

# IN VITRO FERTILIZATION

In vitro fertilization (IVF) is a procedure generally defined whereby eggs are removed from a female (the female patient or an “egg donor”) and fertilized in the lab (“in vitro”) with the partner’s or donor sperm. The resulting fertilized eggs (or embryos) are transferred to the uterus (the patient’s uterus or that of a “gestational carrier”) usually through the cervix after 3-5 days.

In vitro fertilization was originally developed to remedy infertility caused by fallopian tube disorders such as blocked or absent tubes. In recent years, it has become common to use IVF for treatment of unexplained infertility, male factor infertility, endometriosis and pelvic adhesive disease. This technology also allows achieving pregnancies in cases where eggs cannot be obtained from the female partner (IVF with donor egg) and/or where the female partner cannot carry the pregnancy (IVF with “gestational carrier”).

## COLLECTION AND PROCESSING OF A SEMEN SPECIMEN

For identification purposes, it is of vital importance that all semen samples collected are labeled with the subject’s name and clinic ID number.

*Under no circumstances will the lab accept unlabeled specimens!*

The optimal method for semen sample collection is masturbation. Samples should be collected following 2-5 days of sexual abstinence. It is RMIA’s preference that samples be collected on-site, but special conditions exist to facilitate off-site collection. All off-site collections require the use of a sterile container pre-tested for toxicity to sperm, which may be acquired from the RMIA lab staff. All samples should be delivered to the lab within 30 minutes of collection and kept protected from temperature extremes during delivery. It is extremely important that water, saliva, mineral oil, KY jelly, or any other form of lubricant do not contaminate the sample, as these materials are toxic to sperm. In specific instances where masturbation is not a viable option, the sample may be collected via sexual intercourse using a sterile, non-spermicidal condom obtained from the lab.

## INABILITY TO COLLECT A SPECIMEN

Occasionally patients are unable to collect a semen sample when scheduled. If collection problems are anticipated or your partner may be out of town on the day of collection, there is an option to collect and freeze a specimen in advance of your procedure for possible backup, however, whenever possible, a fresh specimen is always the specimen of choice.

Please be advised: In the event a fresh sample is obtained and the cryopreserved sample is no longer needed, RMIA does not automatically discard the sample. RMIA must obtain a written consent in order to either discard the semen sample or have the sample transferred to a long term storage facility.

## IVF: A STEP BY STEP GUIDE

Every cycle of IVF involves multiple steps, each occurring at a specific time.

### 1. IVF PHYSICIAN ORIENTATION SEMINAR

This presentation, a pre-requisite for all potential IVF patients, is presented by representatives of both our medical and administrative staff.

### 2. OBTAINING MEDICAL RECORDS

Prior to the Program Start appointment, all medical records pertaining to infertility testing or treatment must be sent to RMIA for review.

### 3. PRESCREENING

Prescreening consists of certain diagnostic tests, which **MUST** be completed prior to the Program Start appointment. Please refer to the “IVF Prescreening Checklist.”

### 4. PROGRAM START APPOINTMENT

Once all of the above prescreening has been completed, you will need to call the IVF coordinator to schedule a Program Start appointment.

The Program Start appointment consists of the following:

- You will meet with the medical assistant for ½ hour to review/update your medical history.
- A trial of transfer and sonohysterogram will be performed. This takes approximately 15 minutes. (For further details, see separate instructions for sonohysterogram and trial of transfer).
- You will then meet with the physician to discuss your individual protocol and sign consents. The IVF stimulation protocol takes into consideration your age, Day 3 lab results and prior response to stimulating medications. This consult takes approximately ½ hour.
- Unless additional testing or treatment is deemed necessary, a nurse will then schedule a tentative IVF retrieval date. You will be given specific instructions when to discontinue birth control pills, begin Lupron injections (as it applies to your treatment) and schedule your IVF baseline ultrasound.
- You will also meet with the Business Office personnel. **Payment in full for IVF cycles is due at this time.**

### 5. IVF BASELINE ULTRASOUND

This is a transvaginal ultrasound usually performed after you have discontinued birth control pills. The ultrasound is performed in order to evaluate the lining of the uterus as well as to

ensure there are no ovarian cysts present. At this time, you will have blood drawn for baseline Estradiol, Luteinizing Hormone, and Hemoglobin levels. Instructions for beginning ovarian stimulation will be given.

#### 6. OVARIAN STIMULATION

In order to optimize the chances of success, the production of multiple eggs is needed. Ovarian stimulation or “superovulation” is a process whereby medications are administered to stimulate the ovaries and increase the production of multiple oocytes per cycle. The administered dose of these hormones is greater than what your body would normally produce; therefore the ovaries will typically develop more oocytes than during a natural cycle. Ovarian stimulation may be achieved through a variety of medication regimens involving such fertility treatment drugs as Repronex, Menopur, Gonal-F, Follistim and Bravelle.

#### 7. MONITORING OF DEVELOPING FOLLICLES

Monitoring of follicular development is accomplished utilizing a combination of ultrasounds and blood Estradiol levels. Once administration of stimulation medications have begun, several subsequent office visits are necessary in order to accurately monitor your response to these medications. Schedule flexibility may prove helpful during this 2-3 week period due to the increased number of visits necessitated by patient response to stimulation treatment.

#### 8. FINAL EGG MATURATION/HCG ADMINISTRATION

Once follicular maturity has been achieved, the use of ovarian stimulation medication is no longer necessary. A single intramuscular or subcutaneous injection of HCG (Human Chorionic Gonadotropin: an inexpensive substitute for LH) will be administered 36-38 hours prior to the scheduled IVF retrieval time to provide for final maturation of the oocytes. The decision to administer HCG is based on both the serum Estradiol level, and follicular number, size and maturity.

#### 9. TRANSVAGINAL EGG RETRIEVAL

This procedure is performed 36-38 hours after HCG administration. The retrieval takes place in a procedure room adjacent to the IVF laboratory. A certified registered nurse anesthetist administers intravenous medication to minimize the discomfort that may occur during the retrieval and for several hours following the procedure. Once the anesthetic has been administered, your physician will place an ultrasound transducer into your vagina. He/she will then pass a needle alongside the transducer through the top of the vagina, and into your ovaries. The eggs and follicular fluid are then aspirated into a tube and transferred to the IVF lab where the eggs are examined microscopically. All mature follicles are routinely punctured and aspirated in order to obtain as many eggs as possible. At the completion of the retrieval procedure, you will be taken into a recovery room and observed for approximately 1 hour while the intravenous medication gradually subsides. When you are fully awake, have stable vital signs, and are taking liquids and solids without nausea, you may then be released to go home. It is possible to have some vaginal spotting and lower abdominal discomfort for several days following this procedure. Generally speaking, most patients feel completely recovered within 1-2 days. Most patients are able to return to work the day after retrieval.

Obviously, the number of eggs retrieved is related to the number of ovaries present (one of two), their accessibility and the number of follicles that develop during the administration of stimulating medications. Ultrasound and blood Estradiol levels provide only an approximation of the number of eggs that one can expect to recover. If no eggs are retrieved, there is an emotional let down that couples experience. Should this happen, please know that it is normal to feel depressed and/or experience grief.

**NOTE:** Every effort will be made to schedule your IVF retrieval and transfer with your primary physician. Please be aware, however, that at times, it may be necessary for another physician to perform your procedure.

#### 10. INSEMINATION OF EGGS

Once the follicular fluid is obtained, it is taken into the IVF laboratory where it is examined under a microscope to check for the presence of the egg. Optimal size follicles contain an egg in about 80% of the cases (this may vary with age and diagnosis).

Prior to insemination of oocytes, the semen specimen is prepared through careful washing with a culture medium. The resultant mixture is gently centrifuged so as to separate the active sperm from the seminal plasma. In most cases approximately 5,000-10,000 active sperm are placed in a specially-prepared dish with each oocyte.

#### 11. EMBRYO TRANSFER

The embryo transfer procedure is generally performed 3 days following the egg retrieval. However, depending upon your treatment plan and individual case, the embryo transfer may be scheduled for day 3, 4, or 5 following oocyte retrieval. The procedure itself is nearly identical to the trial of transfer, in that the same catheter type is gently passed through the cervix into the uterus. The embryos are deposited in the cavity along with the small amount of fluid. No anesthesia is required for the embryo transfer, however, to aid in relaxation, you will be asked to take 1-2 Valium tablets one hour prior to the transfer. The day of your transfer and the following day, bedrest is a requirement to help facilitate implantation of the embryo.

#### 12. LUTEAL PHASE SUPPORT

Under normal circumstances, progesterone is made by granulosa cells that remain in the follicle following ovulation. During egg retrieval, however, these cells may be removed along with the egg. Furthermore, there is evidence that pre-treatment with Lupron may, in and by itself, compromise progesterone secretion. Therefore, you will be given supplemental progesterone in order to prepare the uterine lining for implantation and support it during the early phase of your pregnancy. This daily medication will continue until your pregnancy test. If the test is positive, you may be advised to continue to take progesterone for several more weeks (usually until the time of the confirmation of pregnancy ultrasound). About half of the patients can discontinue treatment early (and safely) if they show sufficient progesterone secretion.

### 13. PREGNANCY TEST

A serum pregnancy test is performed 10 and 12 days following the embryo transfer. You will not be informed of the results until after **both** tests have been run. Since the pregnancy test is drawn shortly after the embryo transfer, two tests are necessary in order to ensure there is either an appropriate rise in the value (if positive), or there continues to be a negative value (if negative).

### 14. CONFIRMATION OF PREGNANCY ULTRASOUND/POST-IVF CONSULT

If the results of your blood pregnancy test are positive, you will be asked to schedule two ultrasounds at approximately four to six weeks after embryo transfer in order to confirm the status of your pregnancy. If the results of your pregnancy tests are negative, you will be advised to discontinue medication and schedule a post-IVF consult with your physician. At the post-IVF consult, both you and your physician will thoroughly discuss a plan for either the next fresh IVF cycle or frozen embryo transfer.

**CURRENT GUIDELINES FOR THE TRANSFER OF FRESH EMBRYOS  
 (1/1/2010)**

RMIA bases its embryo transfer guidelines on those issued by the American Society for Reproductive Medicine (ASRM). The recommended number of embryos, to be transferred, is mainly determined by the age of the patient, the stage at which embryos are transferred (day 3 or 5), as well as by factors associated with a “more or less favorable prognosis.”

The standard transfer policy of Reproductive Medicine & Infertility Associates (“RMIA”) is shown by age group.

<b>Patient Age</b>	<b>Number of Embryos Transferred</b>
< 35	Day 3: 2 3 if less favorable* AND patient agreeable Day 5: 2 1 if more favorable**
35-37	Day 3: 3 2 if more favorable*** Day 5: 2
38-40	Day 3: 3 Day 5: 3 2 if more favorable**
> 40	Day 3: 5 Day 5: 3
Recipients of donor oocytes (all ages)	1, 2, or 3 based on the age of donor (see above guidelines)

**\* Less favorable prognosis, day 3:**

- a. Two or more previous failed fresh IVF cycles  
 OR
- b. Poor embryo quality (No “good” embryo OR no ≥ 8 cell graded as “fair”) on a second cycle

**\*\*More favorable prognosis, day 5:**

- a. Previous successful cycle  
 OR
- b. First/second cycle with High quality day 5 embryos (Hatching Blastocyst, grade 2 or better, OR Blastocyst grade 1)

**\*\*\*More favorable prognosis, day 3:**

- a. Previous successful cycle  
 OR
- b. First/second cycle with two “good” embryos

# Reproductive Medicine & Infertility Associates

## IVF PRESCREENING CHECKLIST

*Please Contact RMIA for Specific Instructions Prior to Initiating the IVF Prescreening Process*

### **IVF ORIENTATION:**

- The orientation covers the entire IVF process: prescreening, ovarian stimulation, retrieval, embryo transfer as well as what occurs in the IVF lab
- Held at RMIA the second Thursday of each month (There is a DVD available for patients who live out of town).
- Please contact a scheduler to register

### **PRESCREENING LAB TESTS (FEMALE):**

- Day 3 Labs: E2, FSH, LH (these can be performed cycle day 2, 3 or 4 of your cycle).
  - Call on day 1 of full flow of menses to schedule test
  - These tests *must* be performed at RMIA
- Infectious Disease Testing (it is preferred that blood is drawn at RMIA but if you are an out-of-town patient, it may be drawn at your local clinic. In either case, the blood must be sent to Memorial Blood Centers for testing).

HIV 1&2 Antibodies, Hepatitis B Surface Antigen, Hepatitis C Antibody

  - Needs to be repeated once a year
- Blood Type (ABO Rh) (may be performed at RMIA or your primary care clinic):
- Rubella Titer (may be performed at RMIA or your primary care clinic)
- Antibody Screen (may be performed at RMIA or your primary care clinic)

### **BIRTH CONTROL PILLS:**

- You will be instructed to start birth control pills on cycle day-3 of your period, AFTER any necessary day-3 labs are drawn.

### **PRESCREENING LAB TESTS (MALE):**

- Semen Analysis
  - This test *must* be performed at RMIA and must be current within 6 months
  - 2-5 days of abstinence is required
  - Please refer to semen analysis patient information sheet for further information
- Infectious Disease Testing (it is preferred that blood is drawn at RMIA but if you are an out-of-town patient, it may be drawn at your local clinic. In either case, the blood must be sent to Memorial Blood Centers for testing). Kits are available upon request from RMIA for infectious disease labs, Fedex charges apply).

HIV 1&2 Antibodies, Hepatitis B Surface Antigen, Hepatitis C Antibody (only if partner is the sperm source)

**PROGRAM START: Once all IVF Prerequisites have been completed, a Program Start appointment can be scheduled, a \$500.00 retainer fee will be collected at this time in order to confirm and reserve your Program Start appointment. This \$500.00 will be deducted from the amount owed on the day of your appointment. You should still be on active oral contraceptives at the time of the Program Start, call a nurse if you are close to the end of your pack.**

- Program Start appointment Includes a clinic appointment with the physician, trial transfer, sonohysterogram, consent signing, and initiation of individualized infertility treatment plan, visit with business office including collecting payment for IVF cycle. Injection Teaching and tentative retrieval and transfer dates.
- This appointment will be scheduled when ALL of the above prescreening steps are completed and all previous records have been received**

**If you are using a Gestational Carrier, the following items are required in addition to the tests listed on the other side of this document:**

**\*\*\*NOTE:** no testing should occur until your Gestational Carrier has been approved. Please contact a scheduler to coordinate and schedule her prescreening.

- **QUESTIONNAIRES (FEMALE & MALE):**
  - Donor Prescreening Risk Factor Questionnaire – to be completed via telephone interview
  - Donor Application & Medical/Genetic History - fax the completed form to RMIA
  - Once the above forms/questionnaires have been reviewed/approved by the MD, you will be contacted to schedule the remainder of the IVF prescreening tests
- **PSYCHOLOGIST VISIT:**
  - Contact Debbie Simmons at 763-546-5797 for appointment and pricing.
- **LAB TESTS – INFECTIOUS DISEASE (FEMALE & MALE):**
  - RPR (syphilis blood test)
  - Hepatitis B Core Antibody (blood test)
  - Hepatitis B PCR (blood test)
  - HIV 1&2 plus 0 (blood test)
  - HIV 1 PCR (blood test)
  - GC/Chlamydia PCR (urine test)
  - Hepatitis C PCR (blood test)
  - Repeat testing for female, within 30 days prior to retrieval, for HIV 1&2 Antibodies, Hepatitis B Surface Antigen, Hepatitis C Antibody, RPR, GC/Chlamydia PCR, Hepatitis B Core Antibody, HIV 1 PCR, Hepatitis C PCR and Hepatitis B PCR.
- **LAB TESTS– INFECTIOUS DISEASE (MALE):**
  - CMV (IgG/IgM) (cytomegalovirus blood test)
  - HTLV I&II Antibodies (blood test)

**\*\*\*A cryopreserved semen specimen will be used for insemination of the oocytes (eggs), if at all possible. If the male's initial infectious disease testing is entirely negative, a semen specimen for cryopreservation will be collected within 7 days of the date the initial infectious disease test samples were obtained. If his initial infectious disease testing results are not entirely negative, other testing will be required (including a repeat of the infectious disease tests performed thus far). It is required that a complete panel of infectious disease tests be obtained within 7 days of the collection of the semen specimen. If a cryopreserved specimen cannot be used, then a complete panel of infectious disease tests must be obtained within 7 days prior to the egg retrieval.**

- **PHYSICAL EXAMINATION (FEMALE & MALE)**
- **LEGAL CONTRACT WITH GESTATIONAL CARRIER**

**If you are using Donor Oocytes, the following items are required in addition to the tests listed on the other side of this document:**

**\*\*\*NOTE:** day 3 FSH/LH and estradiol are not required if using donor oocytes (eggs).

- **PSYCHOLOGIST VISIT:**
  - Contact Debbie Simmons at 763-546-5797 for appointment and pricing.
- **QUESTIONNAIRES (FOR YOUR KNOWN DONOR):**
  - Donor Prescreening Risk Factor Questionnaire – to be completed by your known donor via telephone interview
  - Donor Application & Medical/Genetic History - have your known donor complete the form and fax to RMIA
  - Once the above forms/questionnaires have been reviewed/approved by the MD, both parties (recipient and known donor) will be contacted to coordinate and schedule your IVF prescreening.
- **LAB TESTS – INFECTIOUS DISEASE (FEMALE):**
  - RPR (syphilis blood test)
  - Hepatitis B Core Antibody (blood test)
  - GC/Chlamydia PCR (urine test)
  - Varicella titer

# IVF CRITERIA

## SMOKING POLICY

ALL patients (female and male) MUST quit all tobacco use (cigarette, cigar, pipe) one month prior to consent signing. Your IVF cycle will be postponed until tobacco use has stopped completely!

## AGE & BMI GUIDELINES

Program	Age	Body Mass Index (BMI)
Using Own Eggs	<ul style="list-style-type: none"> <li>• Fee for Service: &lt; 46</li> <li>• FCWP: &lt; 39</li> <li>• 100% refundable: &lt; 35</li> </ul>	<ul style="list-style-type: none"> <li>• Fee for Service: ≤ 35.0</li> <li>• FCWP: ≤ 35.0</li> <li>• 100% refundable: &gt; 19 and &lt; 33.0</li> </ul>
IUI FET Using Donor Eggs	<ul style="list-style-type: none"> <li>• Fee for Service: &lt; 51*</li> <li>• FCWP: &lt; 51*</li> <li>• 100% refundable: &lt; 51*</li> </ul>	<ul style="list-style-type: none"> <li>• Fee for Service: ≤ 37.0</li> <li>• FCWP: ≤ 37.0</li> <li>• 100% refundable: ≤ 37.0</li> </ul>

\*Any patient 45-50 will be required to have clearance from a perinatologist before doing any prescreening at RMIA. The letter is to be sent directly to us regarding clearance. And patient must be <51 at time of transfer. **NO EXCEPTIONS!**

## CALCULATING BODY MASS INDEX (BMI)

To calculate your Body Mass Index, find your height (inches) in the column on the left. Slide across to the right to find your weight.

Height (in)	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40
	<b>Body weight (lb)</b>																					
58	91	95	100	105	110	114	119	124	129	133	138	143	148	152	157	162	167	172	176	181	186	191
59	94	99	104	109	114	119	124	129	134	139	144	149	154	159	164	169	174	179	184	188	193	198
60	97	102	107	112	117	122	127	132	138	143	148	153	158	163	168	173	178	183	188	194	199	204
61	101	106	111	117	122	127	132	138	143	148	154	159	164	169	175	180	185	191	196	201	207	212
62	103	109	114	120	125	130	136	141	147	152	158	163	168	174	179	185	190	196	201	206	212	217
63	107	113	119	124	130	135	141	147	152	158	164	169	175	181	186	192	198	203	209	214	220	226
64	111	117	123	129	135	141	146	152	158	164	170	176	182	187	193	199	205	211	217	223	228	234
65	114	120	126	132	138	144	150	156	162	168	174	180	186	192	198	204	210	216	222	228	234	240
66	118	124	131	137	143	149	156	162	168	174	180	187	193	199	205	212	218	224	230	236	243	249
67	121	127	134	140	147	153	159	166	172	178	185	191	198	204	210	217	223	229	236	242	248	255
68	125	132	139	145	152	158	165	172	178	185	191	198	205	211	218	224	231	238	244	251	257	264
69	128	135	142	149	155	162	169	176	182	189	196	203	209	216	223	230	236	243	250	257	263	270
70	133	140	147	154	161	168	175	182	189	196	203	210	217	224	231	237	244	251	258	265	272	279
71	136	143	150	157	164	171	179	186	193	200	207	214	221	229	236	243	250	257	264	271	279	286
72	140	148	155	162	170	177	185	192	199	207	214	221	229	236	244	251	258	266	273	281	288	295
73	143	151	158	166	174	181	189	196	204	211	219	226	234	241	249	257	264	272	279	287	294	302
74	148	156	164	171	179	187	195	203	210	218	226	234	242	249	257	265	273	281	288	296	304	312
75	151	159	167	175	183	191	199	207	215	223	231	239	247	255	263	271	279	287	294	302	310	318
76	156	164	172	181	189	197	205	214	222	230	238	246	255	263	271	279	287	296	304	312	320	328

# OTHER ART PROCEDURES

## CRYOPRESERVATION

### **Semen:**

Prior to treatment cycles, patients may elect to cryopreserve semen samples. This option is often utilized by patients who:

- 1) Anticipate difficulty collecting a semen sample on the day of insemination or oocyte retrieval
- 2) May be unavailable for semen collection on the day of insemination or oocyte retrieval
- 3) May require surgical sperm extraction

Any semen sample cryopreserved at RMIA will be stored on-site for a limited time only. Patients will be advised as to RMIA's storage length limits and consequently be required to indicate their preferences for sample disposition beyond that time limit. These preferences must be documented prior to any cryopreservation. Furthermore, documentation of negative infectious disease testing is also a prerequisite for the cryopreservation of a semen sample. If infectious disease testing is positive and you wish to have a cryopreserved sample, it must be collected and stored at an outside facility. It is then up to you to have the sample shipped to RMIA no later than the baseline ultrasound.

In cases where cryopreserved donor semen is being used, it is the patient's responsibility to order enough semen for that treatment cycle only and to have it shipped to RMIA. The specimen should arrive by the patient's baseline ultrasound. If further treatment cycles are necessary, additional semen will need to be ordered. Since RMIA is not licensed as a long term storage facility, we cannot store donor semen samples for a duration longer than one cycle.

### **Embryos:**

In an ideal IVF case, there will be high quality embryos which are not transferred, a phenomenon which occurs in approximately 30% of all IVF treatment cycles. In these cases, the opportunity exists to save the extra qualifying embryos through cryopreservation. This process involves protecting the embryos from freezing damage through the use of compounds called cryoprotectants. These cryoprotectants replace water contained in the embryonic cells and protect them from ice crystal formation. Once frozen, the embryos are stable for many years and subsequently may be stored for use at a later time. The practical advantage of cryopreservation is that if a patient desires to have more than one child through IVF, the need to repeat a stimulation regimen to obtain more oocytes is eliminated.

There are several key factors in determining whether or not a frozen embryo cycle will be successful. The most important of these factors being the quality of the embryos at the time of cryopreservation. High quality embryos freeze or thaw at a much higher success rate than do poor quality embryos. At the time of fresh embryo transfer, a member of the RMIA staff will advise the patient as to which embryos appear suitable for cryopreservation. On average, of all

embryos frozen, greater than 90% of embryos survive. It must be recognized however that even high quality embryos may not survive the thawing process.

Due to the extended life of most cryopreserved embryos, each patient's intentions for the long-term storage of their embryos must be clearly documented prior to the cryopreservation process. Most clinics, including RMIA have on-site storage limitations for cryopreserved embryos. Therefore, if the patient's desired storage time exceeds RMIA's on-site storage limitations, the embryos will be transferred to a long-term storage facility. All options and requirements for the execution of those options will be explained to patients prior to any IVF treatment cycle.

### **INTRACYTOPLASMIC SPERM INJECTION (ICSI)**

ICSI is a laboratory procedure used to enhance fertilization in cases of poor sperm quality, reduced sperm number, and low fertilization rates. The procedure utilizes highly specialized instruments to microscopically inject a single sperm into each individual egg.

### **ASSISTED HATCHING (AH)**

Assisted Hatching is a laboratory procedure used to enhance the implantation of the embryo to the uterine wall. The technique involves the microscopic creation of a small opening in the shell surrounding the embryo.

# SONOHYSTEROGRAM

IVF preparation requires verification that uterine cavity is structurally normal and free of polyps or fibroids. This can be determined safely and effectively with a sonohysterogram.

This procedure is done between menstruation and ovulation (day 7 and day 10 of your cycle), or while taking the birth control pill. It is important that this test is not performed if pregnancy is possible.

While lying on the exam table, a speculum is inserted into the vagina. A thin catheter is inserted into the opening of the cervix and once properly positioned, the aforementioned speculum is removed. To facilitate uterine visualization, a transvaginal ultrasound transducer will be inserted into the vagina. A small amount of warm saline is injected through the catheter allowing the physician to evaluate the uterine cavity. The entire test takes approximately five to ten minutes. During saline insertion, you may experience a mild pelvic pressure sensation. This discomfort does not require any pre-medication.

*As a full bladder is required for a sonohysterogram **and** a trial transfer (see next page), please empty your bladder two hours before the procedure, drink 4-6 large (8 ounce) glasses of water then abstain from urinating again until after the completion of the procedures.*

*If you are scheduled for a sonohysterogram **only**, please empty your bladder prior to the procedure.*

Following the sonohysterogram, you may notice a slightly pink watery discharge for a few hours. If you notice increased abdominal pain, fever, foul smelling discharge, or heavy bleeding, please call RMIA at (651) 222-6050 for further assistance.

# TRIAL TRANSFER

Prior to undergoing an IVF cycle, it is necessary to assess the ability to insert the embryo transfer catheter as well as the actual depth of the cavity.

The trial transfer is similar to a pelvic exam or intrauterine insemination. After a speculum is placed in the vagina, a small flexible catheter is placed through the cervix into the uterus. You may experience a small amount of cramping as the catheter penetrates the cervix and again as the tip of the catheter touches the top of the uterine cavity. This cramping, similar in sensation to a mild menstrual cramp will resolve within 30-60 seconds.

The trial transfer is usually conducted [between menstruation and ovulation (day seven and day 10 of your cycle)] or while you are taking the birth control pill.

*As a full bladder is required for the procedure, please empty your bladder two hours before the procedure, drink 4-6 large (8 ounce) glasses of water and abstain from urinating until after the completion of the procedure.*

If you experience heavy vaginal bleeding, foul smelling discharge, fever or abdominal pain following this procedure; please call RMIA at (651) 222-6050 for further assistance.

# OVARIAN HYPERSTIMULATION SYNDROME

If ovulation induction medication is used to stimulate the ovaries, both a high level of estradiol and a large number of follicles may result. These changes in both the vascular system and the ovaries may result in the accumulation of fluid in the abdominal area, a condition known as ovarian hyperstimulation syndrome or OHSS. Ovarian hyperstimulation may range from mild to severe as symptoms often develop 7-10 days after the initial HCG injection.

## Signs and Symptoms

- Mild, moderate, or severe pelvic pain
- Nausea/vomiting
- Increased abdominal bloating
- Weight gain (greater than two pounds per day)
- Decreased urine output or very dark urine
- Difficulty breathing
- Constipation
- Diarrhea

## Managing Symptoms

- Increased rest in a reclined position
- Decreased activity level
- Increased fluid intake (Gatorade is the beverage of choice) 1 liter/day
- Psyllium products for constipation (i.e. Metamucil, Citrucel, etc.)
- Tylenol for pain management – 2 Extra Strength Tylenol every 4 hours as needed
- Increase intake of protein, i.e., chicken, steak

## Monitoring Symptoms

(The following parameters may be monitored in order to assess the severity of the OHSS)

- Body weight
- Abdominal girth
- Fluid intake and output
- Lab work

Please call our office immediately if you notice any of these symptoms or have questions regarding OHSS. (651) 222-6050

# FROZEN EMBRYO TRANSFER

The use of cryopreserved embryos affords our patients a second or even third opportunity to achieve pregnancy without undergoing another round of ovarian stimulation and egg retrieval.

Embryos may remain frozen indefinitely, and are usually transferred during a cycle in which the uterine lining has been stimulated using both synthetic estrogen and progesterone. (Note: greater than 90% of embryos survive cryopreservation and the thawing process. Those embryos may implant and develop into ongoing pregnancies at a somewhat lower rate than do fresh embryos.)

A frozen embryo transfer, like many other IVF procedures involves multiple steps, each of which occurs at a specific time during the menstrual cycle.

## 1. CONTACT CLINIC

If you are returning to the clinic for an FET following a pregnancy or delivery, please call the clinic and speak with a scheduler regarding which prescreening tests need to be updated, as well as what delivery information is needed.

## 2. SCHEDULE PRESCREENING TESTS

If the FET cycle is occurring immediately following a fresh IVF cycle, much of the necessary prescreening has already taken place. However, if the completion of your previous IVF prescreening was longer than 6 months from the current date, the following infectious disease tests may need to be updated.

- HIV 1 & 2
- Hepatitis B antigen
- Hepatitis C antibody

## 3. SCHEDULE CONSULT / SONOHYSTEROGRAM / TRIAL TRANSFER

To assist in scheduling both the sonohysterogram and trial transfer, you may be asked to begin taking birth control pills on day 3 of your menstrual cycle. This will be discussed with a nurse prior to scheduling.

# CRYOPRESERVED EMBRYO STORAGE

## **Regular IVF Program**

At a cost of \$60 per month, any remaining embryos may be stored at RMIA for up to one year.\* Upon the conclusion of this year, any remaining embryos left in storage will automatically be transferred to ReproTech Ltd., a long-term cryopreservation storage facility located in St. Paul, Minnesota. (Please refer to insert)

## **Fertility Cost Warranty Program**

Any remaining embryos may be stored at RMIA for up to one year at no cost.\* Upon the conclusion of this year, any remaining embryos left in storage will automatically be transferred to ReproTech Ltd., a long-term cryopreservation storage facility located in St. Paul, Minnesota. (Please refer to insert)

\*Note: If either the female or male patient has tested positive for an infectious disease, their embryos will not be stored at RMIA under any circumstances. In these instances, the patients incur payment of all possible charges associated with cryopreservation including transportation and storage fees.

The primary fear of my patients is that embryos could get mixed-up or that a problem may occur during shipping. I have full confidence in Reprotech to keep paperwork organized and accurate, keep embryos well categorized and keep the embryos completely safe during transport. That gives my patients confidence as well.

— Randle Goffman, M.D., Ph.D.

We store embryos for one year and then transfer everything to Reprotech. This process gives me great peace of mind because Reprotech is now keeping track of patients' records and is responsible for the final disposition of the embryos. And they do a terrific job at it, freeing me of the emotional, ethical and potential legal concerns.

— Neil Roberts, Lab Supervisor

Since Reprotech works directly with our clients and their longterm storage needs, it's important that they represent themselves extremely well. Reprotech has proven they have a higher standard in this than we would ask of ourselves. They have shown me through their organizational practices that they can be trusted. They have an established protocol for semen or embryo transfer that never varies. The same is true for documentation. Everything is tightly controlled. Deliveries are scheduled well in advance and always on time.

ReproTech has done an excellent job for us and I strongly recommend anyone needing longterm storage to trust the process to Reprotech.

— Klaus E. Wipmer, Ph.D.



**REPROTECH**  
LIMITED

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1/06



**REPROTECH**  
LIMITED

## The Cryostorage Experts You Can Trust



integrity

experience

reliability

understanding

## What is ReproTech, Ltd.?

ReproTech, Ltd. (RTL) is a one-stop resource specializing in effective solutions to the challenges faced in today's ever-changing field of Reproductive Medicine. ReproTech's experienced staff provides expert consultation services for long term storage of reproductive tissues and donor program management to assist in compliance with regulatory agencies.

## Why Use ReproTech, Ltd.?

Credentials\* - ReproTech, Ltd. is proud to be:

- Established in 1990 as a long term storage cryobank
- Inspected and Accredited by the American Association of Tissue Banks
- Inspected and Licensed by the New York State Department of Health
- Licensed by the California State Department of Health
- Member of the American Society of Reproductive Medicine
- Each regional facility is staffed by experienced personnel

\*Not all sites share the same credentials. Please see our website for site specific credentials.

## Service

In some cases, clinics find the responsibility involved in long term cryopreservation warrants third party involvement. ReproTech, Ltd. is equipped to meet the specific needs of these patients, thereby releasing the clinician and laboratory staff of a long-term commitment. By acting as the contract holder with the patient, RTL assumes responsibility for transfer and storage of cryopreserved tissue.

## Potentially Infectious

RTL provides storage services for patients who have tested positive for a sexually transmitted

disease such as HIV, Hepatitis B, Hepatitis C, HTLV I & II, syphilis or any communicable disease. In addition, we supply a shipping tank into which these cryopreserved tissues are immediately transferred and shipped to RTL for storage. We have separate shipping and storage tanks that are used only for potentially infectious tissue.

## Storage Management

Many IVF clinics agree to store their patients' specimens for a short time (one year or less), thereby reducing the need for clinics to purchase additional storage tanks. At the end of that time, the patients are required to decide whether to continue with long term storage, dispose of, or use their gametes and/or embryos. Specimens from patients choosing to continue storage are transferred to RTL.

## Safety

RTL uses state-of-the-art storage tanks which are replenished regularly and are continuously monitored 24/7 with a state-of-the-art system which detects temperature changes as small as .01 of a degree Celsius. In keeping with AATB Standards, documentation of storage tank function is maintained. Documentation of effective specimen transfer is completed using quality control measures.

AATB and NY State inspections have confirmed the effectiveness of RTL's procedures for specimen transfer and storage.

## Testing Requirements

Standard storage fees are assessed for individuals who have completed at least Anti-HIV 1&2(AIDS) testing. Specimens will be accepted without Anti-HIV 1&2(AIDS) testing at a higher storage fee.

Standards and/or Regulations require that patients complete the following serology/virology testing prior to release of specimens from RTL for transfer back to patients' clinic for their use: HBsAg and Anti-HCV, in addition to Anti-HIV 1 & 2.

## Transfer Of Specimens

ReproTech uses specially designed dry liquid nitrogen transport shippers for specimen transfer via an overnight air courier. Due to the valuable nature of the specimens, RTL's standard shipping protocol recommends the use of two transfer shippers in order to split the shipment. We make all of the arrangements for the transfer and prepare the necessary return shipping paperwork. Documentation verifying transfer of specimens follows each shipment.

RTL documents the successful transfer of transported specimens through the use of a temperature exposure indicator which monitors the cryoflask environment throughout shipping.

## Withdrawing Specimens

The patient may have his/her/their specimens withdrawn at any time upon the request of a licensed physician or designee. Patients must complete RTL's notarized Authorization to Release and required testing. With a nominal charge for shipping, the specimens can be easily transported to the requesting physician.

## Disposition Options for Embryos

Three options are provided for final disposition of embryos: anonymous or directed donation to another recipient, donation for research (stem cell, embryo development, etc.), or destruction. Donation options depend on specimen quality and/or donor screening/testing results. RTL requires documentation of final disposition, including notarized signatures of our patients.

Visit our web site at [www.reprot.com](http://www.reprot.com) for a complete listing of RTL's services and fees.

## Fee Schedule

STORAGE FEES	Standard	Potentially Infectious
<b>Sperm or Egg</b>		
Quarterly	\$75	\$113
1 Year	\$275	\$413
2 Year	\$490	\$735
3 Year	\$705	\$1058

*Inquire about longer term storage fees.*

<b>Embryo</b>		
Quarterly	\$106	\$159
1 Year	\$400	\$600
2 Year	\$700	\$1050
3 Year	\$1000	\$1500

*Inquire about longer term storage fees.*

**ADMINISTRATIVE**  
Account Setup Fee **No Charge**  
Handling Fee **No Charge**

**SHIPPING**  
**Local Medical Courier\*\* \$75-125**

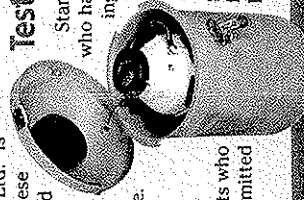
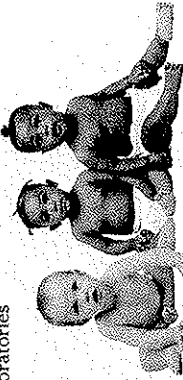
**Overnight Air Courier**  
One Tank **\$190**  
Two Tanks\*\* **\$350**  
Potentially Infectious (one tank) **\$190**

\*Available within metro area of each RTL Office  
\*\*Two tanks recommended if specimens packaged in multiple storage cases.

Shipping Fee may be reduced if clinic arranges for group shipments from clinic to RTL.

**Consultation Services**  
Reproductive Clinics & Laboratories

Call for pricing



*Each of our three regional storage facilities are staffed by experienced personnel.*

**ReproTech Mission Statement**  
ReproTech, Ltd. (RTL) is committed to maintain the highest level of expertise and competency in the field of Reproductive Medicine. Our quality services ensure safe and effective shipment and long term storage of cryopreserved reproductive tissues. We are dedicated to assist our clinical partners in meeting regulatory requirements in the areas of tissue storage for our patients and donor embryos.

## **SAMPLE INTEGRITY & CHAIN OF CUSTODY**

We at Reproductive Medicine and Infertility Associates are totally committed to providing you the best chance for success in your efforts to achieve a family. Part of our efforts rest in ensuring that all samples are properly identified, appropriately handled, and processed in a timely manner. This entire process begins with sample identity. You will notice as you progress through the program that there are several points at which you will be asked identifying information (ie. name, clinic ID number, birthdate). The most critical points at which you will be asked this information include:

- 1) When a semen sample is delivered to the lab for processing – At this point, a chain of custody system is put in place so the sample can be identified and tracked at each process or use point while in the lab. Even when any unused portion of the sample is discarded, that discard is documented. The tracking system begins with patient verification that the sample presented is authentic. This verification is required whether the sample was collected on-site or off-site, and is accompanied by patient signatures to that effect.
- 2) At the time of oocyte retrieval – As you will see, prior to the oocyte retrieval, several members of the clinical and laboratory teams will ask you identifying information such as name, birthdate and clinic ID number in an effort to be absolutely sure the patient being retrieved is correctly identified. There are too many people in the world with the same name to rely simply on name as an identifier.
- 3) At the time of embryo transfer – As with the retrieval, several members of the clinical and laboratory teams will ask you identifying information to ensure accuracy of patient identification prior to treatment.

Several other measures are taken to ensure the care and integrity of samples while in the laboratory. For example, all sample tubes and petri dishes are labeled with name, unique identifying numbers, and are also color coded prior to use. All of this information is checked at each step of sample processing. Also, at the time of your egg retrieval, you will wear a wristband with your personal identifying information on it that will be checked frequently throughout the remainder of your IVF procedure to ensure proper patient identification.

At times, these information requests may seem a bit impersonal. But keep in mind; these efforts are solely to ensure that you receive accurate treatment and to maximize your safety. Even for those who have visited our office often and those we know, this information will be requested. It is our safeguard to ensure that your samples are handled appropriately.

# IVF CYCLE – POTENTIAL COMPLICATIONS

## ➤ **CYCLE CANCELLATION**

Cycle cancellation, although infrequent (approximately 5% of all IVF cycles are cancelled) may occur after you have begun taking your medications. The most commonly cited reasons for cycle cancellation are the failure of a patient's system to "down-regulate" during pre-stimulation with Lupron or poor follicular development during the stimulation phase. In the event of cycle cancellation, you will receive further instruction from your physician regarding preparation for a new treatment cycle.

## ➤ **NO OOCYTES RECOVERED DURING TRANSVAGINAL RETRIEVAL**

Occasionally, no oocytes are recovered at the time of retrieval (a phenomenon that occurs in less than 1% of all egg retrievals). The most common reason for this occurrence is the eggs being released prior to the retrieval. Prior to another round of attempted stimulation, the physician or nurse practitioner will instruct the patient on ways to prevent spontaneous ovulation.

## ➤ **UNEXPECTED POOR SPERM QUALITY**

Prior to the initiation of any IVF cycle every attempt will be made to identify patients who have sub-optimal sperm quality. A semen analysis will be performed and all other test results reviewed, so as to increase the likelihood of achieving a pregnancy utilizing the patient's sperm. Those patients identified as having sub-optimal sperm will be counseled regarding the use of ICSI for their IVF cycle. Occasionally, patients may provide a sub-optimal sperm sample on the day of the oocyte retrieval despite having previously exhibited normal semen parameters. If this occurs, the sample may not be suitable for routine insemination and in all likelihood, ICSI will be utilized. Therefore, all patients should readily anticipate the possibility that ICSI may need to be incorporated into their IVF treatment cycle, and authorize RMIA to perform this procedure beforehand.

## ➤ **FERTILIZATION FAILURE**

In less than 5% of all IVF cases, total fertilization failure may occur. This may be due to an undiagnosed male factor, meaning no fertilization occurred even though all previous semen samples, including the sample used on the day of the egg retrieval appeared normal. This problem may be prevented through the utilization of ICSI. However, if fertilization failure occurs, it is not possible to then treat those unfertilized oocytes with ICSI. Total fertilization failure may also be due to poor oocyte quality, in which case the physician will discuss options for future cycles.

In the event of total fertilization failure, most embryos are not transferred. However, if the fertilization failure resulted from the retrieval of immature oocytes, it may be possible to utilize ICSI once the oocytes have matured and eventually transfer these potentially fertilized embryos. Please be aware of the concerns posed by this scenario such as the normality of embryos resulting from fertilization of oocytes matured in the laboratory.

➤ **FAILURE OF EMBRYOS TO DEVELOP**

It is possible, although rare, that embryos resulting from IVF fertilization may not develop. A probable explanation for this phenomenon is usually poor oocyte quality. In these cases, embryo transfer is usually cancelled. Your physician will discuss possible remedies with you prior to the start of any future cycles.

➤ **POOR EMBRYO QUALITY**

It is an altogether uncommon phenomenon for all of the embryos produced by a patient in an IVF cycle to be of a lower quality. If such an event does occur, focus is often directed toward oocyte quality, as it is believed that embryo quality is generally a reflection of oocyte quality. Embryo quality may also be influenced by other factors including maternal age, male factor, or poor response to ovarian stimulation.

Embryo quality plays an important role in deciding how many embryos to transfer, and acts as a reliable indicator for likelihood of implantation. Also, poor quality embryos do not survive the freeze/thaw process as well as higher quality embryos. Therefore the decision to cryopreserve embryos should be based largely on the quality of your additional embryos.

➤ **FAILURE OF EMBRYOS TO SURVIVE CRYOPRESERVATION**

Occasionally, all embryos may not survive the cryopreservation and thawing processes. (This is an uncommon occurrence as greater than 90% of embryos survive both processes.) The likelihood of this problem occurring is generally related to embryo quality at the time of initial cryopreservation. However, on occasions, even high quality embryos may not survive the process.

➤ **FAILURE TO BECOME PREGNANT**

Despite your best efforts and those of the RMIA staff, you may not achieve pregnancy. In the event of this unfortunate occurrence, we will do our best to help you cope with your disappointment. Certain staff members are able to assist you through this time.

➤ **MULTIPLE PREGNANCIES**

We at RMIA do not believe in the “more is better” philosophy when it comes to the potential for developing a multiple pregnancy. From a statistical standpoint, those patients who have achieved multiple pregnancies are often at an increased risk for a variety of medical problems. The key factor is that the uterus can only hold so much – normally, one or two developing fetuses. The more fetuses there are, the shorter the pregnancy will be, and in turn, the higher the risk for complications. Depending on numerous factors (the age of the patient being one of them), embryos usually have a 15 to 50% chance of implanting, and this is why we currently don’t recommend transferring one single embryo by choice to all patients. However, for specific patients (high likelihood of success) the transfer of a single embryo is a reasonable option.

A method for dealing with multiple pregnancies is selective reduction. This procedure involves terminating one or more of the developing fetuses. Most of the time selective reduction does not affect the remaining fetus(es), however it is considered an invasive procedure and therefore poses a certain degree of risk, including loss of the entire pregnancy.

➤ **PREGNANCY LOSS**

As is the case with naturally achieved pregnancies, those achieved using IVF are at risk for loss. While the data is not entirely clear, there are some indications that the loss rate of IVF pregnancies is comparable to those pregnancies achieved naturally.

➤ **CONCEPTION OF AN ABNORMAL BABY**

The evidence for or against IVF (including ICSI) contributing to children at a higher risk for abnormalities than those conceived naturally is unclear. The one exception may be in cases where ICSI is utilized with specific types of male factor infertility. Some men carry genes (referred to as “Y deletion” genes) that may be the cause of, or at least contribute towards their infertility. However, when ICSI is utilized to override this lack of sperm function in order to achieve a pregnancy, the resulting child (particularly if male) may then inherit the same genetic tendency toward lowered fertility when he eventually attempts to create a family.

# DISCLOSURE STATEMENT

Each Program applicant will be required to sign RMIA's Informed Consent and Authorization forms as appropriate. In addition to those disclosures made elsewhere in this booklet, each applicant should know:

- A. IVF may lead to a series of complications, e.g., ovarian hyperstimulation syndrome, infection, bleeding, multiple pregnancy, tubal pregnancy, and spontaneous abortion. These risks are limited but present, regardless of whether or not the patient will be included in the program. It is RMIA's intention to provide the same high quality of care to all of its patients.
- B. In the event of complication, while most such complications may be covered under the applicant's own health insurance, the fees and expenses associated with the treatment of such complications shall be the sole responsibility of the Program applicant. **Treatment of complications is not covered under this Program.**
- C. The couple may terminate the Program at any time with the approval of their RMIA physician.
- D. The Program does not cover prenatal and delivery fees and expenses.
- E. Participation in the Program is contingent upon meeting the requirements of the screening and qualification process and paying the required fees. Applicants will be served on a first come first serve basis.
- F. RMIA retains the right to terminate or amend the program at any time, provided such termination or amendment shall not adversely affect the medical condition of those applicants already accepted into the Program.
- G. Each couple must understand and accept the risk of the multiple pregnancies. Selective reduction services are not provided by RMIA nor are the cost of such services included in the Program.
- H. RMIA is not in the business of long-term storage of cryopreserved pre-embryos. Patients that are participating in the **FCWP** will have storage covered for one year from the date they first cryopreserve their embryos. After that year expires the embryos will be automatically transferred to Repro Tech, Ltd ("RTL"). In the **Regular IVF** Program, the patient will be billed for storage on a monthly basis from the time those embryos are first stored. Patients will be asked to execute a pre-embryo storage agreement with RTL, or a similar facility, prior to transfer.
- I. Patients who have had two previous tubal pregnancies or extensive damage to their tubes will need to undergo a tubal ligation or excision prior to IVF in order to be eligible for this Program. **The Program does not cover costs associated with tubal ligation.**
- J. Ultimately, the decision of which IVF program a patient enters into is at the discretion of the RMIA physician.