phlebotomy) allows measurement of hormones 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 issues may arise which may prevent the completion of an ART cycle. Most visits for this are scheduled well in advance. Inability to comply with scheduled office visits may require rescheduling or cancelling of a cycle. Treatment may be stopped prior to retrieval of eggs at a physician's discretion, for any reason that is believed to be medically appropriate. Cycle cancellation and changes can result in lost medication and some monitoring costs. Planned embryo cryopreservation, or its unexpected use for hyperstimulation (OHSS), has additional expense associated with delayed embryo transfers.

The MOST common reason to cancel treatment is for a low or poor response with few follicles and/or low estrogen levels. At times, one or two follicles grow too far ahead of others, reducing the total of mature follicles. Such cancellations occur in about 10-15% of started cycles but are much more often with higher female age, or when there is low ovarian reserve. It is important to realize, ovaries can respond variability between months, and that variability increases with maternal age. A low responding cycle may be converted to intra-uterine insemination (IUI), if the fallopian tubes are open, and follicle number is appropriate. Whether it is best to cancel and try again, convert to IUI, or to proceed to egg retrieval will depend on many factors, but generally, ART has higher success than IUI with 3 or more eggs. Other conditions may arise that lower chances of successful implantation by affecting the uterine lining. Overstimulation, or a premature rise in progesterone (breakthrough ovulation), or too rapid estrogen rise, polyps, or retrieval of many more eggs than expected may require cancellation or delayed embryo transfer. When some risks are known, it may be recommended in advance to "Freeze-Only" developing embryos and later perform a frozen-thawed embryo transfer (See section on FET).

When might delaying embryo transfer (freeze only) be recommended?

Both patients and the team of professionals desire the fastest and safest route to conception. Studies have consistently shown a lower chance of implantation and pregnancy when the uterine lining (endometrial lining) is over stimulated (too many eggs, too much estrogen) and when the embryo and the lining are not synchronized. The latter can occur if the embryos grow slowly, sometimes placing them behind the endometrium in a planned cycle of egg retrieval and fresh embryo transfer. Other research is suggesting that pregnancy complications (bleeding, hypertension, etc) may be reduced by frozen/thawed embryo transfer (FET cycles). Therefore, in some situations, if these concerns arise, your embryo transfer (ET or FET) will be postponed to a later month. These delays result in

additional costs in medications, cryopreservation, and thawing of embryos for a later transfer. While disappointing, these efforts offer the benefits of higher chances of successful and healthy pregnancy. Decision to delay embryo transfer is based on your stimulation, history, ultrasound findings and reports from the embryology laboratory.

Ovarian Hyper-Stimulation Syndrome (OHSS)

This is the most severe side effect of stimulating the ovaries. Signs of OHSS include increased ovarian size, nausea, vomiting, a buildup of fluid in the stomach, and weight gain >2 pounds per day. You may also have trouble breathing. In some cases, OHSS increases the level of red blood cells, and causes kidney and liver problems. In the most severe cases, it can cause blood clots, kidney failure, or death. All of these complications occur very rarely (in only 0.2% of all treatment cycles). OHSS may occur at two stages:

- EARLY, 1 to 5 days after egg retrieval (as a result of the hCG trigger); and
- LATE ONSET, 10 to 15 days after retrieval (because of rising hCG, if pregnancy occurs).

The risk of severe problems from OHSS is much higher if you become pregnant. For this reason, your doctor may suggest that your embryos be frozen for later use instead of transferring them in the fresh cycle. A frozen transfer can be done later, when there is no risk of OHSS. Management of OHSS may require DAILY assessments, lab tests, ultrasound and sometimes removal of abdominal or pelvic fluid that accumulates. To manage the fluid imbalances, hospitalization will sometimes be necessary. Rarely, removal of the ovaries may be required and other major complications such as internal bleeding, blood clots, stroke and kidney failure are possible.

It is impossible to reliably predict who will develop OHSS and it seems to be unique to some women but not others. When risk for OHSS development is suspected, some additional preventive and alternate medications may be prescribed during the ART cycle. If you experience 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.

EGG RETRIEVAL, FERTILIZATION AND EMBRYO TRANSFER

What is transvaginal egg retrieval or Ovum Pick Up, "OPU"?

Retrieval of eggs is critically timed to about 35 hours after the ovulation trigger. Therefore, you will be specifically instructed on when and how to administer this ovulation trigger injection (either hCG or Lupron). Eggs are retrieved in a medical office setting, routinely with pain management by deep conscious sedation. A special needle is guided by ultrasound through the right and the left corners of the vagina to enter the ovaries and each visible and safely accessible follicle (egg sac). Fluid suctioned from mature follicles usually contains one egg, but not every follicle yields an egg, and not every follicle is safely accessible. Occasionally, particularly with age >35 and low ovarian reserve, no useable eggs are found. This ultrasound-guided procedure usually takes 5-10 minutes.

What are risks of egg retrieval?

Surgical complications of egg retrieval are uncommon (less than 0.1%), but include, but are not limited to: internal bleeding and/or puncture of blood vessels, injury to bowel, bladder, ureters, uterus, ovaries and/or any other abdominal organ. Potentially serious and even life-threatening complications may require immediate surgery and/or blood transfusion. If major bleeding is recognized during egg retrieval, and does not resolve, surgery and other procedures may be required with hospitalization. Serious pelvic infections (including Pelvic Inflammatory Disease also known as PID) are rare (less than 0.1%) but 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 reduce your chance of future conception.

Anesthesia methods and risks of anesthesia will be discussed again prior to the procedure. Sedation may be administered under the direction of your physician by a qualified intravenous sedation nurse, anesthetist or other qualified personnel. A 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 and include but are not limited to, allergic reactions and side effects of drugs such as nausea or vomiting. In rare cases, use of anesthesia has resulted in breathing problems, cardiac arrhythmia / arrest, neurologic injury and death.

Failure to safely access some or any follicles, or failure to find any healthy, normal eggs is an uncommon complication of transvaginal egg retrieval. Other surgical approaches have been used to retrieve eggs, such as laparoscopy, but the ability to quickly arrange for surgery with general anesthesia at a local facility prevents it's use as a ready alternative.

Laboratory insemination, fertilization, and culture of eggs and embryos

Immediately after retrieval, eggs are transferred to the embryology laboratory where they are identified and placed in "culture media", fluid that supports the eggs in the incubator. For conventional insemination ("In Vitro Fertilization"), sperm are placed with the eggs in the culture media. For sperm injection (see ICSI below) cumulus cells surrounding eggs are removed to assess the egg maturity by microscopy. Egg maturity can only be assessed after the cumulus cells are removed. It is common and expected for 10-30% of eggs to be immature and not likely to fertilize. ICSI is always required for pre-implantation genetic testing (PGT) of embryos and commonly used for male infertility or use of testicular sperm. Once inseminated, eggs are returned to the incubator.

NOTE: Though not recommended, a patient/couple may elect to limit the number of eggs inseminated, and should discuss this topic making their preferences known at the time of providing written consent.

Embryo development usually proceeds along the following schedule:

- *Day 1*: This day eggs and sperm are expected to have combined and are checked for signs of fertilization. At this stage, the normally fertilized egg is still a single cell with 2 nuclei, called a 2PN or zygote.
- *Day 2*: Normal embryos will divide into 2 to 4 cells, usually remain in the incubator and not assessed.
- *Day 3*: Normally developing embryos will continue to divide and contain 4 to 8 cells.
- *Day 4*: The cells of the embryo begin to merge to form a solid ball of cells called a morula.
- *Day 5*: Normal embryos now have 100 cells or more and are called blastocysts, that have an inner, fluid-filled cavity and a small cluster of cells on the inside called the inner cell mass.

What is Intra-Cytoplasmic Sperm Injection (ICSI) and its risks?

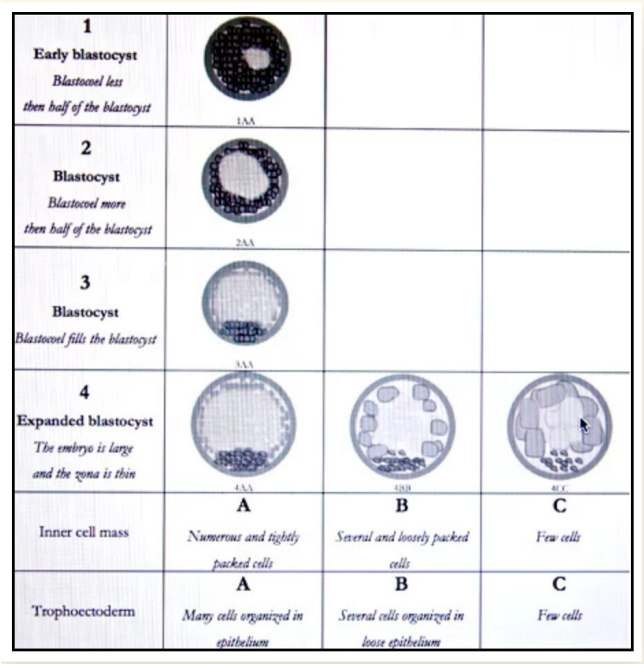
Intra-cytoplasmic sperm injection (ICSI) is a specialized, microsurgical form of insemination where a single sperm is placed into an individual egg to aid fertilization. With conventional insemination (IVF), very low fertilization rates are common for men with low numbers or abnormal sperm or semen. ICSI may provide live birth rates very close to those of IVF in men with normal sperm. In some cases, ICSI allows fertilization by sperm that are not motile but, contain normal DNA. As its use evolved, ICSI has become common for most ART cycles to avoid unpredictable and detrimental fertilization problem. ICSI is recommended for sperm retrieved directly from the testicle (vasectomy) and required for cases where genetic testing is planned for the resulting embryos.

ICSI involves direct handling of eggs/sperm and therefore adds to the chance of damage in the laboratory. Experience of the embryologist serves to reduce that risk to a minimum (1-5% of eggs). ICSI may be associated with a slightly higher risk of birth defects. It is hard to know if the increased risk is due to the ICSI procedure itself or to defects in the sperm. The risk of birth defects after ICSI is still quite small (4.2% compared with 3% in children conceived naturally). Experts are still debating the impact of ICSI on the mental and physical development of children. Most recent studies have not detected any differences in the development of children born after ICSI, regular IVF, or natural conception. Children conceived by ICSI have slightly more problems with their sex chromosomes (the X and Y chromosomes) than children conceived by IVF alone, but only by a very small margin (0.8% to 1.0% for ICSI pregnancies compared to 0.2% for IVF pregnancies). The reason for the difference is not clear. It may be caused by the ICSI procedure itself, or by the father. Men with sperm problems such as very low count and low motility are more likely to have genetic abnormalities. They often produce sperm with abnormal chromosomes, especially with abnormal sex chromosomes (X and Y). If sperm with abnormal chromosomes produce pregnancies, the pregnancies will likely carry the same defects. Translocations (a re-arrangement of chromosomes that can cause miscarriage or birth defects) may be more common after ICSI. Some men with extremely low sperm counts or no sperm have small deletions on their Y chromosomes. In some of these cases, sperm can be obtained to fertilize eggs with ICSI. Any sperm containing a Y chromosome microdeletion will pass on the deletion to any male child. These male children will also carry the microdeletion and may be infertile. A Y chromosome microdeletion can often, but not always, be detected by a blood test. This is because the chromosomes in the sperm may not always be the same as those seen when tested in the blood.

How are my embryos graded at the blastocyst stage?

While in culture, embryos are observed carefully and regularly by microscopy. A gradual reduction in number of viable embryos (attrition) is expected between egg retrieval and embryo transfer or freezing and embryos that stop growing are not viable. The visible appearance prior to transfer is important, but ultimately, the embryo quality is also reflected by the "invisible" DNA. A complete set of normal chromosomes is essential for establishment and maintenance of a healthy pregnancy (see Preimplantation Genetic Testing, PGT). It is believed that many, if not most, eggs and early embryos do NOT have normal chromosomes. Allowing embryos to grow to the blastocyst stage, usually Day 5 or 6, helps identify embryos with the best prognosis and is routine in this practice. Faster growing embryos with proper size and structural appearance are graded best. **Note**: Despite these efforts, grading of an embryo is not an absolute predictor of probability of pregnancy, so that "low grade" embryos will sometimes make "beautiful babies."

Table of Blastocyst Grading.



1 **Early blastocyst** *Blastocoel less then half of the blastocyst*	1AA		
2 **Blastocyst** *Blastocoel more then half of the blastocyst*	2AA		
3 **Blastocyst** *Blastocoel fills the blastocyst*	3AA		
4 **Expanded blastocyst** *The embryo is large and the zona is thin*	4AA	4BB	4CC
Inner cell mass	**A** *Numerous and tightly packed cells*	**B** *Several and loosely packed cells*	**C** *Few cells*
Trophoectoderm	**A** *Many cells organized in epithelium*	**B** *Several cells organized in loose epithelium*	**C** *Few cells*

What is Assisted Hatching and when might it be used?

Human eggs are surrounded by a 'shell' (zona pellucida or simply "zona") composed of a soft gel-like substance that after fertilization, holds the embryo 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 called "hatching." 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, but not all. This procedure is referred to as assisted hatching. The evidence does not suggest benefit in all cases, therefore its use may be recommended in individual cases before the ART cycle (primary assisted hatching), or may be recommended by an embryologist from assessment of the embryos (secondary assisted hatching). Assisted hatching is used frequently and as part of genetic testing of embryos. Hatching was most utilized PRIOR to use of blastocyst (Day 5) transfers. Assisted hatching is not routinely performed on healthy-appearing 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 in an effort to ease exit of the embryo that should take place within

the uterus and allows the embryo to establish direct contact with the lining of the uterus. The technique of embryo transfer is not changed by assisted hatching.

Potential Risks and Benefits

Each step of an ART process that involves direct handling of embryos in the laboratory, as with Assisted Hatching, some risk of damage exists. 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

What procedures and indications exist to obtain sperm?

Although ICSI has improved the outcomes for men with low semen quality, for some males, healthy sperm cannot be obtained from a semen sample, or semen cannot be produced. For example, the cause of some male infertility is an absence of the duct ("vas deferens" as in "vasectomy") bringing sperm from the testicle into the body. Other men will have blockage (obstruction) of this duct due to infection or surgery, such as 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, thus, avoiding the alternative of using donor sperm.

How are Testicular Sperm Aspiration/Extraction (TESA/TESE) performed?

Sperm may be aspirated from the epididymis located adjacent to the testicle, called Percutaneous Epididymal Sperm Aspiration, PESA, or directly from the testicle called Testicular Sperm Aspiration, TESA. In the most difficult cases, a aspiration is not adequate and a tissue biopsy of the testicle(s) is required to locate and remove sperm producing tissue, called Testicular Sperm Extraction, TESE. These approaches have offered great hope to infertile men to produce a genetically related child. Testicular sperm from these methods are usually few in numbers and may initially lack adequate motility as well. For this reason, microsurgical insemination (see section on ICSI) is required to optimize the possibility and percentage of eggs fertilized. Sperm from TESA and TESE are usually retrieved in advance, with TESE samples being cryopreserved for later use. In general, freshly retrieved sperm are preferred and TESA sperm are routinely kept fresh, incubating until the female's eggs are obtained. If sperm were confirmed on a previous testicular biopsy (TESE) and frozen, a fresh sample may be preferred, keeping the frozen sample as a "back up". Couples may be recommended and elect to order donor sperm as a "back up" option so that if sperm are not retrieved, the female's egg retrieval and ART cycle will not have to be cancelled.

What are potential risks and complications of sperm retrieval?

Anesthesia for sperm retrieval by TESA and TESE routinely involves topical anesthetic cream ("EMLA") and locally injected anesthetics (ie lidocaine), similar to how vasectomy is performed. Intravenous sedation may be offered for some cases. Deep conscious sedation may be provided by an intravenous sedation nurse or anesthetist or other qualified personnel. Most urologists will request general anesthesia for open surgical testicular biopsy (TESE). The type of technique used, and the risks of anesthesia will depend on findings and will be discussed prior to the procedure. Some TESE biopsies will be deemed inadequate for ICSI, despite rare sperm seen on a pathology report. 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 organs, and testicular failure/loss. The risks and benefits of these therapies will be discussed with your physician prior to consents and initiation of treatment.

EMBRYO TRANSFER

How do I prepare for Embryo Transfer (ET)?

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. A "trial" or practice transfer is not needed in every case. In some patients with cervical or uterine issues, the ease of transfer may be determined prior to the actual ART cycle by a trial transfer using an empty plastic catheter (tubing). If there are any concerns or prior difficulty, plans are made to optimize the actual transfer, by using special catheters or other instruments and occasionally dilating the cervix in advance. In the majority of 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 a 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.

How is it determined for a safe number of embryos to be transferred?

Not every embryo transferred during ART will implant, and not every embryo that implants will result in a "clinical" pregnancy (visible on ultrasound) or a live born infant. Age of the woman is likely the most important factor and allows more embryos to be safely transferred as maternal age increases. Other factors unique to a patient/couple affect success such as number, grade and growth rate of blastocysts available and whether genetic testing ("euploid embryo", See PGT) was used. Therefore, considerations for transferring more than one fresh (not frozen/thawed) embryo are best made when more information is available on the day of transfer. Patients may decline, if offered to transfer more than one embryo.

Multiple births (twins, triplets, etc.) significantly raise the risk of premature birth/complications and is to be avoided whenever possible and the routine use of blastocyst culture (see above) has helped significantly. NewLIFE adheres to the guidelines published by the American Society for Reproductive Medicine (ASRM) and will deviate from these (transfer more) when medically indicated or less if patient concerns or risks exist.

Recommendations for the limit to the number of embryos to transfer, (ASRM 2021)

Cleavage-Stage Embryos

Prognosis	Age <35	Age 35-37	Age 38-40	Age 41-42
Euploid[a]	1	1	1	1
Other Favorable[b]	1	1	≤ 3	≤ 4
Not Euploid or favorable	≤ 2	≤ 3	≤ 4	≤ 5

Blastocysts

Prognosis	Age <35	Age 35-37	Age 38-40	Age 41-42
Euploid[a]	1	1	1	1
Other Favorable[b]	1	1	≤ 2	≤ 3
Not Euploid or favorable	≤ 2	≤ 2	≤ 3	≤ 3

[a]Demonstrated euploid embryos, best prognosis

[b]Other favorable = Any ONE of these criteria: **Fresh cycle**: expectation of 1 or more high quality embryos available for cryopreservation, or previous live birth after a prior transfer with sibling embryo(s). **FET cycle:** availability of vitrified day-5 or day-6 blastocysts, euploid embryos, 1st FET cycle, or previous live birth after an IVF cycle.

Another influence in the decision to transfer additional embryos may be the couple's attitude regarding fetal reduction ("Selective reduction"), a procedure employed in early pregnancy to reduce the risk of a triplet of higher pregnancy down to twin or singleton pregnancy. Women with a higher pregnancy, and other health risks may have a general medical recommendation for fetal reduction because of the higher risk for premature delivery, infant death and babies with lifelong disabilities. Several publications suggest that fetal reduction is safe and effective for multiple 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, or employ pre-implantation genetic testing (see PGT). Please discuss this with your partner and with your physician or other medical personnel BEFORE providing written consent for ART, 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, Eggs, Sperm, and Tissues

Freezing (Cryopreservation or "Cryo") of living cells was developed, applied and has been successfully advanced over many years. The first birth with a frozen/thawed human embryo was in Australia in 1985. The best available data from around the world suggest similar chances of the usual birth defects in children born with and without use of cryopreserved embryos in an age-matched group of women. Cryopreservation of others, such as sperm, eggs and testicular tissues have advanced as well.

As the majority of risk, inconvenience and expense of ART arises from oocyte stimulation, retrieval and laboratory services, it is desirable to gain as much benefit from these steps. Use of cryopreservation with ART allows optimized ovarian stimulation, for more, good quality eggs without the obligation to transfer too many embryos at one time. And further, as presented above, postponement of embryo transfer is desirable or required if impairment of implantation or risks are suspected for a fresh transfer. Before starting an ART cycle, patients may choose to cryopreserve embryos for later attempts, when excess normally growing embryos (Day 5 or 6 blastocysts) result. Cryopreservation of embryos is required for use of Pre-implantation Genetic Testing (See PGT).

Embryos are routinely frozen using a process called "vitrification". With this process, structurally normal embryos are expected to survive cryopreservation and thaw at a high rate, approaching 90%. Among other factors, the age of a woman when the embryos were generated is likely the most important determinant of successful thaw/transfer and pregnancy. Embryos are usually thawed one at a time and after an initial thaw, failed survival or poor quality may suggest the need to thaw one or more additional embryos, if available. Despite extensive experience with these technologies, no guarantee can be made of a healthy pregnancy from a frozen-thawed embryo and damage to embryos from cryoprotectant agents, cryopreservation and long-term storage may have yet to be discovered.

What are legal concerns for cryopreservation and Long-term Storage (LTS)?

The laws regarding cryopreservation, ownership, control and disposition of cryopreserved embryos and other tissues are not completely developed or settled. 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 reproductive partners while in possession of this practice. Where donor eggs or sperm (gametes) are being used, the embryos are treated in a manner mutually agreed upon by the receiving patient/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 or recipient patient). And this decision shall be contingent upon their mutual consent or upon a legally binding and enforceable agreement, in writing, signed by these parties involved. If such embryos are legally determined to be property, the couple shall hold them jointly with all rights in the survivor.

Why is formal permission required for cryopreservation, storage and disposition?

Contingency Situations: In the event that a member of the couple should die, unless otherwise designated, the remaining partner will 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. Similar designations will be requested of couples in the events of separation/divorce and disappearance with failure to update contact information, resulting in inability to make changes in disposition.

Embryos cannot be donated unless the donating couple has fully assumed the responsibility of being screened for infectious diseases. This would allow the embryos to be readily donated anonymously to another infertile patient/couple. These screening tests need to be obtained at least 6 months after the cryopreservation of the embryos. If the embryos(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 or other parties regarding disposition of the embryos, the physician / 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 / 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 / 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.

It is practice policy to insist that each partner, or donor recipient patient, agrees, for himself and for herself and for his or her successors and heirs, to reimburse and indemnify the physician(s) / 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.

NOTE: Planned disposition of cryopreserved embryos/tissues: It is the policy of this practice to maintain only short-term storage of cryopreserved tissues for “imminent use”. When the use of stored embryos or other tissues is not imminent, the practice will routinely transfer such to a “long-term storage facility” (LTS). Therefore, it is inherent that couples recognize the right of this practice to transfer cryopreserved tissues to LTS after which maintenance and costs remain with the couple. After transfer, any future arrangement for disposition of these tissues 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. WITHOUT proper documentation for transfer to long-term storage or for other disposition, cryopreserved tissues retained at NewLIFE will be discarded at a time and in a manner AT THE SOLE DISCRETION of this practice.

Patients/couples will be informed from time to time of the fact that they have embryo(s) in storage at NewLIFE. Storage fees will be charged regularly with the right reserved by this practice to change such fees. If the patient/couple fails to pay for storage, or maintain current records, or provide notification of a change of address, or is unable to be located by phone or certified letter to their last known address, the tissues will be disposed of in an appropriate manner. The patient/couple recognizes that failure to reply to such notice within 30 days of the issue date, embryos or other tissues may be discarded AT THE SOLE DISCRETION of the practice. In requesting cryopreservation services, the patient/couple understands that: 1) their right to terminate cryopreservation services at any time is reserved, but requires a current, witnessed written request, 2) upon terminating those services, the patient/couple will be asked for instructions regarding what they wish to do with any embryo(s) then cryopreserved.

NOTE: Waiver of and limited liability for loss of cryopreserved tissues: 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/tissue cryopreservation, the patients/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 precluding maintenance of the cryopreservation containers, loss of liquid nitrogen supplies, governmental interference or regulation, war, rebellion, malicious intent and natural disasters, or any other cause not within the direct and immediate control of personnel and practice. This release extends to damage or loss of embryos in transit through standard courier services.

Egg Cryopreservation for Future Reproduction

When is egg cryopreservation for future reproduction recommended?

Cryopreservation technology advances allow storage of unfertilized eggs for future use, as an approach to fertility preservation. The most profound is the recognition that for most women, reproductive ability (the chance to conceive) gradually and progressively declines with age to menopause. With societal changes in the developed world, women are waiting longer to have families. This delay comes with increasing likelihood of infertility. Other health issues,

unique to a particular woman, may affect reproductive decisions as well. In general, common reasons and medical conditions for which a woman might consider egg cryopreservation are:

1) Expectation of a delay in childbearing until mid to late 30's;
2) Diagnosis of a cancer requiring chemotherapy and/or pelvic radiation that may reduce the number of eggs;
3) Female relatives (mother, sisters, maternal aunts) that have experienced earlier menopause, before age 45;
4) Diagnosis of advanced stage or aggressive endometriosis;
5) Having had extensive or repeated ovarian surgery for cysts, tumors, or other loss of ovarian tissue.

To cryopreserve eggs, women undergo ovarian stimulation and retrieval (see ART services above). Eggs are examined microscopically for quality and maturity, then cryopreserved without fertilization, and sent for long term storage (LTS). If and when they are needed in the future, eggs may be thawed with an expectation for survival and fertilization rates dependent on the age of the woman at the time of egg retrieval. Though relatively new, outcomes can be generalized from Donor Egg experiences. Donated eggs from women in early to mid-20's have uniformly good prognosis for conception and delivery, but this is not so with older women. Of course, some women may never need to use their stored eggs, but this service allows her to retain the sense of reassurance as a backup option.

What preparation is needed for Frozen Embryo Transfer (FET)?

During a natural menstrual cycle, the hormones produced by the egg's follicle prepares the uterine lining ("endometrium") for implantation of the embryo. With use of frozen/thawed embryos or with donated eggs or donated embryos, the uterine lining must be prepared synthetically using the same hormones, estrogen and progesterone. Natural cycles will, without notice, be abnormal, making synthetic cycles more reliable. Various preparations of these hormones may be used, including transdermal adhesive patches, oral pills and vaginal pills, inserts, creams or suppositories and injections. Absorption and effect of these are checked by ultrasound and blood testing prior to thaw/transfer of embryos. and assessments must be scheduled and performed at the specific times. If concerns arise, the type and/or route of hormone administration may be changed. Vaginal progesterone alone will not raise levels detectably in blood but acts directly in the uterus. Other medications that may be used for FET include antibiotics, steroids, subcutaneous Lupron®, metformin and low dose aspirin and heparin. A growing pregnancy requires ONGOING supplementation with estrogen and progesterone, so these medications should NOT be stopped unless and until directed by your fertility team.

What kinds of uterine abnormalities can affect ART outcomes and how are they tested/treated?

Congenital uterine malformations (bicornuate, septum anomalies) and acquired abnormalities, such as polyps, fibroid tumors and adhesions can lower implantation and pregnancy success. Scarring and adhesions may arise from a D&C, myomectomy, C-sections and other uterine surgeries. Additionally, "endometrial receptivity" can be reduced by the presence of inflammation, and endometrial dysfunction, possibly related to endometriosis. Women with some uterine abnormalities may be at greater risk for miscarriage, premature delivery and pregnancy complications such as breech presentation and placental abnormalities, and possibly ectopic pregnancies. Multiple pregnancy should be avoided in women with uterine abnormalities to avoid a much higher risk of obstetrical complications.

ROUTINE ANNUAL uterine cavity assessment is performed by one of three methods: saline-infused ultrasound (SIS), office hysteroscopy or less reliably, hysterosalpingogram ("HSG" or "dye test"). Reassessment should be performed after clinical pregnancies, uterine surgery, and vaginal or C-section deliveries. Testing for endometrial receptivity is less well defined, but may be assessed by ultrasound changes, endometrial sampling for microscopic inflammatory cells, genetic markers (Endometrial Receptivity Assay, ERA) or markers of inflammation and endometriosis (BCL-6) and progesterone-resistance (BCL-6).

Management varies by abnormality, with surgery needed for a septum, polyps, fibroids and adhesions. Antibiotics and steroids may be used for inflammation. Pre-cycle endometrial suppression or laparoscopic surgery has been suggested for women with repeatedly failed implantation and positive BCL-6 testing or endometriosis. Changing of hormone regimens and addition of other medications have been used to improve endometrial response and timing.

Why is testing required for infectious diseases and HIV (Human Immunodeficiency Virus)

Practice guidelines of the American Society for Reproductive Medicine (ASRM) and regulations by Food & Drug Administration (FDA) require that patients/couples be tested for the presence of HIV and other infectious diseases

(Hepatitis B, C). HIV(Human Immunodeficiency Virus) is the virus that causes AIDS (acquired immuno-deficiency syndrome). Tests for previous exposure to the HIV virus are routinely performed on blood samples obtained from both male and female undergoing ART. A positive screening test requires additional testing to exclude or confirm that you have been infected with the HIV virus and are able to infect others. The purpose of testing is to prevent transmission of HIV/AIDS and the other diseases to offspring. Women who harbor HIV, but have no symptoms of AIDS, may pass this serious disease to their offspring. Fortunately, when detected, the rate of fetal transmission may be reduced with treatment during a woman's pregnancy. Men and women, whether or not they are symptomatic, may pass these viruses to their sexual partners. Needle sharing with infected persons and blood products used medically are other ways of transmitting AIDS and other viruses.

Infected people may harbor HIV 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 reliable 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 to you of this education document and other materials acknowledges consent, if ART is elected. In consenting to having testing for HIV, each patient or member of a 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, syphilis, and for pregnancy planning women, chlamydia and gonorrhea). Patients/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.

NewLIFE maintains a policy to prioritize the safety and well-being of patients and potential offspring. Therefore, the following guidelines regarding infectious diseases and fertility treatment apply. NewLIFE reserves the right to defer/refer fertility treatment for patients with active infectious disease until the risks from the disease is appropriately managed. This precautionary measure is implemented to minimize the risks of transmission to potential offspring, and/or worsening disease related to a pregnancy. In order to protect unaffected partners and potential offspring, NewLIFE also reserves the right to decline fertility treatment for couples where the male intending to provide sperm tests positive for HIV/AIDS, hepatitis B,h hepatitis C, while the female partner does not. However, such coules have the option to proceed with treatment if they choose to use a donor for their sperm source.

Concerns regarding mosquito-borne ZIKA virus infection and fetal complications are a recent development. Patients planning to conceive should seek guidance from the Centers for Disease Control for the latest Travel Warnings and guidelines (https://wwwnc.cdc.gov/travel/page/zika-travel-information). Because a person infected may have no symptoms, a person or a partner who is potentially exposed (travels to a place known to have Zika-carrying mosquitos) is asked to delay conception for a variable time, and current serologic (blood) testing may not be a reliable predictor of exposure or infection. It is the patient's/couple's responsibility to inform the healthcare providers of their travel plans and potential exposures. Management will be based on review of current CDC guidelines and counseling.

What outcomes can be expected for pregnancy and birth after 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 successful pregnancy with a live birth depends on many factors unique to the patient/couple. Whatever the course of treatment, the response of any individual patient cannot be predicted with certainty. It is realistic to consider that multiple attempts may ultimately be needed or that none of the treatment may be successful. While it is important to discuss average success rates and use of data analytic services (such as UnivFy, and others) for estimation of individual success rates, there are no guarantees of an outcome.

Even after a completed ART cycle, a normal pregnancy may not result with principal reasons as follows:

- Embryos may not attach (failed implantation);
- Embryos may implant with a positive pregnancy test, but then may fail to progress (biochemical loss);
- Pregnancy may be visualized by ultrasound but may stop development (clinical loss, or miscarriage). Chance of miscarriage increases with age and ART pregnancies are lost at similar rates to non-assisted pregnancies in women at the same age. ART patients are generally older than the fertile population.
- Twins and triplets should be avoided for higher risks obstetric complications, loss and fetal malformations.
- Ectopic or "tubal" pregnancies are uncommon with ART but occur with greater frequency in infertile women than in general populations. They may be treated medically or surgically, and early diagnosis is essential for safe management.
- Obstetrical complications later in the pregnancy may result in a loss and may be related to maternal age, ART or being in an infertile population. 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 Table below summaries some risks of pregnancy with ART and with multiple gestation.

Risks of Pregnancy with ART

	Singleton Pregnancies			Twin Pregnancies		
	Incidence in IVF Pregnancies (%)	Risk compared to other infertile women	Risk compared to fertile women	Incidence in IVF Pregnancies (%)	Risk compared to other infertile women	Risk compared to fertile women
Gestational diabetes	8.2%	No difference	41% higher	10.7%	No difference	23% higher
Pregnancy-induced hypertension	12.6%	No difference	No difference	25.5%	No difference	15% higher
Placental complications	5.2%	95% higher	281% higher	4.9%	No difference	83% higher
Primary cesarean delivery	32.2%	10% higher	20% higher	65.4%	8% higher	17% higher
Low birthweight (<5.5 pounds)	7.7%	21% higher	65% higher	50.4%	No difference	No difference
Preterm birth (<37 weeks gestation	10.3%	26% higher	70% higher	53.8%	No difference	7% higher

Multi-fetal pregnancy reduction: 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 in advance a specific number to transfer, but will make the decision on the transfer day, when all information from the cycle is available.

What are risks to my baby conceived with ART?

The discovery of abnormal development, through ultrasound, or other tests, might lead the patient/couple to consider or decide on a medical termination of pregnancy. Because infertile patients have risks above that of fertile ones,

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. Risks to both the mother and baby persist in an apparently normal ongoing pregnancy, and thus a normal delivery at term of a normal infant is uncertain. In ART pregnancies, as in pregnancies resulting from intercourse, serious unforeseen obstetrical complications occur, which 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. Chances of premature delivery are increased with multiple (twin, triplet, etc) pregnancies (See Multiple Pregnancy) and possibly for ART singletons. ART babies are 5% more likely to have birth weight less than 5lb 8oz (2500 grams) than natural conceptions.

Does ART change the chance of babies with congenital malformations, "Birth Defects"?

The chance of birth defects in children conceived without ART in a fertile population is about 4.4% with severe birth defects is about 3%. Babies conceived with ART have birth defects about 5.3% and severe birth defects about 3.7%. Major birth defects increase with the parents' ages and may be increased by the abnormal reproductive function of the parents, infertility. Congenital malformations are also more common in multiple pregnancies. Examples of the types of defects include cleft lip, clubbed feet, cardiac and bowel defects, etc. Reports exist that associate hypospadias (abnormal penile urethral opening) with ICSI (See section on ICSI).

Imprinting Disorders are rare and are caused by genes of the mother or father that are not working. It is unknown whether such problems are linked to ART. Beckwith-Weidemann Syndrome (obesity syndrome) may be linked with ART but as with all defects the differences in rates are small. There is no increased risk of childhood cancers with ART except possibly for retinoblastoma (a cancer behind the eye). Long term development appears to be normal from most studies, and for babies without the risk of prematurity.

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 (Non-Invasive Prenatal Test, NIPT), 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.

When is use of Freeze Only (no fresh embryo transfer) cycles helpful?

Embryo cryopreservation techniques allow for successful storage, thaw and transfer for pregnancy. Accumulating evidence and clinical experience suggest that embryos may implant (attach) to the uterine lining at a similar or higher rate when transferred in a non-stimulated, controlled Frozen-thawed Embryo Transfer (FET) cycle. This suggests that for some women, uterine lining to be less receptive when stimulated. This concern exists for other conditions, such as Polycystic Ovary Syndrome (PCOS), endometriosis, recurrent pregnancy loss, or recurrent implantation failure and women with higher maternal age (>35), and/or low ovarian reserve, and delayed embryo development. Planning to Freeze-Only ("FO", no fresh embryo transfer) may reduce or circumvent some concerns.

When fertility injections are used to produce more than one egg, more estrogen production results. This excess hormone may cause the uterine lining to be "out of synch" with the developing embryos. This effect is exaggerated when more follicles grow than expected, a common finding with PCOS women. Women with endometriosis may suffer from a less receptive lining regardless of ovarian stimulation and early trials suggest that pre-cycle suppression of the lining prior to an ART cycle may give improvement. For other conditions where embryo quality is also a concern (age, low reserve, recurrent miscarriage), combining FO and PGT may improve the outcomes. In fact, some evidence reports that the combination of FO+PGT makes the couple's infertility diagnosis irrelevant to their success.

Results from well-controlled studies suggest that the improved implantation rates seen with freeze-only ART cycles may actually REDUCE the time to healthy delivery, and the overall cost of a delivery. This seems feasible, as there would be less failure and time in the fresh cycles, and more pregnancies per embryo transferred in the FET cycles. From the obstetrical perspective, early evidence also suggests that conceptions occurring in non-stimulated cycles

may have a lower risk of other complications such as elevated blood pressure, pre-eclampsia, low birth weight, and premature labor and delivery.

The “freeze only” approach allows full stimulation to generate more eggs and embryos, and use of blastocyst culture to cryopreserve better prognosis embryos, with or without PGT. In FO cycles, the chance of OHSS is markedly reduced or eliminated. Additionally, a patient’s stimulation regimen can be optimized for egg quality without regard for the uterine lining. Patients in FO cycles will not require the routine medications used to support the uterine lining, and their stimulation regimens are usually less expensive, saving enough to apply to the additional cost of FET. Additionally, FET enjoys more flexible scheduling. Your provider may discuss a Planned FO cycle with you.

PRE-IMPLANTATION GENETIC TESTING (PGT)

What is PGT and how can it impact ART outcomes?

Normal human cells have 23 pairs of chromosomes, one of each pair comes from a person's mother (egg) and father (sperm). Abnormal chromosome number, called "aneuploidy," is known to be the most common cause of miscarriages, and may be a common reason for an unsuccessful ART cycle. One example of aneuploidy is Down Syndrome (an extra chromosome 21, trisomy 21). Aneuploidy most often arises from the egg and the chances of aneuploidy increase with the age of the woman's eggs. As eggs become older it is more common that chromosome pairs do not split evenly resulting in too many or too few chromosomes in the egg and resulting embryo. The goal of PGT (formerly PGS, preimplantation screen) is to identify which embryos that are less likely to have chromosomal abnormalities, e.g. missing one chromosome (monosomy) or extra chromosome (trisomy) and higher potential for successful pregnancy. Most embryos with an abnormal number of chromosomes will fail to grow, fail to implant, or miscarry early in the pregnancy. Rarely, aneuploidy will result in a birth, but possibly with birth defects and health problems. Down Syndrome (Trisomy 21) and Turner's Syndrome (45X) can result in viable births, whereas other aneuploidies are lethal. PGT-A is screening for aneuploidy. PGT-M is screening for "monogenetic" single gene disorders, such as cystic fibrosis, sickle cell disease, etc, which can arise when BOTH male and female are "genetic carriers" or the genetic condition is Autosomal Dominant, meaning it can be passed from one parent to an affected child. Couples are routinely offered carrier screening before treatment and pregnancy. PGT-SR screens for uncommon structural rearrangements within chromosomes such as segmental loss or gain of DNA. PGT may detect embryos that appear to have mixtures of cells with different DNA, called "mosaic." Mosaicism can be limited to early placental cells and not always reflect the early fetus, and some mosaic findings may spontaneously resolve. Physical birth defects occur in 3-5% of all babies (cleft lip, clubbed feet, etc.) and may be due to multiple genes, maternal conditions or exposures ("multifactorial") and these may not be detected by PGT. PGT may not detect a condition of "balanced translocation" where embryos have complete DNA complement, but with rearrangements. PGT is also applied to determine the gender of an embryo, female XX or male XY.

Advances in genetic technology, while expensive, have allowed testing for all 24 distinct chromosomes (1-22, X, Y) contained within embryonic cells. Chromosomally abnormal embryos may be identified and withheld from use. Identifying and transferring normal embryo(s) may raise the chances of successful pregnancy and may reduce risk of miscarriage for the embryo chosen for transfer. In cases where no normal embryos result, transfer is not possible.

PGT does not guarantee that a pregnancy will occur, even if embryo testing is normal. Factors other than the genes also influence pregnancy rates. Screening the embryo's chromosomes, or testing for one specific genetic disease, does not guarantee that the embryo will be healthy and free of other disorders. For example, some common disorders that cannot be checked with PGT are autism and diabetes. Some birth defects can also occur even if chromosome screening is normal. An example of this would be a cleft lip or palate (failure of the lip and upper mouth to join properly).

Procedures to Genetically Test Embryos

Embryology Laboratory Services: An embryologist will make an opening in the shell (zona) surrounding the embryo to extract 3-10 cells from the early placental cells (trophectoderm) containing the DNA required for PGT. These cells are placed in a protective solution in an appropriately labeled container. While this is a tedious, critical process that requires expensive equipment and laboratory expertise, the embryology lab in this practice does NOT perform the genetic testing. These samples are sent via express mail to an outside genetic laboratory for testing.

Genetic Laboratory Services: The DNA in the few cells must be amplified many times to provide enough DNA material to tag with markers designed to show the presence or absence of each chromosome. The results are usually available 1-2 weeks afterward. PGT necessitates cryopreservation, thawing and transfer of embryos in a later Frozen Embryo Transfer cycle (See FET) which carries additional costs.

Findings from PGT have been enlightening, revealing that a majority of eggs and resulting human embryos are genetically abnormal. Aneuploidy is common and seems to explain why humans do not conceive in every month. It is expected that half or more of embryos sampled will test abnormally, and the rate will vary with maternal age and ovarian reserve. Embryos deemed as abnormal, "aneuploid" or "severe, high-level mosaic" will generally not be

transferred or maintained in cryopreservation. Cryopreserved embryos reported as abnormal, unsuitable or ineligible for transfer will be routinely discarded. Embryos may have variable degrees of mosaicism and will usually be reported as unsuitable for transfer, unless the abnormality is considered mild, limited or self-correcting. It is presumed that for decades prior to PGT, mosaic embryos were transferred without knowing, and negative consequences were not identified. Notwithstanding, consultation report from a Certified Genetics Counselor is required prior to planning the elective transfer of mosaic embryos, which should be a last resort when other options do not exist.

Potential Risks and Benefits of Pre-implantation Genetic Testing

Several concerns persist with PGT, generally categorized as:

Technical issues - inability to perform a biopsy or inadequate biopsy;
Missing, lost, delayed, damaged or destroyed samples during shipping;
Laboratory issues - DNA that is degraded or fails to completely amplify;
Uncertainty - DNA signals may not reach confidence limits set by the lab, reporting an "unknown" result;
Cell sampling that does not represent the fetus (ICM) - placental cells may differ from fetal cells (mosaic);
Abnormalities that are not detected or are too small to be detected;
Misdiagnosis – an abnormal embryo is reported as normal, or a normal embryo is reported abnormal;
Failure of cryopreserved embryos to survive thawing for transfer;
Other genetic/egg factors not detected by PGT - persistent effect of maternal age on successful pregnancy.

Technical issues will prevent testing or reporting in some cases. For example, embryo biopsy may not be possible. Cells from embryos may not result in adequate DNA amplification, preventing genetic analysis, resulting in an embryo with UNKNOWN status. In such situations, the embryo may be transferred unknown, or re-biopsy and retesting may be considered, though not recommended at this time, as it requires thawing, biopsy and re-freezing of the embryos, and may impair implantation. Single gene disorders (cystic fibrosis, sickle cell, etc) and small deletions, duplications and unbalanced translocations may not be detected by PGT-A. Thus, embryos with "normal" test results may still contain other abnormal chromosomes that were in cells not tested. Therefore, when a couple conceives after PGT, Non-Invasive Prenatal Testing (NIPT) of maternal blood, and sometimes by direct chromosome analysis by chorionic villus sampling (CVS) or amniocentesis remain 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. NIPT is performed in the first trimester of pregnancy and requires only a maternal blood sample. Fetal DNA found in the mother's blood can be tested for some chromosome abnormalities.

The risks to offspring resulting from micro-manipulation for biopsy of embryos are not fully known but are believed to be acceptably low as the world-wide experience with PGT has not suggested significant detrimental effects to date and recent, blinded PGT studies inferred no detriment of the biopsy process on implantation and birth rates. 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, or of the reliability of testing, or the genetic outcome, as not all genetic disorders can be identified. In addition, and summary:

Potential benefits from the use of PGT are:

Increasing the chance of a normal pregnancy,
Reducing the chance of miscarriage,
Identifying embryos that do not have a disorder or condition carried by parents,
Reducing the chance of conception with a high multiple pregnancy,
Gaining information that may be applicable to your future care and fertility treatments and decisions

Potential risks of PGT include, but are not limited to:

Causing a detrimental effect that may reduce the chance of pregnancy for the total ART cycle,
Detriment to embryos that is recognized or as yet unknown,
Decreasing the number of excess embryos that may otherwise be cryopreserved and stored,
Errors in diagnosis due to biological (sample of different cells) and laboratory technology issues,
Missing the diagnosis of a genetic abnormality due to limitations of technology,
Assignment of a genetically normal embryo as "abnormal" or the reverse (false positive, false negative)

What do I need to know to decide and consent for use of PGT?

A normal PGT result cannot guarantee a healthy baby or obstetrical outcome. The use of PGT is voluntary. Therefore provision of your consent is required. Consultation with a Genetics Counselor is recommended and available prior to requesting PGT to provide details and answer specific questions. After reviewing your medical findings, your physician will decide whether PGT may be offered but not recommended, recommended but declined by you, or not offered to you as being not indicated or potentially harmful in your particular situation. It is important to realize that embryos have been transferred fresh in ART for decades without use of PGT and without an observed increase risk for abnormal offspring. Accordingly, there remains some debate as to which patients benefit from and should use PGT. Note that similar genetic information may be obtained in the first trimester of pregnancy by NIPT, or with CVS or amniocentesis, as discussed above. Your decision whether to use PGT will not affect your current or future care in this practice. Consent to use PGT may be cancelled at any time, well in advance of the embryo biopsy or testing. By providing your signed consent, you have not waived any other legal rights as a patient.

The fees for PGT are additional expenses to your ART treatment and you are responsible for payment, even if results do not reveal useful information. As genetic testing is relatively new, insurance rarely provides coverage and you may be asked to make a deposit in advance. Information obtained during testing for genetic findings 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.

THIRD PARTY & DONOR SERVICES

USE OF DONOR OOCYTES (EGGS)

Oocyte (egg) donation involves harvesting one or more oocytes from the ovaries of a woman with normal ovaries ("egg donor"), insemination with the sperm of the intended father and transferring a number of any resulting embryos to the uterus of the intended, recipient 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.

This Practice does NOT recruit donors or procure eggs for donation. Working with national egg banks, this Practice 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 egg donor 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.

Egg banking programs recruit, screen and collect eggs from donors. The recipients will have 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 through national egg banking services.

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. This Practice 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. Embryos are kept in culture (see above ART sections) and reassessed on Day 3 and cultured until Day 5 or 6, 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

When there is a reduction in the number or quality or absence of available sperm, or for single females, or women 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 such as ICSI (see above) has allowed the use of a male partner's semen sample, even when the number of sperm and/or motility is extremely low.

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 such is found, the alternatives are 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. This Practice only offers use of donor sperm from FDA-approved sperm banking facilities and does NOT offer use of donor sperm from known (non-anonymous) donors.

Prior to initiation of a treatment protocol with donor sperm, a patient will be asked to select a sperm bank, peruse a current donor catalog and to provide a list of their choices in descending order. This is necessary because sometimes a first or second choice is unavailable at the time the order is placed.

NOTE: The patient will place a hold on the donor sperm selected and will order delivery to the Practice with sufficient notice to have the sample on hand prior to the ART or IUI procedures. However, the specimen should not be ordered until instructed to do so by staff. Samples delivered prematurely and not utilized will be discarded, if other storage arrangements are not made in advance. This Practice does NOT provide for long term storage of semen or donor sperm samples. Similarly, if the patient does not give sufficient time to make arrangements for delivery, the cycle may need to be delayed, postponed or canceled at the discretion of the physicians and other staff. A separate CONSENT FORM is required for use of donor sperm samples.

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 questions to guide members through their search for a sperm bank.

Some banks 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 indicated. 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 established under a physician's care for that physician and practice to receive and use a donor sample. The patient may 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's office in small liquid nitrogen containers that can store samples for up to 1 week. Sometimes delivery is made directly to the patient's address to be transferred to the physician's office for thaw and use. Samples will be shipped by one of any commercial shipping agents including FedEx, UPS, Delta Dash, or US Postal Service.

Below is a limited, non-selected list of commercial semen donor companies, addresses and web sites for example.

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

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

Biogenetics Corporation
187 Mill Lane
Mountainside, NJ 07092
800-637-7776 or 908-654-8836
Email: director@sperm1.com
www.sperm1.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

USE OF DONATED EMBRYOS

A Donor Embryo Service is designed to address infertility arising from conditions which limit a patient's/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 the administration of hormones.

Embryo Donation Categories

Potential embryo donors fall into two categories:

(1) In the case of **non-anonymous donor**s, 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. This Practice does not offer "known" or non-anonymous embryo 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 recipients for this service 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 (see Preparation for Frozen Embryo Transfer). 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 characteristics 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 SERVICE - NOTE: NewLIFE does not procure embryos to provide this service)

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. Because this type of assisted reproductive technology, 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. 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.

Notes and Questions: