Dear patient:

This handbook and video have been designed and utilized over the past 22 years with input from staff, educators and patients and it serves as an “all-inclusive” source of information for your IVF/ART process.

- Please read this handbook cover to cover and view the video as they have been designed to serve as a guide for each phase of your IVF/ART process.

- Keep this handbook accessible at all times.

In order for you to keep your costs down, we ask that this handbook be used for answering questions as they arise. Fees may be applied for additional calls or inquires made to staff regarding information available in this material.
The Midwest Center for Reproductive Health, P.A. (MCRH) was founded in 1992, bringing together a group of innovative and specialized reproductive health care professionals, led by reproductive endocrinologist, Randle S. Corfman, Ph.D., M.D. The vision of The Midwest Center is to provide patients with state-of-the-art reproductive health care while maintaining a very personal and caring approach to patient care. Achieving this goal has been facilitated by combining cutting edge medical and surgical knowledge with high tech andrology and embryology skills. Holistic and specialized care is delivered by specially trained nurses, a health educator, and administrative staff. This synthesis provides a unique environment which we feel improves the quality of care and the quality of life for our patients while optimizing chances for pregnancy.

The andrology and embryology teams provide the latest technology in the assisted reproductive technologies, including micromanipulation of sperm, oocytes (eggs) and embryos. Currently, this includes intracytoplasmic sperm injection (ICSI) and assisted zona hatching (AZH) of embryos and preimplantation genetic diagnosis (PGD).

You will find that The Midwest Center excels in the area of patient education by providing on-site educators. It is our belief that by educating our patients in the assisted reproductive technologies, we can better prepare them for participation in decision making. This active participation contributes to stress reduction while improving the quality of the experience. Our nursing staff also excels in the area of patient education and in coordinating treatment plans, helping you gain a better understanding of your infertility treatment. When appropriate, our nurses will maintain timely communication with satellite staff in order to ensure smooth and “seamless” transitions for patients traveling from great distances.

In the past, IVF has been perceived as one of the most stressful experiences a couple faces. We feel that we can help you minimize the stress, in part, by providing a social worker whom is particularly experienced in counseling couples struggling with infertility.

Meticulous preparation for IVF contributes greatly to the success experienced at The Midwest Center. We are committed to your success and feel strongly that much of the success experienced at The Midwest Center is a result of complete investigation of the infertile couple. Our IVF Coordinators specialize in assisting couples with all of the pre-IVF testing requirements. Each piece of
information is important in determining which treatment protocol will most likely result in pregnancy. While occasionally perceived as bothersome, we rely extensively upon the pre-IVF testing.

Finally, we are aware that the financial burden for completing IVF is substantial. Our business office will assist you in satisfying the financial requirements of the program, providing helpful and up-to-date information.

We are excited to have you participate in the assisted reproductive technologies at MCRH. We hope you will find our team approach complete, satisfying, and rewarding. We are eager to assist you as you embark upon this important journey.

Please visit our website at www.mcrh.com

The Midwest Center for Reproductive Health Staff
FACING IT TOGETHER

Facing IVF can be a daunting or overwhelming process for many people. The Midwest Center for Reproductive Health has instituted a support program called “FIT” (Facing It Together), for individuals or couples who would benefit from the support of someone who has previously been through the IVF process. If this program is of interest to you, please return this form and we will do our best to find you a match. Sharing of personal information is left to the discretion of the individuals themselves. Your first name and email address you provided is the only information given by MCRH.

If you have any additional questions, please contact the Nurseline at 763-494-7726.

I give permission to give my first name and email address to an individual chosen by the staff of Midwest Center for Reproductive Health:

____________________________________                         __________________________
Patient’s name printed                                         Signature

____________________________________                         __________________________
Spouse/Partner’s name                                          Signature

Date signed: __________________

Email address: _______________________________________________

Please return to:

FIT Coordinator
Midwest Center for Reproductive Health
12000 Elm Creek Blvd. North
Suite #350
Maple Grove, MN 55369

Fax: 763-494-7706

Email: info@mcrh.com
Section I

Introduction and Overview
IN VITRO FERTILIZATION

In vitro fertilization (IVF) is probably the best known and most widely used of the Assisted Reproductive Technologies (ART) options. In this procedure, eggs are removed from the woman and mixed in the laboratory with the partner/donor sperm in order to achieve fertilization. The resulting embryos are incubated an additional 2-5 days in the laboratory after which they are returned to the woman’s uterus through the cervix.

In vitro fertilization (IVF, as it will be referred to throughout this document) was originally developed to remedy infertility caused by fallopian tube disorders such as blocked or absent tubes. In recent years, it has become more common to use IVF for treatment of unexplained infertility, male factor infertility, endometriosis, and pelvic adhesive disease. In order for a woman to be eligible for IVF, she must have a uterus and at least one functional and accessible ovary unless utilizing a third party option.
Assisted Reproductive Technology Overview

Consultation
- Proceed
- Adoption
- Childfree Alternatives

Preparation

Clinical / Laboratory Requirements
- Blood type with Rh factor, HIV 1 and 2 antibody and Hepatitis B & C serology for both patient and partner
- Rubella
- Varicella
- Lupus Anticoagulant, Beta 2 Glycoprotein Antibody 1 and Anticardiolipin Antibody, Factor V Leiden if indicated
- Antithrombin Antibody, if indicated
- Day 3 FSH, Estradiol (E2), luteinizing hormone (LH), AMH if indicated
- Semen analysis, cryopreservation recommended
- Sonohysterogram/Uterine Profile, if indicated
- If no previous tubal evaluation, Hysterosalpingogram (HSG) or Laparoscopy, if indicated

Lifestyle / Psychosocial (e.g., discontinue smoking)
- Stop smoking
- Lupus Anticoagulant, Beta 2 Glycoprotein Antibody 1 and Anticardiolipin Antibody, Factor V Leiden if indicated
- Antithrombin Antibody, if indicated
- Day 3 FSH, Estradiol (E2), luteinizing hormone (LH), AMH if indicated
- Semen analysis, cryopreservation recommended
- Sonohysterogram/Uterine Profile, if indicated
- If no previous tubal evaluation, Hysterosalpingogram (HSG) or Laparoscopy, if indicated

Team Member Involvement
- IVF Coordinator: informs of and reviews screening requirements and consents
- MD: IVF review, sonohysterogram and uterine profile
- Embryologist: review gametology and embryology – per patient need
- Nursing: coordinate patient care and prescriptions, medication outline and injection training
- Business Office: financial arrangements

Final Preparation for Stimulation (Down Regulation)

Birth control pills: one tablet once daily as directed
- Norethindrone Acetate (Aygestin) one tablet once daily for 10 - 20 days
- Pituitary desensitization (if indicated): GnRH agonist (Leuprolide Acetate (Lupron), subcutaneous)
  - for minimum of 10 days or until down regulation has been achieved
- * Ultrasound & estradiol (E2)

Ovarian Stimulation Cancellation Rate=20%
- Human menopausal gonadotropin (Menopur)
- Follicle stimulating hormone (Follistim, Gonal-f, Gonal-f RFF pen, Bravelle)
- GnRH antagonist (Ganirelix Acetate, subcutaneous) – if indicated
  - for approximately 5 days in conjunction with stimulation medications until hCG administration
- * Ultrasound & estradiol (E2)
- * All ultrasound and estradiol (E2) results must be received in our office by 12:00 p.m. CST/CDT.

hCG (Pregnyl/Novarel) with or without Lupron Trigger
- Follicles 80%
- Oocytes + Sperm 80%
- Embryos

Oocyte (Egg) Retrieval
- Semen Collection
  - (36 hours from trigger)
  - Oocytes
  - In vitro fertilization
    2-5 days
    Assisted Zona Hatching (AZH) if indicated
    Embryo Transfer - +/- embryo cryopreservation

B-hCG level
- (approximately 14 and 16 days from transfer)

Ultrasound Confirmation = Clinical Pregnancy
- Intrauterine Pregnancy per Retrieval (approximately 21 days from positive BhCG)
- Delivery = Delivery per Retrieval (33 weeks)

Risks & Complications of Retrieval
- Injury to blood vessels, bladder or bowel, any of which could require laparotomy
- Infection requiring antibiotics or surgical removal of ovary

Risks & Complications of Transfer
- Ectopic pregnancy
- Multi-fetal reduction
- Multiple births
- Ovarian cancer
- Ovarian hyperstimulation syndrome (OHSS)
STATISTIC REPORTING

MCRH is a member of The Society for Assisted Reproductive Technology (SART). Membership requires complete documentation of all pregnancy outcomes and/or deliveries. This information also enables us to provide patients with updated statistics and information regarding our center. Cycle-specific data is reported to the Society for Assisted Reproductive Technology (SART) on a yearly basis for the purpose of publishing an annual report. All personal identifiers submitted are protected under the Privacy Act. Patient names are not reported to SART.

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

On a periodic basis, SART clinic programs will be reviewed by outside professional reviewers to validate information. Each patient may be contacted by the professional reviewers and asked to confirm information provided in the chart and/or database.
Section II

Guidelines

Lifestyle and Activity
GUIDELINES

General Information
Much of this information may have already been addressed along your treatment process, but to clarify our recommendations, the following guidelines are provided to optimize your treatment.

Office Phone Calls
Our staff is available to answer specific questions and to refill medications during office hours (8:00 a.m. to 3:00 p.m. CST/CDT). They can be reached by calling (763) 494-7700 or (800) 508-9763. All calls will be routed to the department where a confidential message may be left. Calls will be returned by the appropriate staff member by the end of the business day unless received after 3:00 p.m.

After clinic hours and on weekends, non-emergency calls should be made to the nurses’ line at (763) 494-7726. Messages may be left at any time and will be addressed the following business morning by a nurse.

In case of an emergency, the on-call nurse may be paged at (763) 494-7700. A nurse will return your call and appropriate medical direction will be given to you.

Any non-emergency pages after hours and on weekends will be billed appropriately.

The Midwest Center utilizes a confidential phone system to enhance our communications with you during your treatment cycle. Patients will receive a communication bulletin with their assigned personal identification number and the date to begin checking messages. **Please access your private voicemail system daily between 3:00 p.m. and 4:00 p.m. CST/CDT during your treatment cycle.** Patients can expect to receive messages on all monitoring days regarding test results and future treatment plans and occasionally, there may be other communications left for patients throughout their treatment cycle. If you have not received an anticipated message by 4:00 p.m. CST/CDT, please contact the nurse line at (763) 494-7726 for further instructions. Questions may then be answered during office hours.

We require that you have an answering machine/voice mail where we can leave detailed messages regarding medication and monitoring instructions as a backup to the confidential phone system.

**With sincere sensitivity to all of our patients, we ask that those of you with children not bring them along to appointments or procedures.**

Phone Numbers:

General Office Phone................................................................. (763) 494-7700
Toll Free....................................................................................... (800) 508-9763
Fax.............................................................................................. (763) 494-7706
Patient Voicemail................................................................. (763) 494-7799
Toll Free....................................................................................... (888) 253-MCRH

Under extremely rare cases, when you call (763) 494-7700 or (800) 508-9763 and cannot reach our clinic, you may hang up and dial our nurse on-call pager at (612) 613-2579 and enter your 10 digit phone number. This is to be used ONLY when unable to contact us by getting a busy signal on several attempts indicating our phone system is out of order.
LIFESTYLE/ACTIVITY

Exercise/Activity
You are encouraged to exercise with moderation. Walking and swimming are encouraged. **High impact aerobics/exercises should be avoided.** Hot tubs and saunas should not be used by men at least two months prior to the IVF cycle and throughout treatment. (This is especially true for males with low sperm counts). Women should avoid hot tubs and saunas once stimulation medications have begun.

Diet/Smoking/Alcohol Consumption/Caffeine
Healthy eating habits/normal weight range. All couples are **required to avoid smoking, secondary smoke and tobacco usage** as research indicates that it is harmful to the ovaries and sperm and has a negative impact on chances for conception and pregnancy. Couples are also **required to avoid the use of alcohol** throughout the treatment cycle. **Caffeine intake** should be minimal or avoided with pregnancy. However, caffeine intake during the IVF stimulation process may help to alleviate symptoms of ovarian hyperstimulations syndrome. Therefore, between retrieval and transfer, it is recommended to consume 2-3 servings of caffeinated beverage daily following your retrieval. In addition, a diet high in protein along with increasing your fluid and sodium intake will help alleviate some of the bloating and constipation that are typical post-retrieval. Referrals to dietary and smoke cessation programs are available through The Midwest Center.

Medications
Over the counter medications that can be used throughout treatment include Tylenol, Actifed, Sudafed, and Robitussin. If additional medications and/or treatment are necessary, be sure your prescribing physician is aware that you are trying to achieve pregnancy. Please inform our staff of any prescription medications you are currently taking and of any medical conditions that may require additional attention (i.e. heart or thyroid condition, diabetes, or artificial joints).

Influenza Vaccination (Flu Shot)
Flu shots are recommended for anyone who is pregnant or attempting to conceive.

Travel
We request that any previous or future travel plans be discussed with the MCRH Team prior to your IVF cycle. A deferral of 6 months may be required to minimize the risk of ZIKA virus transmission. The MCRH Team will help determine if a potential deferral is necessary.
The American Society for Reproductive Medicine is closely following developments related to the Zika virus. At this point, it seems clear the virus has implications for reproduction and that it can be transmitted through sexual activity and reproductive tissues.

We urge patients who are pregnant, who are considering becoming pregnant, or those who may be involved as donors or recipients of reproductive tissues to exercise caution.

Due to the rapidly evolving understanding of Zika, we strongly recommend that our members and their patients follow the information and recommendations made available from the Centers for Disease Control and Prevention (CDC). The CDC has issued “Level 2 Practice Enhanced Precautions” recommendations for certain areas, urging those pregnant or seeking to become pregnant to avoid travel to those areas, or use enhanced prevention and follow-up activities if such travel cannot be avoided.


It is Dr. Corfman's recommendation that both you and your partner avoid travel to those areas designated as cautionary for the Zika virus. Please refer to the CDC website for a list of these areas. If you or your spouse/partner have already travelled to one of these areas in the past 12 months, please discuss this with our MCRH team to determine the timeframe for proceeding with your treatment plan.

If you have additional questions regarding this information, please contact the MCRH Nurse line at (763) 494-7726.
What do I need to know about Zika virus and trying to have a baby?

The Zika virus:
- Is found in South America, North America, the Caribbean, and Singapore.
- There is currently no vaccine or medicine to prevent or treat Zika.
- Symptoms can be mild or not present, making it difficult to know if you have it.
- Is spread primarily through daytime-active mosquitoes.
- Can be transmitted through intimate sexual contact, blood transfusion, and from mother to fetus.

What are symptoms of Zika virus?
Common symptoms include fever, rash, joint pain, conjunctivitis (red eyes), muscle pain, and headache. The incubation period is likely just a few days and the symptoms last 2-7 days. But most people will not have symptoms.

What about Zika virus and pregnancy?
The World Health Organization (WHO) reports that the Zika virus can cause microcephaly when transmitted from mother to fetus. Microcephaly is a medical disorder where the head is smaller than normal and is associated with brain shrinkage and cell death, causing serious developmental problems in the child. Infection with Zika virus during pregnancy is also linked to miscarriage, impaired growth, eye defects, and hearing loss in the child.

Should I be tested for Zika virus?
A blood or urine test can confirm Zika infection. If Zika virus is found in the blood or urine, it is assumed to be present in semen or other bodily fluids, although there is no completely reliable commercially available test.

Negative blood or urine test would not necessarily mean the virus is not present in semen or other bodily fluids. Testing of semen or vaginal fluids is not recommended to determine whether a person could pass Zika virus to their partner during sex because available tests are not yet reliable for these fluids.

When trying to get pregnant, women and men with possible exposure to Zika virus but without clinical illness can consider testing for Zika within 2 weeks of suspected exposure. However, this testing strategy will not necessarily guarantee they are not infected with Zika. Testing for Zika is not universally available or recommended and its cost is not always covered by insurance. Your healthcare provider should know what tests are available in your community, the limitations of these tests, which patients will be allowed testing, and whether testing is covered by insurance.

Will the Zika virus affect my plans to undergo assisted reproduction procedures?
For men and women planning pregnancy who live in an area of active transmission, the risk is always present due to continuous potential exposure. The safest option is to delay pregnancy; however, this is not always possible particularly in those women older than 35 years.

Individuals using only their own eggs and sperm should follow the same precautions as for a non-assisted pregnancy. For those using donated eggs, sperm, or embryos, the United States Food and Drug Administration (FDA) states: use of sperm, eggs, and embryos from living persons are not allowed if the donors:
- Had a diagnosis of Zika virus infection in the past 6 months.
- Resided in or traveled to an area with active Zika virus transmission within the past 6 months.
- Have had sex with a man within the past 6 months who, during the 6 months before this sexual contact:
  - Was diagnosed with Zika virus disease.
  - Experienced an illness consistent with Zika virus disease.
  - Or traveled to an area of active Zika virus transmission.

If I've been infected, exposed, or think I might have been exposed to Zika virus, should I wait to get pregnant?
Guidance from the CDC, WHO, and ASRM about timing pregnancy is summarized in the table below.

Other considerations:
- In areas where Zika virus-carrying mosquitos have been identified, women of reproductive age, particularly those who are attempting pregnancy, should take measures to prevent breeding of mosquitos and prevent bites. For the latest information on minimizing Zika infections, please visit http://www.cdc.gov/zika/prevention/index.html.
- For the latest information about where the Zika virus-carrying mosquitos have been found, please visit the CDC website at http://www.cdc.gov/zika/geographic/index.html.
- If you are using donated embryos, eggs, or sperm, you should consider the potential exposure of the embryos to Zika virus, particularly if they were frozen at a time before these screening processes were in effect.
- Laboratory techniques that have been used to prevent the transmission of other viruses, such as HIV, have not been shown to prevent Zika virus at this time.
- Information about Zika virus, including how it is transmitted, ways to test for it, and what effects it has on babies and adults, is changing daily. Guidance published today may not be accurate for counseling and treatment of individuals tomorrow. Check with your healthcare provider and the CDC and FDA for the latest information.

For more information on this and other reproductive health topics, visit www.ReproductiveFacts.org

Created 2016

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<table>
<thead>
<tr>
<th>Population</th>
<th>ASRM</th>
<th>WHO</th>
<th>CDC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Those with symptoms</td>
<td>Wait 6 months</td>
<td>Wait 6 months</td>
<td>Men-wait 6 months, Women-wait 8 weeks</td>
</tr>
<tr>
<td>Those with possible exposure, no symptoms, and a positive test</td>
<td>Wait 6 months</td>
<td>Wait 6 months</td>
<td>Men-wait 6 months, Women-wait 8 weeks</td>
</tr>
<tr>
<td>Those with possible exposure, no symptoms, and a negative test</td>
<td>Wait 8 weeks</td>
<td>Wait 6 months</td>
<td>Men-wait 6 months, Women-wait 8 weeks</td>
</tr>
<tr>
<td>Those with possible exposure, no symptoms, and no test</td>
<td>Wait 6 months</td>
<td>Wait 6 months</td>
<td>Men-wait 6 months, Women-wait 8 weeks</td>
</tr>
</tbody>
</table>

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Helpful links to information about Zika virus:
- FDA: http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm486812.htm
- WHO: http://www.who.int/mediacentre/factsheets/zikafacten/
Smoking and infertility

Can smoking affect my ability to have a child?
Most people understand that smoking increases the risk for heart, vascular, and lung disease. Many do not realize that smoking can also lead to problems with fertility in both men and women. Erectile dysfunction and pregnancy complication rates are also increased with smoking.

Will smoking affect my eggs or sperm?
Chemicals (such as nicotine, cyanide, and carbon monoxide) in cigarette smoke speed up the loss rate of eggs. Unfortunately, once eggs die off, they cannot regenerate or be replaced. This means that menopause occurs 1 to 4 years earlier in women who smoke (compared with non-smokers).

Male smokers can suffer decreased sperm quality with lower counts (numbers of sperm) and motility (sperm's ability to move) and increased numbers of abnormally-shaped sperm. Smoking might also decrease the sperm's ability to fertilize eggs.

How can smoking impact my ability to conceive?
Women who smoke do not conceive as efficiently as nonsmokers. Infertility rates in both male and female smokers are about twice the rate of infertility found in nonsmokers. The risk for fertility problems increases with the number of cigarettes smoked daily.

Even fertility treatments such as IVF may not be able to fully overcome smoking's effects on fertility. Female smokers need more ovary-stimulating medications during IVF and still have fewer eggs at retrieval time and have 30% lower pregnancy rates compared with IVF patients who do not smoke.

Because smoking damages the genetic material in eggs and sperm, miscarriage and offspring birth-defect rates are higher among patients who smoke. Smokeless tobacco also leads to increased miscarriage rates. Women who smoke are more likely to conceive a chromosomally unhealthy pregnancy (such as a pregnancy affected by Down syndrome) than nonsmoking mothers. Ectopic pregnancies and preterm labor also occur more often among female smokers.

Can smoking affect my children?
Men whose mothers smoked half a pack of cigarettes (or more) a day had lower sperm counts. Smoking during pregnancy also can lead to growth restriction of the baby before birth. Children born with lower-than-expected birth weights are at higher risk for medical problems later in life (such as diabetes, obesity, and cardiovascular disease). Children whose parents smoke are at increased risk for sudden infant death syndrome (SIDS) and for developing asthma.

I don’t smoke but my partner does. Could this secondhand smoke affect my fertility?
Women exposed to secondhand smoke can suffer all the above health risks.

If I stop smoking, will my chances for conceiving and having a healthy pregnancy improve?
Yes. Quitting smoking can improve fertility though the decrease of the egg supply cannot be reversed. The rate of pregnancy complications due to smoking decreases the longer a person has not smoked.

Quitting smoking can be very, very difficult but studies show that the chance for success is much higher if you work with your health-care provider and/or a support group. Sometimes, temporary use of a nicotine replacement (such as nicotine gum or patch) and/or prescription medication called bupropion can improve quitting smoking rates, and you can use these while trying to conceive, if needed. Though it generally isn't advised to use these during pregnancy, you and your health-care provider might consider their use during pregnancy after weighing the risks and benefits.

Revised 2014
For more information on this and other reproductive health topics, visit www.ReproductiveFacts.org
Stress and infertility

It is not clear how exactly stress impacts fertility. It is not known whether high levels of stress can prevent pregnancy or affect a woman’s chance of conceiving. We do know that reducing stress provides a better quality of life during times of intense personal challenge.

**What is stress?**
Stress is often defined as an event that a person sees feels is threatening. In order to protect itself, the body responds with a "fight or flight" response.

**How can stress impact a fertility patient?**
Sometimes, infertility patients respond to the stress of being unable to conceive by aggressively pursuing treatment and procedures. Other patients withdraw and isolate from family, friends, and community. Neither of these extremes is ideal for patients who seek to treat their infertility and build a family.

**How can I reduce my stress?**
Having less stress in your life while pursuing fertility treatment may not, in and of itself, result in a pregnancy. However, developing better coping strategies to manage stress related to an infertility diagnosis and treatment can help you feel more in control and improve your overall well-being.

It has been shown that stress does interfere with making rational and well-thought-out decisions. Reducing stress can allow patients to research, explore, and consider all the options available with a clearer mindset. By reducing stress, the pros and cons of one treatment course over another can be more effectively weighed and considered.

Reduced stress is good for your health. While no one expects patients to approach fertility treatment stress-free, finding ways to minimize stress while pursuing treatment can help. It is helpful for patients to look for ways to reduce the burden of infertility treatments and medical protocols.

There are many stress-reducing techniques; some of the more popular methods recommended to fertility patients are:
- Acupuncture
- Aerobic exercise (may be reduced during treatment)
- Collaboration with experts in stress reduction
- Guided imagery
- Journaling
- Listening to music
- Massage therapy
- Meditation
- Mind-body groups
- Mindfulness
- Progressive muscle relaxation
- Psychotherapy and cognitive behavioral therapy
- Self-help books
- Support/educational groups
- Visualization
- Walking/hiking
- Yoga

**How can I help my friend/loved one?**
Friends and loved ones are facing a challenge. Telling patients to be less stressed can make them feel more responsible for "causing" their own infertility and feel blamed. Telling someone to relax can cause greater stress. However, asking how couples/friends are doing and suggesting concrete and pragmatic ways to reduce stress will enhance quality of life and give the patient back some sense of control. For many struggling with infertility, just having friends/loved ones available for listening is greatly appreciated.

The goal of stress reduction is to minimize, not eliminate stress, by finding the technique that serves the patient's needs the best.

Revised 2014

For more information on this and other reproductive health topics, visit www.ReproductiveFacts.org
Section III

Consent Forms
CONSENT FORMS

The following pages contain examples of the consent form for IVF and FET. This is for your reference only. Prior to initiating treatment, you will receive a consent packet containing consents appropriate to your care. Please take time to review these in detail prior to signing so that any clarifications or questions you have may be answered.

These consents are mandatory and must be signed, witnessed/notarized and returned by the designated date or treatment may be postponed.

3-1
The Midwest Center for Reproductive Health, P.A. (MCRH)
Consent for Assisted Reproductive Technology (ART)

I/We have been informed of the assisted reproductive technology treatments available to us at MCRH, and it is our intention to proceed with my/our individualized treatment plan outlined by my/our physician. I/We further understand it is my/our responsibility to notify MCRH staff of any changes in my/our health status or prescribed medications throughout my/our treatment.

I/We have read the handbook, viewed the video and fully understand their content. As with any medical procedure, I/we acknowledge there are risks of complications.

I/We hereby consent to and authorize MCRH to perform routine diagnostic procedures, laboratory tests and treatment protocols necessary during my/our ART process. I/We have been given and understand the information regarding medications, the routes of administration and associated side effects.

I/We understand that my/our physician has outlined specific treatment regarding methods of fertilization. I/We realize semen parameters may vary on the day of retrieval and therefore, are permitting MCRH staff to proceed with ICSI and/or RICSI as deemed medically necessary. Additionally, I/we have been given the option of cryopreservation of a backup semen specimen and understand the significance as outlined in the handbook. In the event the backup semen specimen was provided and not used on the day of retrieval, I/we understand this specimen will be stored for 6 months and then discarded without further notification.

I/We understand that on the day of transfer, assisted zona hatching (AZH) will be performed if indicated. I/We understand and permit the transfer of the agreed upon number of embryos and allow cryopreservation of our additional embryos, unless specifically advised against by our physician. In addition, authorization is hereby given to MCRH staff to dispose of all non-viable or poor quality embryos, abnormally fertilized oocytes, and unfertilized oocytes in accordance with laboratory standards and regulations.

I/We understand that MCRH is not a long term storage facility and therefore, I/we authorize the automatic transfer of our cryopreserved embryos to ReproTech and have completed the necessary ReproTech registration and agreement forms.

I/We have been assured that all information regarding our treatment will be handled confidentially and neither our identity nor specific medical details will be revealed without our prior written consent. Specific anonymous medical details may be revealed in professional publications and to the SART licensing board as long as our identity is concealed. Data from our ART procedure will also be provided to the Center for Disease Control and Prevention (CDC). The 1992 Fertility Clinic Success Rate and Certification Act requires that CDC collect data on all assisted reproductive technology cycles performed in the United States annually and report success rates using these data. Additionally, we consent to having medical observers throughout this process for the purpose of advancing medical education.
I/We have been given cost information and itemization and understand that if additional treatment or procedures are performed, they will be charged according to the variable costs listed, and I/we will be responsible for payment of these services. I/We understand that all IVF billing will be through The Midwest Center for Reproductive Health (MCRH), which is out-of-network with all insurance companies.

I/We shall keep MCRH informed at all times, in writing, of our current address and telephone numbers for any matter requiring notification. This consent is valid until new consents are signed or until MCRH is provided with and agrees to any changes in writing.

I/We hereby waive, release and forever discharge MCRH, its officers, directors, employees, agents, and other representatives, from and against any and all claims, demands, charges, causes of action, liabilities, penalties, costs and expenses, including attorneys’ fees, that any third party or party to this Agreement may have, against MCRH, its officers, directors, employees, agents, and other representatives whether direct or indirect, foreseeable or unforeseeable, arising from, relating to or in connection with this Agreement unless caused by the intentional misconduct or gross negligence of MCRH. Further, the parties agree to protect, defend, indemnify, and hold harmless MCRH, its agents, attorney, any representatives, officers and employees, from and against any and all claims, demands, charges, causes of action, liabilities, penalties, costs and expenses, including attorneys’ fees, brought by any third party or party to this Agreement, and arising from, relating to, or in connection with this Agreement unless caused by the intentional misconduct or gross negligence of MCRH. In clarification of the foregoing, I/we understand and agree that (i) MCRH utilizes outside vendors for certain services associated with my/our treatment, including without limitation laboratory testing and diagnostics, and (ii) MCRH is not responsible for the acts and/or omissions of such third parties, and such third parties shall not be, (i) responsible for any third party service vendor, or/and (ii) negligent for its actions and/or other information/materials provided to MCRH by such third party service vendors in connection with my treatment. I/We acknowledge that MCRH is relying on this release and indemnification and, that but for this release and indemnification, MCRH would not enter into this Agreement.

This agreement shall be binding upon each of us, our assigns, heirs, executors and administrators.

Patient Legal Name (printed) _____________________________________________

Patient Legal Signature ________________________________ Date ___________

Witness Signature ________________________________ Date ___________

Spouse/Partner Legal Name (printed) ___________________________________

Spouse /Partner Legal Signature ________________________________ Date ___________

Witness Signature ________________________________ Date ___________

IVFC/Consent-FreshIVF11/14
The Midwest Center for Reproductive Health, P.A. (MCRH)
Consent for Assisted Reproductive Technology (ART)
Frozen Embryo Transfer

I/We have been informed of the assisted reproductive technology treatments available to us at MCRH, and it is our intention to proceed with my/our individualized treatment plan outlined by my/our physician.

I/We have read the handbook and fully understand its content. As with any medical procedure, I/we acknowledge there are risks of complications.

I/We hereby consent to and authorize MCRH to perform routine diagnostic procedures, laboratory tests and treatment protocols necessary during my/our ART process. I/We have been given and understand the information regarding medications, the routes of administration and associated side effects.

I/We authorize MCRH laboratory staff to thaw our cryopreserved embryos in the manner that I/we have discussed. In addition, I/we hereby permit MCRH staff to dispose of all non-viable or poor quality embryos according to laboratory standards and regulations.

I/We understand that on the day of transfer, assisted zona hatching (AZH) will be performed if indicated. I/We understand and permit the transfer of the agreed upon number of embryos.

I/We understand that MCRH is not a long term storage facility and therefore, I/we authorize the automatic transfer of any remaining cryopreserved embryos to ReproTech and have completed the necessary ReproTech Specimen Transfer and Medical Information Release Authorization.

I/We have been assured that all information regarding our treatment will be handled confidentially and neither our identity nor specific medical details will be revealed without our prior written consent. Specific anonymous medical details may be revealed in professional publications and to the SART licensing board as long as our identity is concealed. Data from our ART procedure will also be provided to the Center for Disease Control and Prevention (CDC). The 1992 Fertility Clinic Success Rate and Certification Act requires that CDC collect data on all assisted reproductive technology cycles performed in the United States annually and report success rates using these data. Additionally, we consent to having medical observers throughout this process for the purpose of advancing medical education.

I/We have been given cost information and itemization and understand that if additional treatment or procedures are performed, they will be charged according to the variable costs listed and I/we will be responsible for payment of these services. I/We understand that all IVF billing will be
through The Midwest Center for Reproductive Health (MCRH), which is out-of-network with all insurance companies.

I/We shall keep MCRH informed at all times, in writing, of our current address and telephone numbers for any matter requiring notification. This consent is valid until new consents are signed or until MCRH is provided with and agrees to any changes in writing.

I/We hereby waive, release and forever discharge MCRH, its officers, directors, employees, agents, and other representatives, from and against any and all claims, demands, charges, causes of action, liabilities, penalties, costs and expenses, including attorneys’ fees, that any third party or party to this Agreement may have, against MCRH, its officers, directors, employees, agents, and other representatives whether direct or indirect, foreseeable or unforeseeable, arising from, relating to or in connection with this Agreement unless caused by the intentional misconduct or gross negligence of MCRH. Further, the parties agree to protect, defend, indemnify, and hold harmless MCRH, its agents, attorney, any representatives, officers and employees, from and against any and all claims, demands, charges, causes of action, liabilities, penalties, costs and expenses, including attorneys’ fees, brought by any third party or party to this Agreement, and arising from, relating to, or in connection with this Agreement unless caused by the intentional misconduct or gross negligence of MCRH. In clarification of the foregoing, I/we understand and agree that (i) MCRH utilizes outside vendors for certain services associated with my/our treatment, including without limitation laboratory testing and diagnostics, and (ii) MCRH is not responsible for the acts and/or omissions of such third parties, and such third parties shall not be,(i) responsible for any third party service vendor, or/and (ii) negligent for its actions and/or other information/materials provided to MCRH by such third party service vendors in connection with my treatment. I/We acknowledge that MCRH is relying on this release and indemnification and, that but for this release and indemnification, MCRH would not enter into this Agreement.

This agreement shall be binding upon each of us, our assigns, heirs, executors and administrators.

Patient Legal Name (printed) __________________________________________

Patient Legal Signature ______________________________ Date __________

Witness Signature __________________________________________ Date __________

Spouse/Partner Legal Name (printed) __________________________________

Spouse /Partner Legal Signature ______________________________ Date ______

Witness Signature __________________________________________ Date ________

F:IVFC/Consent-FETIVF-11-14
Section IV

Program/Testing Requirements
CYCLE PREPARATION/TESTING

In attempts to provide information, complete testing, and alleviate some of the stress involved with your treatment cycle, you will receive extensive education regarding the in vitro fertilization process. At MCRH we recognize that a picture is sometimes worth a thousand words. With this in mind, we have prepared a DVD which provides a visual overview of what you will experience when you choose to undergo IVF at MCRH. You will be able to familiarize yourself with the IVF experience, from the time you are welcomed into our doors through the moment you leave our facility. The videos can be found on our website at www.mcrh.com under the Resources and Links.
This form is an example of the checklist completed by Midwest Center staff and filed in your chart.

THE MIDWEST CENTER FOR REPRODUCTIVE HEALTH, P.A.
IVF MEDICATION OUTLINE

PATIENT NAME: ___________________________ PARTNER NAME: ___________________________
Date prepped: __________________ By: __________________ Series: ______

______ IVF Video Viewed
______ Answering Machine/Voicemail system
______ Medication Outline ________________
______ Kardex Monitoring Sheet
______ Donor Sperm, if Yes # _________
______ ICSI
______ Copy of previous ART Monitoring Sheets
______ Injection experience discussed/direction provided re: training

__________________________________________________________________

______ Current Medications_____________________

______ Zika virus travel restrictions/risks discussed with patient

Prescriptions
______ Norethindrone Acetate 5mg tablets, #___, refills x 1
______ Leuprolide Acetate (Lupron) 2.8 ml vial #____, vials refills x 2
______ Ganirelex Acetate 250 mcg, #9, refills x 1
______ Follistim 600 iu #2 and 300 iu #3, refills x 2 each
______ Gonal-f RFF 450 iu Pen #4, 300 iu Pen #1 (fill both quantities), refills x 2 for 450 iu
Pen, refills x 2 for 300 iu Pen
______ Bravelle 75 iu #____, refills x 2
______ Menopur 75 iu #____, refills x 2
______ Pregnyl 10,000 USP Units or Novarel 10,000 USP Units, DAW refills x 1
______ Estradiol 2mg TID Qty #90, refill x 3
______ Prenatal Plus Vitamins #100, refills x 1
______ Doxycycline 100mg tablets, #10, refills x 1
______ Spouse/Partner Doxycycline 100 mg tablets, #32, refills x 1
______ Methylprednisolone, 4 mg tablet, #16, refills x 1
______ Endometrin 100 mg #____, refills x 4
______ Vaginal Progesterone Suppositories 200 mg, #90, refills x 4
______ Vaginal Progesterone Suppositories 50mg, #60, refills x 4
______ Progesterone in Oil 50mg/ml (10ml Vial), #4, refills x 4
______ Lovenox 30mg SQ every 12 hours, 2 week supply x 4 refills

If Satellite
______ Satellite Location: ____________________ Contact Person: ______________________
______ Monitoring sheet/orders faxed by __________________________ Date _______
______ Monitoring requirements reviewed with patient

______ Patient verbalizes understanding of information presented.
______ Above instructed by __________________ Date: ____________ Units: ____________

By phone: Y N
PROGRAM REQUIREMENTS

The following procedures and blood tests are requirements and recommendations of both our clinic and the American Society for Reproductive Medicine for participation in our assisted reproductive program. It is necessary for all testing to be completed and reports to be in our office before any stimulation medications will be initiated.

FEMALE TESTING

Procedures

- **Sonohysterogram** (within one year of IVF cycle or if a pregnancy loss has occurred since last test was performed)
  A procedure in which sterile water is inserted via a catheter into the uterus. By then placing an ultrasound probe into the vagina, this allows any potential abnormalities to be outlined and identified on an ultrasound monitor. If a defect is found and a follow-up procedure is necessary, this may alter the timing of your IVF cycle.

- **Uterine profile/catheter fitting** (within one year of IVF cycle, if indicated) - performed by Dr. Corfman at office visit or via ultrasound pictures for satellite patients
  For uterine evaluations performed in the office, a catheter will be inserted through the cervix and into the uterus to determine the correct placement of the embryos at the time of the embryo transfer. Knowing this information will also diminish any cramping or bleeding at the time of the embryo transfer.

  Please note: In the month this is scheduled, barrier contraception or abstinence from intercourse is required.

- **Ovarian Volume with Pre-Antral Follicle Count (PAF)** (within one year of IVF cycle)—This is a measurement of the ovaries performed via ultrasound. This must be performed either while the patient is on birth control pills or prior to cycle day 5 if not on birth control, and can be performed in conjunction with the Sonohysterogram if the patient is on birth control pills.

  If an evaluation of the fallopian tubes has never been performed:

- **Hysterosalpingogram (HSG)**
  An x-ray study in which a contrast dye is placed into the uterus to show the contour of the uterine cavity and patency of the tubes (if they are present).

  **OR**

- **Laparoscopy**
  An examination of the outside of the uterus, tubes, and ovaries. It is done on an outpatient basis under general anesthesia. It may include a tubal dye study.

- **Tubal Evaluation**
  Completed during the sonohysterogram by Dr. Corfman or another provider.

  **May be indicated by Dr. Corfman as a pre-screening requirement:**

- **Mammogram**
- **PAP**
  You will be asked to provide a current PAP result with any history of abnormal. We recommend also scheduling any routine or annual exam with your primary physician prior to beginning the process.

**Women ≥ 42 years of age** must undergo an evaluation to detect underlying heart disease. The incidence of cardiovascular compromise increases significantly in women 40 years of age and over due to increased cardiac output in pregnancy. The cardiac evaluation should be done by someone other than your OB/GYN (i.e. cardiologist, perinatologist, or internist). The evaluation should include an electrocardiogram (EKG) as well as any other tests indicated by your physician. In addition, a cardiac clearance letter must be obtained from a cardiologist, perinatologist, or internist and forwarded to our office in order to proceed.

**BMI**
A BMI ≤ 30 is required prior to being placed in an IVF cycle.
FEMALE TESTING

Blood Tests

- **Rubella Immune Status**
  Rubella is a common infectious disease caused by a virus. About 1 in 7 women of child-bearing age in this country is still susceptible to Rubella. The lack of immunity can endanger the fetus if a woman contracts Rubella during pregnancy, especially during the first three months. This can result in miscarriage, stillbirth, or birth defects of numerous types.

  A blood test to determine Rubella immunity should be done during your fertility work-up. This titer will establish if an exposure to German measles and/or vaccination has occurred. If this immunity has not been established, there are risks associated if you should become pregnant.

  Because of the risks to the unborn baby, women of childbearing age should receive a vaccine only if they are not pregnant. Women should not become pregnant for four weeks after vaccination. Pregnant women should wait to get the MMR vaccine until after they have given birth. Women should not get the MMR vaccine if they have ever had a life-threatening allergic reaction to one of the following: gelatin, previous dose of MMR vaccine, or the antibiotic Neomycin.

  It is our recommendation that women who are not immune receive a vaccination and wait four weeks before attempting pregnancy.

- **Varicella Immune Status**
  Varicella, the primary infection associated with varicella zoster virus (VZR) or chicken pox, may cause serious maternal complications when contracted during pregnancy. In addition, it may lead to fetal varicella syndrome (FVS) or infection of the newborn. Infection of the fetus in the first or early second trimester of pregnancy may result in serious abnormalities including fetal limb atrophy, scarring of the fetal skin, and central nervous system deficiency. Therefore, a blood test to determine varicella immunity should be performed prior to initiating fertility treatment.

- **Blood type with Rh factor** (done once in a lifetime)
  In preparation for your upcoming treatment cycle, you will have a blood test to find out your blood type. As there are different blood types, there is also an Rh factor. The Rh factor is the type of protein on the red blood cells. When the Rh factor is present, an individual’s blood type is designated Rh+ (Rh positive); when the Rh factor is absent, the blood type is Rh- (Rh negative). If an Rh negative female conceives using sperm from a male whom is Rh positive, it would constitute an Rh incompatibility. As this is a manageable condition, The Midwest Center would make you aware of this incompatibility requiring further evaluation and treatment by your obstetrician should you have a successful outcome.

The following tests measure ovarian reserve. If the results are abnormal, patients will be advised of their options.

- **Follicle Stimulating Hormone** (FSH) cycle day 3* (within one year of IVF cycle)
- **Estradiol** (E2) cycle day 3* (within one year of IVF cycle)
- **LH** cycle day 3 (one time as indicated by physician)
  * If indicated, these must be drawn on day 3 of your menstrual cycle. If the blood tests are requested to be drawn on the cycle in which your medications begin, be sure to obtain them before any medications are started. If results are elevated, stimulation may be discontinued.
FEMALE TESTING

- HIV 1 and 2 antibody (acquired immune deficiency, AIDS)
- Hepatitis B surface antigen ** - regardless of immunization status
- Hepatitis C antibody **

Required within one year of an IVF cycle.

Please inform our staff if vaccination for or exposure to any of these diseases has occurred.

** These viruses can cause infection of the liver and lead to liver failure; therefore, testing will be done to ensure your health prior to your IVF cycle.

If any of these test results are abnormal, you will be referred to an infectious disease specialist for further evaluation and your treatment may be delayed.

Please be advised that while some infectious disease testing is performed for your IVF cycle, not all diseases are screened for or tested. Communicable disease transmission is a possibility since bodily cells/fluids are involved in the IVF process. If you would like further discussion about communicable disease transmission, please set up a consult with your physician.

- TSH
- Prolactin (fasting)

Immune System Evaluation

- Anticardiolipin Antibody (ACA)
- Lupus Anticoagulant (LAC)
- Beta 2 Glycoprotein Antibody 1
- Factor V Leiden

If a patient has experienced a previous pregnancy loss, additional evaluation of the immune system may be necessary to determine if an abnormal antibody production has occurred. These are blood tests ordered to determine the presence or absence of antibodies which may negatively impact chances for pregnancy.

It is thought that if any of these test results are positive, the woman receiving embryos may be producing antibodies that “attack” the placenta, causing blood clots to form. These blood clots may reduce transfer of nutrients from the mother to the fetus, jeopardizing the pregnancy.

Low dose aspirin and/or heparin may be prescribed to treat such at risk individuals by lowering the likelihood of blood clot formation at the placental implantation site.

- Antichlamydial Antibody

This blood test may be ordered if the patient has a history of Chlamydia, pelvic inflammatory disease, or hydrosalpinx. This test is necessary to determine if an antibody is present resulting from a previous Chlamydia exposure/infection.

It is thought that if these antibodies are present, the woman receiving embryos may develop antibodies that “attack” the placenta, causing blood clots to form, thereby reducing transfer of nutrients from the mother to the fetus. This might jeopardize the pregnancy.

Doxycycline, an antibiotic, may be prescribed as treatment for both patient and partner to treat a potential underlying infection. Low dose aspirin and/or heparin will be prescribed to treat such at risk individuals by lowering the likelihood of blood clot formation at the placenta.
MALE TESTING

Semen Analysis (within one year of IVF cycle)
Prior to ART/IVF procedures, a number of preparatory steps need to be performed. For the male, this requires the collection of at least one semen sample. The sample should be collected at MCRH or an approved off-site facility. A private, soundproofed room equipped with a VCR/DVD (visual materials are included) and magazines will be provided for the collection. This should be collected by masturbation in the sterile container provided. The sample should be collected after a 2-7 day abstinence period. The microscopic study of the semen sample will include the following:

Volume
The quantity of ejaculate. Quantities of $\geq 1.5$ cc (or ml) are considered normal.

Sperm Density
This is simply a calculation of how many sperm are present in the sample. Values of $\geq 15$ million sperm per milliliter are considered normal. A mandatory frozen back-up semen sample may be required if outside normal parameters. Your IVF coordinator will notify you if indicated for your treatment.

% Motility
This figure indicates the proportion of the sperm that are moving. A value of $\geq 40\%$ is considered normal.

Morphology
This value is indicative of the sperm shape. A value of $\geq 15\%$ is considered normal.

Presence of White Blood Cells
The presence of white blood cells is important as it may indicate the presence of infection. Such a situation must be corrected prior to undergoing ART/IVF. The antibiotic most commonly used to treat this is Doxycycline. It is an oral medication that is taken twice daily with meals. Photosensitivity is associated with the use of this drug; therefore, exposure to the sun and tanning devices should be avoided while using this medication.
MALE TESTING

Blood Tests

- **Blood type with Rh factor** (done once in a lifetime)
  
  In preparation for your upcoming treatment cycle, you will have a blood test to find out your blood type. As there are different blood types, there is also an Rh factor. The Rh factor is the type of protein on the red blood cells. When the Rh factor is present, an individual’s blood type is designated Rh+ (Rh positive); when the Rh factor is absent, the blood type is Rh- (Rh negative). If an Rh negative female conceives using sperm from a male whom is Rh positive, it would constitute an Rh incompatibility. As this is a manageable condition, The Midwest Center would make you aware of this incompatibility requiring further evaluation and treatment by your obstetrician should you have a successful outcome.

- **HIV 1 and 2 antibody** (acquired immune deficiency, AIDS)
- **Hepatitis B** (surface antigen)**
- **Hepatitis C** (antibody)**

Required within one year of an IVF cycle or if never completed prior to a previous IVF cycle.

Please inform our staff if vaccination for or exposure to any of these diseases has occurred.

** These viruses can cause infection of the liver and lead to liver failure; therefore, testing will be done to ensure your health prior to your IVF cycle.

If any of these test results are abnormal, you will be referred to an infectious disease specialist for further evaluation and your treatment will be delayed.

Please be advised that while some infectious disease testing is performed for your IVF cycle, not all diseases are screened for or tested. Communicable disease transmission is a possibility since bodily cells/fluids are involved in the IVF process. If you would like further discussion about communicable disease transmission, please set up a consult with your physician.
MALE TESTING

SEMEN TESTING FOR IVF PATIENTS:

The staff at MCRH wishes to provide you with the highest quality of care and understands the importance of semen testing. With this in mind, patients undergoing in vitro fertilization are required to have a semen analysis done within a specified time period.

For your convenience, you may elect to have this semen testing completed outside our office. However, due to the variability among andrology laboratories, it is necessary to first verify that the lab you desire can meet the following parameters for semen analysis. By verifying this prior to testing, unnecessary repeat testing and associated costs should be minimized. Listed below are the specific reporting parameters that MCRH requires for semen analysis. Please take this to your selected testing site to verify that their reporting capabilities meet our requirements.

Semen Analysis
According to the World Health Organization guidelines.
Backup Cryopreservation of Semen Sample

Though optimal fertilization results are obtained when a fresh sample is used, it is strongly encouraged to cryopreserve (freeze) an additional semen sample for “emergency IVF backup”. This cryopreserved sample could be used if a fresh sample cannot be obtained, or it may be used to augment a fresh sample of poor quality. If a backup sample is not provided and a semen sample is not available the day of egg retrieval, the in vitro process cannot proceed, and the eggs must be discarded.

There are risks associated with cryopreservation, including possible failure of the equipment or mechanical support system, and possible damage to the sperm during the freezing and thawing process. Complications of pregnancy and childbirth, including the possibility of the birth of an abnormal child (or children) may occur from a pregnancy following cryopreservation. However, available data suggested the risk associated with using cryopreserved semen is not greater than when using fresh semen.

In the event the cryopreserved sample is not used, it will be automatically discarded six months from the collection date without further notification.

For satellite patients wishing to consider the backup semen cryopreservation option, a kit with semen transport media is made available to you. This sample collection may take place in the convenience of your home. Arrangements to receive this kit can be made by calling Midwest Center’s Reproductive Biology Laboratory at (763) 494-7716 or (800) 508-9763 option 6.

Prior to cryopreserving a semen sample, male infectious disease testing (HIV 1 and 2, Hepatitis B surface antigen and Hepatitis C antibody) will be required and a negative result must be received by MCRH.

If you have tested positive for an infectious disease, you can still cryopreserve a back-up sample if you desire. MCRH lab does not have the capability to store an infectious sample and, therefore, we transfer the sample to Reprotech, Ltd. for long term storage. Additional paperwork must be completed for Reprotech to allow them to set up an account for your storage.

Reprotech Storage Fees for Infectious Semen Samples (subject to change)

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<tr>
<td>Quarterly</td>
<td>$113.00</td>
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A local courier would be used to send samples between MCRH and Reprotech. Approximate cost for the courier is $160.00 to have samples sent to RTL initially and then back to MCRH for IVF cycle).

There is an additional cost for cryopreservation and for a transport kit, if needed. Refer to the “Financial” section of this handbook under Male Screening for associated costs.
LATEX SENSITIVITY

Allergy to natural latex rubber has become a serious health risk for many health care professionals and patients. Allergic reactions to latex range from mild skin irritations to full body system involvement which may result in chronic illness, disability, or death.

MCRH has attempted to identify and minimize the use of latex-containing products where possible. We provide a “latex-safe” environment for patients and cannot guarantee a “latex-free” environment.

If you have a latex sensitivity and/or have had a previous reaction, we suggest testing be done through your physician/allergist. You will be given a medical release form granting medical approval to proceed. This must be completed by your physician and returned with the laboratory results in order to proceed through the treatment cycle.
Section V

Initiating Treatment and Down Regulation
PREPARATION FOR IVF TREATMENT

To allow planning for your IVF cycle, our center currently has “uptimes” approximately 5 times a year (2-3 weeks in length). It is during this time that retrievals and transfers will be performed. However, testing and medications will begin 2-3 months prior to your egg retrieval.

Once medications are initiated, subsequent office visits are needed for the ultrasound monitoring of your response to these medications, as well as blood tests. Due to the number of visits in this 2-3 week period of treatment, flexibility in your schedule is needed. In an effort to provide you with timely information, please access your private voicemail system daily between 3:00 p.m. and 4:00 p.m. CST/CDT during your treatment cycle. Patients can expect to receive messages on all monitoring days regarding test results and future treatment plans and occasionally, there may be other communications left for patients throughout their treatment cycle. If you have not received an anticipated message by 4:00 p.m. CST/CDT, please contact the nurses. Questions may then be answered during office hours for your convenience. We require that you have an answering machine/voice mail where we can leave detailed messages regarding medication and monitoring instructions as a backup to the confidential phone system.

The monitoring of ovarian stimulation is performed either at MCRH or one of our satellite clinics. Egg retrieval and embryo transfer will be performed at MCRH in Maple Grove, a northwestern suburb of Minneapolis, Minnesota.

TO BEGIN IVF TREATMENT CYCLE

Please recognize there will be references made to three different types of days.

Cycle Day  
Relating to the day of your menstrual cycle

Down Regulation  
Relating to the days on the birth control pill, Norethindrone Acetate (Aygestin) and Leuprolide Acetate (Lupron), if indicated, for ovarian suppression

Stimulation  
Relating to the days on stimulation medications and Leuprolide Acetate (Lupron) or Ganirelax Acetate

- Call the IVF coordinators at (763) 494-7702 with the onset of menses 2-3 cycles prior to your planned IVF cycle.

- Since the adverse effects of these medications on a possible pregnancy are unknown, barrier contraception or abstinence is required upon starting the birth control pill. Patients are to abstain from vaginal intercourse after the start of stimulation medications until documentation of fetal heart motion.

- Fill prescription(s) for the down regulation medications at least 2 weeks prior to initiating treatment.

You will be given your individualized medication outline prior to initiating treatment.
DOWN REGULATION MEDICATIONS

Oral Contraception (Birth Control Pill)
Patients may be placed on the birth control pill prior to initiating treatment. The intent of this medication is to suppress the system for a period of time to optimize response to the stimulation medications. If indicated, patients will be instructed by The Midwest Center staff when to begin the birth control pill. This medication is not given as a form of birth control; therefore, patients must use barrier contraception or abstinence throughout this time period. Light bleeding/spotting while on oral contraceptives is normal and you should continue taking the birth control pill as instructed. If you experience heavy bleeding, please contact our nurse line at (763) 494-7726. If you have previously taken birth control pills and have experienced a reaction in which you were advised to discontinue use, please contact our office prior to initiating oral contraception. Please make staff aware if you have a history of blood clots, hypertension, severe headaches, and/or if you smoke.

Common reactions to oral contraceptives may include visual changes, inability to wear contact lenses, fluid retention or bloating, elevated blood pressure, splotchy darkening of the skin called melasma, nausea, vomiting, change in appetite, headache, nervousness, depression, dizziness, loss of scalp hair, rash, and vaginal infection. The most serious dangers of oral contraceptives include heart attack, stroke, blood clots in lungs, legs, or eyes, increased risk of birth defects including heart and limb defects if taken by pregnant women, acceleration of the onset of gallbladder disease requiring surgery, and formation of tumors (rare, non-malignant tumors of the liver, cancer of the breast, cervix, vagina and liver has been reported in laboratory animals given estrogen). If you experience any of the following warning signals while taking oral contraceptives, please call our office: chest pain, shortness of breath, pain in the lower leg calf, headaches, vomiting, dizziness, disturbances of vision or speech, numbness in an extremity (arm or leg), stomach pain, and/or yellowing of the skin or eyeballs accompanied frequently by fever, fatigue, loss of appetite, dark colored urine, or light colored bowel movements. Please refer to the package insert for more detailed information on oral contraceptives and side effects.

Norethindrone Acetate (Aygestin) is a synthetic hormone similar to progesterone. It is a tablet given to shed the endometrial lining prior to initiating stimulation medications. A menses generally occurs one to four days after discontinuing this medication. However, bleeding/spotting while on Norethindrone is normal.

Leuprolide Acetate (Lupron) is a synthetic hormone that mimics human gonadotropin releasing hormone (GnRH) by suppressing luteinizing hormone (LH). It is a subcutaneous injection given initially to down regulate/suppress the natural hormone from the pituitary gland. This will enable an even stimulation with the stimulation medications. It will continue during the stimulation phase until the follicles are mature (≥16 mm) and ready for egg retrieval. It also helps to prevent spontaneous ovulation.

Ganirelix Acetate (Cetrotide) is a GnRH antagonist designed to inhibit gonadotropin secretion, thus helping to prevent a premature LH surge. It is supplied in a sterile, prefilled syringe and is administered subcutaneously. You will receive instructions regarding when to initiate this medication. It continues for approximately 5-7 days in conjunction with stimulation medications until hCG administration.
Side effects of Norethindrone, Leuprolide Acetate (Lupron) and Ganirelix Acetate may include hot flashes, vaginal dryness, headaches, changes in mood, and decreased interest in sexual activity. Other less common side effects include dizziness, depression, arrhythmias, angina, peripheral edema, nausea and/or vomiting, increased liver enzyme levels, pulmonary embolism, and transient bone pain.
DOWN REGULATION

- Call our IVF coordinators at (763) 494-7702 with the onset of your period two to three months prior to your treatment cycle.

- If indicated, birth control pills will begin as instructed.

- Norethindrone Acetate (Aygestin) will begin as instructed.

- If indicated, Leuprolide Acetate (Lupron) will begin as instructed. Refer to Leuprolide Acetate administration instructions.

- It is normal to experience vaginal bleeding of varying amounts during down regulation.

- To confirm that suppression has been achieved, a vaginal ultrasound and serum estradiol (blood test) will be performed.

- Once down regulation has been achieved, stimulation medications will begin on the day instructed by The Midwest Center nursing staff.

- Stimulation medications may begin on the same day as your down regulation check. Therefore, fill prescriptions for the stimulation medications and hCG, and keep track of injection supplies. Begin taking your prenatal vitamin by the initiation of stimulation medications if you have not already begun taking it.

- Refer to Down Regulation outline.
PREPARATION OF LEUPROLIDE ACETATE (LUPRON)

1. Clean the work surface that will be used to prepare the injection with soap and water, or swab with alcohol, and wash your hands thoroughly.

2. Assemble the necessary materials: Leuprolide Acetate (Lupron), insulin syringe and needle, alcohol wipes, and disposal container. The needles and syringes are intended for one time use only.

3. Check medication label for proper type of medication and expiration date (medication should be clear and free of particles).

4. Using your thumb, remove flip top cap from Leuprolide Acetate bottle. The medication does not need to be recapped after use.

5. Wipe top of vial with an alcohol swab and allow alcohol to dry. Do not touch the rubber stopper after it is wiped.

6. Remove syringe from packaging and draw air into the syringe by pulling plunger back to amount prescribed (see patient outline).

7. Insert needle straight down through the center circle of the rubber stopper of the vial.

8. Inject air into the Leuprolide Acetate vial equal to or greater than the amount of medication to be withdrawn.

9. Without removing the needle, turn the bottle upside down. Slowly pull back the plunger filling the syringe to slightly more than the prescribed dose and then adjust the plunger to your prescribed dose to clear away air bubbles. Make sure the tip of the needle remains in the medication to avoid withdrawing large amounts of air. It may be necessary to back the needle out of the vial to ensure the needle tip remains below the level of medication.

10. Inject excess medicine and air bubbles back into Leuprolide Acetate bottle.

11. Once the plunger is set at your prescribed dose, remove the syringe needle from the vial.
SUBCUTANEOUS ADMINISTRATION OF LEUPROLIDE ACETATE (LUPRON)

1. Make yourself comfortable by sitting or lying down.
2. Choose an injection site (abdomen, thigh, or upper arm).
3. Clean the injection site with an alcohol swab and allow it to air dry.
4. Carefully uncap the needle by pulling the needle cap from the syringe.
5. Holding the syringe in one hand, use the other hand to pinch a fold of skin at the prepared injection site.
6. Holding the syringe like a pencil, quickly insert the entire length of the needle into the skin at a 90° angle.
7. Inject prescribed amount of Leuprolide Acetate into the subcutaneous tissue by slowly and steadily depressing the plunger. Be careful not to move the syringe and needle while you are injecting.
8. After injecting all the medication, release the pinch.
9. Gently withdraw the needle.
10. Dispose of the syringe and needle safely. Please check with your individual disposal company for specific information regarding disposal. Pharmacies will generally supply Sharps containers or you may dispose of the needle and syringe by placing them in an empty plastic liter bottle. For safety reasons, please do not bring to the office for disposal.
11. Place a tissue or gauze over the skin where you gave the injection. If any bleeding occurs, apply gentle pressure for 10-15 seconds.
12. Alternate injection sites.
ALWAYS PAY CLOSE ATTENTION TO THE DOSE OF LEUPROLIDE ACETATE PRESCRIBED FOR YOU BY YOUR PHYSICIAN. CAREFULLY CHECK THE EXPIRATION DATE ON THE BOTTLE AND DO NOT USE OUTDATED MEDICINE. CAREFULLY CALCULATE AND MEASURE OUT THE CORRECT AMOUNT.

LEUPROLIDE ACETATE (LUPRON) IS A MULTI-DOSE VIAL.

LEUPROLIDE ACETATE SHOULD BE STORED BELOW 77 ° F (REFRIGERATED OR UNREFRIGERATED). AVOID FREEZING.

IF REFRIGERATING PRODUCT, REMOVE FROM REFRIGERATOR 15-30 MINUTES PRIOR TO SCHEDULED INJECTION TO ADJUST TO ROOM TEMPERATURE.

PROTECT FROM LIGHT - STORE VIAL IN CARTON.
**LEUPROLIDE ACETATE (LUPRON) SYRINGES AND DOSAGES**

<table>
<thead>
<tr>
<th>Insulin Syringe</th>
<th>Lupron Kit Syringe</th>
<th>Tuberculin Syringe</th>
</tr>
</thead>
<tbody>
<tr>
<td>20 units</td>
<td>0.2 ml</td>
<td>0.2 cc (or ml)</td>
</tr>
<tr>
<td>10 units</td>
<td>unmarked line</td>
<td>0.1 cc (or ml)</td>
</tr>
<tr>
<td></td>
<td>(line closest to needle)</td>
<td></td>
</tr>
<tr>
<td>5 units</td>
<td>1/2 of unmarked line</td>
<td>1/2 of 0.1 cc (or ml)</td>
</tr>
<tr>
<td>2.5 units</td>
<td>1/4 of unmarked line</td>
<td>1/4 of 0.1 cc (or ml)</td>
</tr>
</tbody>
</table>

* Your prescription is written for the insulin syringe measuring in units. Medication doses provided by Midwest Center staff are based upon insulin syringe measurements. Please utilize this conversion table if necessary.
OVERVIEW

- Call our IVF coordinators at (763)494-7702 with the onset of your period two to three months prior to your treatment cycle.

- If indicated, birth control pills will begin as instructed.

- Norethindrone Acetate (Aygestin) will begin as instructed by staff.

- If indicated, Leuprolide Acetate (subcutaneous injections) will begin as instructed. Refer to Leuprolide Acetate (Lupron) administration directions.

- It is normal to experience vaginal bleeding of varying amounts during down regulation.

- To confirm that suppression has been achieved, a vaginal ultrasound and serum estradiol (blood test) will be performed.

- A down regulation check will be performed for those patients instructed to administer Leuprolide Acetate (Lupron). Once down regulation has been achieved, stimulation medications will begin as instructed by Midwest Center staff. For patients taking Ganirelex Acetate, a baseline monitoring will occur prior to initiating stimulation medications. Ganirelex Acetate will generally start on stimulation day 4-5 and will be taken for approximately 5-7 days in conjunction with stimulation medications, and is continued until hCG administration.

- Vaginal intercourse using condoms is permitted until the initiation of stimulation medications. Abstinence is required from the start of stimulation medications until fetal heart motion is documented.

- Begin taking one prenatal vitamin daily when stimulation medications are initiated, if not before.

- Ultrasounds and blood tests will be obtained periodically (every 2-6 days) while on stimulation medications.

- When your follicles are determined to be mature (≥15 mm), you will receive an injection of hCG (after approximately 8-12 days of stimulation medications).

- Patients will receive final instructions regarding retrieval the day of hCG.

- Approximately 36 hours after hCG administration, the egg retrieval will be performed (for example, hCG at 8:30 p.m. CST/CDT Wednesday -- egg retrieval at 8:30 a.m. CST/CDT Friday). For those patients living in a different time zone, please inform a nurse who can help you adjust your medication times accordingly.

- Begin taking your progesterone as instructed by Midwest Center staff.

- Embryo transfer occurs two to five days after egg retrieval.

- You will have a pregnancy test (quantitative BhCG) approximately 14 and 16 days after embryo transfer.
Section VI

Ovarian Stimulation
OVARIAN STIMULATION

Menopur (LH and FSH) and Follistim/Gonal-f RFF Pen/Bravelle (recombinant FSH) are medications used to stimulate the ovaries to develop and mature multiple follicles. The Midwest Center considers a follicle to be mature when it measures equal to or greater than 15 mm. Having multiple eggs for IVF increases your chance for pregnancy. Frequent ultrasounds and blood work (estradiol levels) are needed to assess follicle growth and maturity (≥15 mm). This monitoring also helps ensure that your dosage of medication is appropriate and aids in determining the optimal time for administering hCG (Pregnyl/Novarel).

Side effects of stimulation medications include irritation at the injection site, hot flashes, dizziness, nausea, bloating, left or right side cramping, breast tenderness, blurred vision, mood swings, headaches and fluid retention. These side effects are uncommon but they can occur together or separately. Should you experience severe side effects, please notify the nursing staff at (763) 494-7726.

Stimulation medications continue for approximately 8-12 days. Keep in mind that this is an estimation and we are unable to tell you the exact date of retrieval until hCG is administered. It is recommended that your spouse/partner administer any intramuscular injections you may need. An injection instruction class is offered at our clinic and satellite clinics to ensure a comfort level with administering injections.

- Begin taking prenatal vitamins daily when stimulation medications are started if you have not already done so.

- If instructed to take Leuprolide Acetate (Lupron), it will continue daily until hCG is administered. If Ganirelix Acetate is prescribed, it will begin as instructed by Midwest Center staff and continue until hCG administration.

- **No vaginal intercourse after start of stimulation medications.** Abstain from vaginal intercourse until fetal heart motion is documented.

- Keep inventory of medications once stimulation has begun to anticipate when refills are needed. Original prescriptions have enough refills to complete the cycle.

- Day 1 of stimulation, spouse/partner should begin Doxycycline, 100 mg, twice a day through the evening before egg retrieval.

- To obtain sperm with maximum motility for fertilization of the oocytes on the day of retrieval, we require that the **last ejaculation occur on stimulation day 7**. This ejaculate does not need to be saved and should **not** be produced by having vaginal intercourse.
Dear Patients:

It is our desire to continually improve our ability to serve your needs. Below please find a partial listing of resources that provide pharmaceutical supplies and medications. Please be aware that it is entirely your choice whether or not you utilize any of these services for your pharmaceutical needs.

<table>
<thead>
<tr>
<th>Pharmacy</th>
<th>Phone #</th>
<th>Fax #</th>
<th>Address</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glen Rock Medical Pharmacy</td>
<td>866-888-3200</td>
<td>201-444-5792</td>
<td>210 Rock Road, Glen Rock, NJ 07452</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><a href="http://www.glenrockmedicalpharmacy.com">www.glenrockmedicalpharmacy.com</a></td>
</tr>
<tr>
<td>Mandell’s Clinical Pharmacy</td>
<td>877-252-0553</td>
<td>877-252-0450</td>
<td>7 Cedar Grove Lane, Somerset, NJ 08873</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><a href="http://www.mandellspharmacy.com">www.mandellspharmacy.com</a></td>
</tr>
<tr>
<td>Walgreens Specialty Pharmacy</td>
<td>800-424-9002, then press 1,1</td>
<td>800-874-9179</td>
<td>7164 Technology Drive, Ste 100 Frisco, TX 75034</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><a href="http://www.walgreenshealth.com">www.walgreenshealth.com</a></td>
</tr>
<tr>
<td>**Walgreens 24-hour Fertility Pharmacy</td>
<td>612-377-3308</td>
<td>612-377-5670</td>
<td>2426 Hennepin Ave S, Minneapolis, MN 55405</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><a href="http://www.freedomfertility.com">www.freedomfertility.com</a></td>
</tr>
<tr>
<td>Fairview Specialty Pharmacy- University Village</td>
<td>612-672-1430</td>
<td>612-672-1431</td>
<td>2545 University Ave SE, Minneapolis, MN 55414</td>
</tr>
<tr>
<td>Freedom Fertility Pharmacy</td>
<td>800-660-4283</td>
<td>888-660-4283</td>
<td>12 Kent Way, Byfield, MA 01922</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><a href="http://www.freedomfertility.com">www.freedomfertility.com</a></td>
</tr>
</tbody>
</table>
Ganirelex Acetate Information Sheet

Ganirelex Acetate

By definition, it is a GnRH (gonadotropin releasing hormone) antagonist. Its action is to inhibit gonadotropin secretion, thus helping to prevent a premature LH surge.

- The recommended dose is **250 mcg** each day, but may increase to twice daily.
- It is supplied in a sterile, prefilled 1cc syringe (containing 250mcg/½ cc of medication) and should be injected **subcutaneously**. The primary sites are the lower abdomen and the upper thigh where the skin is loose.
- Administration may begin as early as stimulation day 3 depending on how quickly your estradiol level rises. The nurses will give you specific instructions regarding when to initiate the medication. The length of time that you are on this medication varies but averages 5-7 days. Once initiated, Ganirelex injections will continue daily until administration of hCG.
- Once this medication is initiated, it is very important that you do NOT miss a dose as this may lead to premature ovulation before egg retrieval. Therefore, if you feel you may need a refill of this medication, please allow enough time for the pharmacy to dispense the refill so you do not miss a dose of the Ganirelex.

Cetrotide 0.25mg is an equivalent medication to Ganirelex Acetate and may be used as a replacement medication if your pharmacy is unable to fill the Ganirelex Acetate. Cetrotide is supplied as a powder and water that needs to be reconstituted prior to administration. This medication needs to be refrigerated.

Please call the nurse line at (763) 494-7726 with any questions regarding these medications.
PREPARATION OF FOLLISTIM (300 IU and 600 IU)

If you do not receive a follistim pen from your pharmacy, please contact our office.

Preparing the Injection
1. Clean the work surface that will be used to prepare the injection with soap and water, or swab with alcohol, and wash your hands thoroughly.
2. Pull off the Follistim Pen™ cap and set cap aside.
3. Unscrew the pen body from the cartridge holder and set them aside.
4. Take a Follistim AQ cartridge out of its package and clean the rubber stopper with alcohol. Place the cartridge into the yellow cartridge holder inserting the metal rimmed cap end first.
5. Lower the pen body containing the black rod into the yellow cartridge holder and screw the body fully onto the cartridge holder. The blue arrow on the cartridge holder and the yellow rectangle on the pen body should be in alignment with no gap.
6. Your cartridge will contain either 300 IU or 600 IU of Follistim. For your prescribed dose, turn the dosage knob until the dot beside the correct number is visible in the middle of the dosage window. If you mistakenly dial past the correct number, do not try to turn the dosage knob backward to fix the error as you will lose some drops of medicine from the tip of the needle. Continue to turn the dosage knob in the same direction past the 450 IU mark and push the injection button in all the way. Start to dial again starting from "0" upwards.
7. Clean the open end of the cartridge holder with alcohol.
8. Peel the protective paper seal off the BD micro-fine pen needle. Do not touch the open needle or place it on any surface.
9. Hold the needle shield in one hand and cartridge holder in the other hand and push the end of the cartridge holder into the outer needle shield. Screw them tightly together.
10. After preparing the injection site, pull off the outer needle shield (leave the inner needle shield covering the needle in place). Do not throw the outer needle shield away as you will need it to dispose of the needle after injecting the medicine.
11. Remove the inner needle shield and discard it.
12. Administer the injection subcutaneously (refer to subcutaneous injection instructions) and leave the needle in the skin for 5 seconds after giving the full injection.
13. The middle of the dosage window should display "0" after the injection has been administered. If the window displays “0”, proceed to step 18.
   If the injection button does not push all the way in, and the number does not read “0”, it means there is not enough medicine in the cartridge. The number in the window indicates the amount of medicine needed to complete your dose. If the number does not read “0”, write this number in the window down and follow steps 15-21.
14. Recap the needle, by placing the outer shield on a flat surface with the opening pointing up. Face the pen pointing needle down and carefully insert the needle into the opening of the needle cap and push down firmly. Grip the shield and unscrew the needle from the cartridge holder. Dispose of your needle and cartridge safely. Please check with your individual disposal company for specific information regarding disposal. Pharmacies will generally supply Sharps containers or you may dispose of the needle and cartridge by placing them in an empty plastic liter bottle. For safety reasons, please do not bring to the office for disposal.

15. Start over with a new Follistim cartridge and new needle by following the instructions previously outlined in steps 4-12.

16. Choose a new injection site.

17. **Use the needle for one injection only.** After administering the injection, place the outer shield on a flat surface with the opening pointing up. Face the pen pointing needle down and carefully insert the needle into the opening of the needle cap and push down firmly.

18. Once the needle is capped tightly, grip the shield and unscrew the needle from the cartridge holder.

19. Dispose of the needle safely. Please check with your individual disposal company for specific information regarding disposal. Pharmacies will generally supply Sharps containers or you may dispose of the needle by placing it in an empty plastic liter bottle. For safety reasons, please do not bring to the office for disposal.

21. If the cartridge is empty, dispose of it in your Sharps container. If medicine remains in the cartridge, put the pen cap on and store your pen in the refrigerator or at room temperature until the next injection. **Never store the Follistim pen with a needle attached to it as the drug may leak out and there is a risk of contamination.**

** The cartridge may be stored at 36°-46° F until the expiration date or at 77° F for 3 months or until expiration date (whichever comes first). Once the rubber stopper of the cartridge has been pierced by the needle, the product can be stored for a maximum of 28 days at 36°-77° F. Do not freeze. Protect from light.

** If you refrigerate the cartridge, remove from refrigerator 15-30 minutes before scheduled injection to adjust to room temperature.

** If you touch the needle, if you blow on the needle, or if it comes in contact with any surface, it is considered contaminated. In the event this occurs, recap and remove the contaminated needle. Attach a sterile needle to the syringe and continue preparation.

Prior to preparing your injection, if it is evident that you do not have enough medicine in the cartridge for another injection you have two options:

#1 - Remove cartridge and insert a new cartridge into the pen and follow steps 4-13 and 18-21.

#2 - Use the remaining medicine before opening a new cartridge. Follow steps 14-21 to inject the remaining drug to complete your dose (this option will require you to administer 2 injections to receive the full dosage prescribed).

-Information taken from Organon’s Follistim Pen™ Instructions for Use
PREPARATION OF GONAL-F (SINGLE DOSE VIAL)

Preparing the Injection

1. Clean the work surface that will be used to prepare the injection with soap and water, or swab with alcohol, and wash your hands thoroughly.

2. Assemble the necessary materials: medication vial(s), prefilled syringe of Sterile Water, 18 G 1½” mixing needle, 27 G ½” injection needle, alcohol wipes, and disposal container.

3. Using your thumb, remove flip top cap from powder vial.

4. Wipe the top of the vial with an alcohol swab and allow alcohol to dry. Do not touch the rubber stopper after it is wiped.

5. Hold the barrel of the prefilled syringe of Sterile Water in one hand. Firmly hold the white plastic cap between the thumb and forefinger of the other hand and with a downward motion, gently snap and pull off the cap. If the gray cap remains, simply remove it.

6. Remove the safety seal cover of the 18 G 1½” mixing needle. Push the needle on the prefilled syringe until it is tight. Holding the base of the needle, secure the needle on the tip of the prefilled syringe and remove the needle cap.

7. Insert the needle of the prefilled syringe straight down through the center circle of the rubber stopper of the Gonal-f powder vial. Slowly inject the water into the vial. Do not shake vial.

8. Turn the vial upside down keeping the needle in the vial so the needle points upward. Back the needle out of the vial to make sure the needle tip remains in the mixture and withdraw the entire contents of the vial. Remove the syringe from the vial.

9. If your dose requires more than one vial of Gonal-f RFF 75 IU, use the mixture in the syringe to reconstitute the next vial of Gonal-f. Use the same 18 G 1½” needle and syringe to mix additional vials.

10. When reconstitution is complete, pull the plunger back to allow a small air space and recap the needle. Twist and pull off the needle from the syringe and discard of it in your disposal container.

11. Remove the safety seal cover of the 27 G ½” needle for injection. Push the needle on the prefilled syringe until it is tight. Holding the base of the needle, secure the needle on the tip of the prefilled syringe and remove the needle cap.

12. Check for air bubbles. If any are visible, point the needle up, tap lightly to collect any air bubbles into the top of the syringe, and gently press the plunger to expel the air.

- **If you touch the needle, if you blow on the needle, or if it comes in contact with any surface, it is considered contaminated. In the event this occurs, recap and remove the contaminated needle. Attach a sterile needle to the syringe and continue preparation.**

- *information taken from Serono’s Reconstituting Gonal-f® RFF 75 IU vial*
PREPARATION OF GONAL-F RFF REDI-JECT PEN (300IU, 450IU AND 900IU)

1. Clean the work surface that will be used to prepare the injection with soap and water, or swab with alcohol, and wash your hands thoroughly.
2. Remove pen cap and wipe gray rubber stopper on pen tip with alcohol wipe.
3. To set the dose, turn the dose knob clockwise until your dose is shown in the display window. Assure you are in good lighting when dialing in your dose.
   *DO NOT* push or pull the dose knob while you are turning it. If you pass your dose, turn the dose knob back to your correct dose.
4. Remove peel tab from outer needle cap.
5. Press rubber stopper end of pen into open end of outer needle cap and twist needle onto pen clockwise until needle is securely attached.
6. Remove outer needle cap (an inner needle cap will remain on the needle).
7. Remove blue cap protecting needle just prior to injection.
8. Administer the injection **subcutaneously** (refer to subcutaneous injection instructions). Press down on the dose knob as far as it will go to complete the full injection. Hold for 5 seconds at completion.
   **If the dose window does not read zero (i.e.: at completion the window displays 75) your dose was not fully given.**
   - You will need a **new pen** to complete your dose as the full amount was **not** available in the pen used.
   - Remove the used needle and discard empty pen (steps 9-12).
   - Open a new pen, dial in and administer remaining dose displayed in empty pen. (steps 1-8)
9. Remove needle and apply pressure with gauze pad/tissue.
10. Hold pen firmly and replace outer needle cap. Grip needle cap firmly and unscrew needle from pen.
11. Dispose of needle safely. Please check with your individual disposal company for specific information regarding disposal. Pharmacies will generally supply Sharps containers or you may dispose of the needle by placing it in an empty plastic liter bottle. For safety reasons, please do not bring to the office for disposal.
12. If the pen is empty, dispose of it in your sharps container. If medicine remains in the pen, replace pen cap and store at room temperature (68°F to 77°F) or in refrigerator for a maximum of **28 days**. Never store the Gonal-f pen with the needle attached.

** Unopened pens may be stored in refrigerator until the expiration date or at room temperature for 3 months.
** If you refrigerate the pen, remove from the refrigerator 15-30 minutes before scheduled injection to adjust to room temperature.
** To determine how much medication you have remaining after administering an injection, record the amount you administer each time and subtract that number from the total number of units remaining in the cartridge.

Information taken from Serono’s Gonal-f RFF Redi-ject instructions for use
PREPARATION OF BRAVELLE

Preparing the Injection

1. Clean the work surface that will be used to prepare the injection with soap and water, or swab with alcohol, and wash your hands thoroughly.

2. Assemble the necessary materials: medication and sterile diluent vials, Q•Cap, 3 cc syringe, 25 G or 27 G ½” or 5/8” needle (if administering injection subcutaneously) or 22 G 1½” needle (if administering intramuscularly), alcohol wipes, and disposal container.

3. Be sure to check medication dosages very carefully. Using your thumb, remove flip top caps from powder and sterile diluent vials.

4. Wipe tops of vials with an alcohol swab and allow alcohol to dry. Do not touch the rubber stoppers after they are wiped.

5. If a capped needle is attached to the 3 cc syringe, remove it and attach the Q•Cap by twisting the connector end until you feel resistance. Do not touch the spike end (pointed portion of the Q•Cap).

6. Draw air into the syringe equal to the amount of diluent you plan to withdraw (i.e. if withdrawing 1 cc, draw 1 cc of air into the syringe).

7. Insert the Q•Cap straight down through the center of the rubber stopper of the diluent vial and inject the air.

8. Without removing the Q•Cap, turn the vial upside down and withdraw the diluent into the syringe by pulling back on the plunger.

- ½ - 1 cc (or ml) for a subcutaneous injection
- 1½ - 2 cc (or ml) for an intramuscular injection

The diluent amount remains constant regardless of the number of powders mixed.

9. Remove Q•Cap from the diluent vial by pulling up on the syringe.

10. Insert Q•Cap into the vial of medication powder. Slowly inject the diluent into the vial to avoid creating bubbles.

11. Leave the Q•Cap in the vial and gently mix by rotating the vial between your fingers until the solution is clear.

12. Invert the vial and withdraw the entire contents of the medication vial into the syringe.

   If instructed to take 150 iu and you have 75 iu of medication, inject all diluent into first 75 iu of powder, withdraw mixture, and inject that into second 75 iu of powder.

13. Remove the Q•Cap from the vial by pulling up on the syringe.

14. Twist the syringe counterclockwise after reconstitution is complete to remove the Q•Cap and attach the needle prior to administration.

   - 25 G or 27 G, ½” or 5/8” for subcutaneous injection
   - 22 G 1½” for intramuscular injection

15. Check for air bubbles. If any are visible, point the needle up, tap lightly to collect any air bubbles into the top of the syringe, and gently press the plunger to expel the air.

* If you touch the pointed portion of the Q•Cap or if it comes in contact with any surface, it is considered contaminated. In the event this occurs, remove the contaminated Q•Cap. Attach a sterile Q•Cap to the syringe and continue preparation.
PREPARATION OF MENOPUR

Preparing the Injection

1. Clean the work surface that will be used to prepare the injection with soap and water, or swab with alcohol, and wash your hands thoroughly.

2. Assemble the necessary materials: medication and sterile diluent vials, Q•Cap, 3 cc syringe, 25 G or 27 G ½” or 5/8” needle (if administering injection subcutaneously) or 22 G 1½” needle (if administering intramuscularly), alcohol wipes, and disposal container.

3. Be sure to check medication dosages very carefully. Using your thumb, remove flip top caps from powder and sterile diluent vials.

4. Wipe tops of vials with an alcohol swab and allow alcohol to dry. Do not touch the rubber stoppers after they are wiped.

5. If a capped needle is attached to the 3 cc syringe, remove it and attach the Q•Cap by twisting the connector end until you feel resistance. Do not touch the spike end (pointed portion of the Q•Cap).

6. Draw air into the syringe equal to the amount of diluent you plan to withdraw (i.e. if withdrawing 1 cc, draw 1 cc of air into the syringe).

7. Insert the Q•Cap straight down through the center of the rubber stopper of the diluent vial and inject the air.

8. Without removing the Q•Cap, turn the vial upside down and withdraw the diluent into the syringe by pulling back on the plunger. 
   
   ½ - 1 cc (or ml) for a subcutaneous injection 
   1½ - 2 cc (or ml) for an intramuscular injection 

   The diluent amount remains constant regardless of the number of powders mixed.

9. Remove Q•Cap from the diluent vial by pulling up on the syringe.

10. Insert Q•Cap into the vial of medication powder. Slowly inject the diluent into the vial to avoid creating bubbles.

11. Leave the Q•Cap in the vial and gently mix by rotating the vial between your fingers until the solution is clear.

12. Invert the vial and withdraw the entire contents of the medication vial into the syringe.

   If instructed to take 150 iu and you have 75 iu of medication, inject all diluent into first 75 iu of powder, withdraw mixture, and inject that into second 75 iu of powder.

13. Remove the Q•Cap from the vial by pulling up on the syringe.

14. Twist the syringe counterclockwise after reconstitution is complete to remove the Q•Cap and attach the needle prior to administration.

   25 G or 27 G, ½” or 5/8” for subcutaneous injection 
   22 G 1½” for intramuscular injection

15. Check for air bubbles. If any are visible, point the needle up, tap lightly to collect any air bubbles into the top of the syringe, and gently press the plunger to expel the air.

* If you touch the pointed portion of the Q•Cap or if it comes in contact with any surface, it is considered contaminated. In the event this occurs, remove the contaminated Q•Cap. Attach a sterile Q•Cap to the syringe and continue preparation.
SUBCUTANEOUS INJECTION ADMINISTRATION

1. Make yourself comfortable by sitting or lying down.

2. Choose an injection site (abdomen, thigh).

3. Clean the injection site with an alcohol swab and allow it to air dry.

4. Carefully uncap the needle by pulling the needle cap from the syringe.

5. Holding the syringe in one hand, use the other hand to pinch a fold of skin at the prepared injection site.

6. Holding the syringe like a pencil, quickly insert the entire length of the needle into the skin at a 90° angle.

7. Inject the medication into the subcutaneous tissue by slowly and steadily depressing the plunger. Be careful not to move the syringe and needle while you are injecting.

8. After injecting all the medication, release the pinch.

9. Gently withdraw the needle.

10. Place a tissue or gauze over the skin where you gave the injection. If any bleeding occurs, apply gentle pressure for 10-15 seconds.

11. Dispose of the syringe and needle safely. Please check with your individual disposal company for specific information regarding disposal. Pharmacies will generally supply Sharps containers or you may dispose of the needle and syringe by placing them in an empty plastic liter bottle. For safety reasons, please do not bring to the office for disposal.

12. Alternate injection sites.

If you experience discomfort administering a medication subcutaneously (i.e. burning at injection site), administer the medication intramuscularly (if the medication is designed to be given either subcutaneously or intramuscularly) by following the intramuscular mixing and administration instructions.
INTRAMUSCULAR INJECTION ADMINISTRATION

1. Choose the area of your upper buttock or thigh where you will administer the injection.

2. Cleanse the area for injection with an alcohol wipe and allow it to air dry.

3. Remove the needle cap.

4. With your other hand, stabilize the skin between your thumb and forefinger.

5. Holding the syringe like a pencil, quickly insert the entire length of the needle at a 90° angle through the skin and into the muscle.

6. Using your stabilizing hand to hold the syringe, pull back (aspirate) the plunger 2-3 units to check that you have not placed the needle into a blood vessel. Aspiration should be maintained for 5-10 seconds. If medication remains clear, inject medication. If blood appears in the syringe, withdraw the needle entirely, properly dispose of the syringe and needle, and repeat the medication preparation process. Under certain circumstances, we recognize that discarding the medication may not be an option and recommend changing the needle before attempting to re-administer the injection. Select and prepare a new site.

7. Inject all of the medication into the muscle steadily and slowly. Medication should be injected at a rate of approximately 1 ml every 5-10 seconds. Be careful not to move the syringe as you are injecting the medication.

8. Wait 5-10 seconds before withdrawing needle to allow time for medication to diffuse into the muscle.

9. Withdraw the needle from the skin and place a tissue or gauze over the site where you gave the injection. Hold in place with gentle pressure for 10-15 seconds.

10. Dispose of the syringe and needle safely. Please check with your individual disposal company for specific information regarding disposal. Pharmacies will generally supply Sharps containers or you may dispose of the needle and syringe by placing them in an empty plastic liter bottle. For safety reasons, please do not bring to the office for disposal.

11. Alternate injection sites.
INTRAMUSCULAR INJECTION SITE LOCATION

- **To locate the appropriate area of the buttock**, envision the division of either buttock into four equal quadrants. Then, further divide the upper, outer quadrant into four equal quadrants—the injection site will be in the uppermost, outermost, quadrant of the buttock following the second division.

![Diagram of buttock showing injection site location]

Relax the muscle on the side in which the injection is being administered.

⇒ *If another person administers this injection*, the patient should either lie face down on a firm surface or stand, leaning forward against a surface using arms to stabilize the body. When leaning, cross one leg behind the other leg and bend the knee of the crossed leg to allow the muscle to relax. Give the injection into the non-weight bearing side.

⇒ *If the pt. self-administers this injection*, sit with knees bent and feet flat on the floor.

***** BE CAREFUL TO NOT ADMINISTER THE INJECTION TOO CLOSE TO THE SPINE OR TOO LOW ON THE BUTTOCK.

- **To locate the appropriate area on the thigh**, the patient should sit with knees bent, feet flat on the floor. The intramuscular injection is administered on top of the thigh. The optimal area to administer this injection is at least four inches above the knee and four inches below the hip. Caution should be used to not inject too close to the knee or hip.

![Diagram of thigh showing injection site location]

Relax the muscle on the side in which the injection is being administered.

⇒ *For injection into the thigh*, the patient should sit while administering the injection to relax the muscle.
IMPORTANT POINTS TO REMEMBER

1. Always pay close attention to the dose of medication prescribed for you. Check medication expiration date.

2. For medication storage information, refer to the individualized package insert. Store all medications away from light. Avoid hot or cold temperature extremes. Single dose stimulation medications should be injected shortly after being mixed, within 1/2 hour.

3. Be sure to alternate injection sites (right side versus left) when administering stimulation medications and Leuprolide Acetate (Lupron) or Ganirellex Acetate.

4. Be consistent with the timing of injections. Give the same time each day.

5. Insert entire needle into the muscle and/or subcutaneous tissue (depending upon the type of administration). The discomfort that is experienced is from the needle penetrating the skin.

6. Swelling and redness sometimes occur where an injection has been given. If the red area is larger than a 50 cent coin or if it lasts for 4 hours or more, contact our office by calling (763) 494-7726.

7. Side effects of fertility medications include soreness at the injection site, hot flashes, bloating, left or right side cramping, breast tenderness, blurred vision, mood swings, headaches, and fluid retention. These side effects are uncommon, but they can occur together or separately.

8. Warm, moist heat before and/or after the medication has been given can greatly reduce the discomfort of injections (i.e. moist washcloth).

9. Dispose of syringes and needles safely. Please check with your individual waste disposal company for specific information regarding disposal. Pharmacies will generally supply Sharps containers or you may dispose of the needles and syringes by placing them in an empty plastic liter pop or bleach bottle. For safety reasons, please do not bring to the office for disposal.
PRENATAL VITAMIN

A prenatal vitamin is an oral vitamin given to supplement your diet by providing you with the vitamins and minerals needed for pregnancy. This vitamin contains the recommended amount of folic acid which will help to decrease the chance of birth defects in early development of the fetus.

Prenatal vitamins are formulated to optimize supplementation for an expecting mother, and it is our feeling that this is also optimal for conception. Given the wide variety of other herbs and vitamins available, and given the lack of studies demonstrating their effect upon reproduction, we ask that you **do not take other vitamins or herbal preparations** while undergoing in vitro fertilization.

**Potential Side Effects of Prenatal Vitamins**

- Constipation
- Darkening of the stools due to iron contained in the vitamins
- Nausea

You may want to drink plenty of water as well as include fiber in your diet to help counteract these effects.

Stool softeners (i.e. Metamucil, Citrucel) may be taken to treat constipation.

Begin taking one vitamin daily when stimulation medications begin if you have not already started.
DAY OF hCG (PREGNYL/NOVAREL)

Pregnyl and Novarel are brand names of hCG (Human Chorionic Gonadotropin). It is a naturally produced hormone which prepares the follicle for retrieval. This is an injection you will administer at a **specific** time (CST/CDT) as instructed by MCRH staff.

- When estradiol levels and the follicle sizes are optimal (≥15 mm), hCG (Pregnyl/Novarel) will be administered with or without a Lupron trigger.

- Instructions will be given regarding retrieval.

- Egg retrieval will be performed approximately 36 hours following the hCG injection. **Timing is very important!!!**

- Once hCG is given, discontinue other medications including **stimulation medications and Leuprolide Acetate (Lupron) or Ganirelix Acetate.**

- Fill all remaining prescriptions and make sure you bring them with you, especially if traveling from out of town.

- **Refer to your individualized patient medication outline.**
PREPARATION OF PREGNYL (10,000 USP Units hCG)

Preparing the Injection

1. Clean the work surface that will be used to prepare the injection with soap and water, or swab with alcohol, and wash your hands thoroughly.

2. Assemble the necessary materials: medication vials, 3 cc syringe, 25 G or 27 G ½” or 5/8” needle (if administering injection subcutaneously), 22 G 1½” needle(s), alcohol wipes, and disposal container.

3. Attach the 22 G 1½” needle to the 3 cc syringe.

4. Using your thumb, remove flip top caps from powder and diluent vials.

5. Wipe tops of vials with an alcohol swab and allow alcohol to dry. Do not touch the rubber stoppers after they are wiped.

6. Remove cover from the needle.

7. Draw air into the syringe equal to the amount that you plan to withdraw (i.e. if withdrawing 1 cc, draw 1 cc of air into the syringe).

8. Insert needle straight down through the center circle of the rubber stopper of the diluent vial and inject the air.

9. Without removing the needle, turn the bottle upside down and withdraw the diluent into the syringe.

   ¾ - 1 cc (or ml) for a subcutaneous injection

   1½ - 2 cc (or ml) for an intramuscular injection

   Back the needle out of the vial to make sure the needle tip remains in the sterile water. This will prevent withdrawing a large amount of air.

10. Remove needle from the diluent vial. Point the needle up and tap lightly to collect any air bubbles into the top of the syringe. Press the plunger to expel air and confirm the correct amount of diluent is in the syringe.

11. Insert needle into the vial of powder containing the Pregnyl 10,000 USP Units. Slowly inject the diluent toward the side of the vial to avoid creating bubbles.

12. Leave the needle in the vial and gently mix by rotating the vial between your fingers until the solution is clear.

13. Turn the vial upside down and withdraw the reconstituted Pregnyl 10,000 USP Units into the syringe. To draw out all the medication, back the needle out of the vial making sure the needle tip remains below the level of medication.

14. Remove the needle from the vial.

15. Recap and twist off the needle after reconstitution is complete and change the needle prior to administration.

   25 G or 27 G ½” or 5/8” for subcutaneous injection

   22 G 1½” for intramuscular injection

16. Check for air bubbles. If any are visible, point the needle up, tap lightly to collect any air bubbles into the top of the syringe, and gently press the plunger to expel the air.

* If you touch the needle, if you blow on the needle, or if it comes in contact with any surface, it is considered contaminated. In the event this occurs, recap and remove the contaminated needle. Attach a sterile needle to the syringe and continue preparation.
**PREPARATION OF NOVAREL (10,000 USP Units hCG)**

**Preparing the Injection**

1. Clean the work surface that will be used to prepare the injection with soap and water, or swab with alcohol, and wash your hands thoroughly.

2. Assemble the necessary materials: medication vials, 3 cc syringe, 22 G 1½” needles, alcohol wipes, and disposal container.

3. Attach a 22 G 1½” needle to the 3 cc syringe.

4. Using your thumb, remove flip top caps from powder and diluent vials.

5. Wipe tops of vials with an alcohol swab and allow alcohol to dry. Do not touch the rubber stoppers after they are wiped.

6. Remove cover from the needle.

7. Draw 1½-2 cc (or ml) of air into the syringe.

8. Insert needle straight down through the center circle of the rubber stopper of the diluent vial and inject the air.

9. Without removing the needle, turn the bottle upside down and withdraw 1½-2 cc (or ml) of diluent into the syringe. Back the needle out of the vial to make sure the needle tip remains in the sterile water. This will prevent withdrawing a large amount of air.

10. Remove needle from the diluent vial. Point the needle up and tap lightly to collect any air bubbles into the top of the syringe. Press the plunger to expel air and confirm the correct amount of diluent is in the syringe.

11. Insert needle into the vial of powder containing the Novarel 10,000 USP Units. Slowly inject the diluent toward the side of the vial to avoid creating bubbles.

12. Leave the needle in the vial and gently mix by rotating the vial between your fingers until the solution is clear.

13. Invert the vial and withdraw the reconstituted Novarel 10,000 USP Units into the syringe. To draw out all the medication, back the needle out of the vial making sure the needle tip remains below the level of medication.

14. Remove the needle from the vial.

15. Recap and twist off the needle used for mixing (22 G 1½”) and attach a new 22 G 1½” needle (equal in length to the one used for reconstitution) prior to administering injection.

16. Check for air bubbles. If any are visible, point the needle up, tap lightly to collect any air bubbles into the top of the syringe, and gently press the plunger to expel the air.

17. This medication is injected intramuscularly.

*If you touch the needle, if you blow on the needle, or if it comes in contact with any surface, it is considered contaminated. In the event this occurs, recap and remove the contaminated needle. Attach a sterile needle to the syringe and continue preparation.*
Lupron Trigger Medication Protocol

For those patients that exhibit an increased response to the stimulation medications, you may be instructed to follow the Lupron Trigger Protocol in an effort to reduce the potential of developing Ovarian Hyperstimulation Syndrome. You will receive specific instructions from the nursing staff regarding administration of a decreased dose of hCG (Pregnyl or Novarel) as well as a subcutaneous trigger shot of Lupron (leuprolide acetate) 80u given 36 hours prior to retrieval. As part of this protocol, there are additional medications that need to be initiated during the luteal phase in order to maximize the potential for a successful IVF cycle. The nursing staff will instruct you to begin these medications the evening after your retrieval at 7pm. The medications are as follows:

- **Estrace (or estradiol) 2mg tablets.** One tablet orally at 7pm the evening after your retrieval and then one tablet orally at 7am/3pm/10pm daily beginning the day after retrieval.

- **Vaginal Progesterone Suppositories 200mg or Endometrin 100mg vaginal tablets.** Insert one vaginally at 7pm the evening after your retrieval and then one vaginally at 7am/3pm/10pm daily beginning the day after retrieval.

- **Progesterone in Oil 50mg.** This needs to be administered intramuscularly once daily into the buttocck beginning at 7pm the evening after your retrieval. This dose is equivalent to 1cc of medication. Please see attached IM injection sheet for detailed administration instructions. If you have questions regarding IM administration, please ask a member of the nursing staff to review it with you on the day of retrieval.

**Mixing A Decreased Dose of hCG:**

Unless otherwise instructed, the Lupron Trigger protocol requires administration of a decreased dose of hCG (either Pregnyl or Novarel). The nursing staff will instruct you regarding the amount of hCG to administer. If giving 1000u of hCG, please use 10cc of diluent, mix with all of the powder, and then draw up only 1cc of the mixed hCG for administration. This 1cc of mixed hCG is equivalent to 1000u. If giving 2000u of hCG, only use 5cc of diluent, mix with all of the powder, and then draw up the 1cc of mixed hCG for administration. **Pregnyl is given SQ (subcutaneously). Novarel must be given IM (intramuscularly).**

The estrace and progesterone will continue daily through your BhCG pregnancy test. If you have a positive pregnancy test, please continue these medications through 12 weeks of pregnancy.

The Lupron Trigger shot will need to be drawn up from a multidose vial of Leuprolide Acetate. The pharmacy will give you an insulin syringe to use for administration. You will have additional medication left over in this vial that will need to be discarded. Please refer to the Specialty Pharmacy List if needing resources for ordering these medications.
DAY FOLLOWING hCG (PREGNYL/NOVAREL) ADMINISTRATION

- Monitoring of patients may be done at MCRH office.

- Please inform the nurses if you have any medication allergies or pre-existing medical conditions (i.e. diabetes or heart condition). Additional antibiotic coverage is necessary if you have a known heart murmur.

- You are required to drink 16 oz. of clear, decaffeinated liquids 3 hours prior to retrieval to prevent nausea and dehydration (i.e. water, juice). Food is not to be consumed 6-8 hours prior to retrieval. These are your last opportunities to eat/drink until after your egg retrieval.

- Refer to your individualized patient medication outline.
DOXYCYCLINE

Doxycycline, an oral antibiotic, will be taken twice daily. This antibiotic is given to prevent infection as a needle will be introduced through the vaginal wall during retrieval. Doxycycline will begin the day following hCG administration and continue for five days (one tablet in the a.m. and p.m.).

If the husband/partner is providing a semen sample the day of egg retrieval, he will be asked to take Doxycycline for approximately a 2 week interval prior to retrieval (this is in correlation with the time frame the wife/partner is on stimulation medications). The husband/partner will begin Doxycycline, 100 mg, twice a day through the evening before retrieval. This is done as a preventative measure to minimize the possibility of infection in the semen specimen for the in vitro fertilization procedure.

Potential Side Effects:

- Nausea--take with meals or light snack
- Sun sensitivity--limit exposure to the sun and tanning devices. If exposure is unavoidable, sunscreen of 30 SPF is recommended.

- Refer to your individualized patient medication outline.
Section VII

Oocyte Retrieval/Fertilization
OOCYTE (EGG) RETRIEVAL

Egg retrieval is a procedure in which the eggs are collected using ultrasound guidance. **You are required to drink 16 oz. of clear, decaffeinated liquids 3 hours prior to retrieval to prevent nausea and dehydration (i.e. water, juice). Food is not to be consumed 6-8 hours prior to retrieval. These are your last opportunities to eat/drink until after your egg retrieval.** On retrieval and transfer days, patients and their partners are asked to not wear cologne, perfume or scented hygiene products. It is also required that patients not wear contact lenses, any type of jewelry (including body jewelry) or fingernail polish.

Egg retrieval will be done as an outpatient procedure and you and your spouse/significant other will need to arrive at MCRH at the time specified by the nursing staff. Adequate time will be allowed for procedure preparation, vital signs and semen collection.

To obtain optimal results, a fresh semen sample needs to be provided on the day of retrieval. A sterile specimen collection container will be provided by the medical center staff and collection will take place in a private area upon admission. We strongly discourage the use of lubricants, however, if one is necessary, we will provide you with a non-toxic mineral oil. You may bring your own visual aids as a VCR/DVD is available. **Before giving the sample to the medical center staff, be sure that the label is filled out completely and attached to the container.** This is critical as the information will be used to verify identification prior to and during insemination.

Valium (Diazepam) 4 mg will be given orally during the admission process. It is a benzodiazepine that exerts temporary anxiolytic, sedative, muscle-relaxant, anti-convulsant and amnestic effects used to facilitation the conscious sedation process.

Upon arriving at the retrieval suite, you will be positioned on the table similar to ultrasound monitoring. An IV will be started by which medications will be given to keep you comfortable throughout the procedure. Medications (Fentanyl and Versed) are injected into the bloodstream inducing a semi-conscious state. Risks of IV sedation include, but are not limited to: injury to a blood vessel (phlebitis), dizziness (vertigo), post-operative nausea and vomiting, an unconscious state which can lead to depressed breathing, and an allergic reaction to the drugs used. Fatigue or sleepiness can be expected for up to 24 to 36 hours following the procedure.

At the start of the retrieval procedure the vagina will be cleansed and the vaginal transducer, along with aspiration needle, will be inserted. The ultrasound image allows the physician to accurately guide the needle through the vaginal wall, into the ovary, and into each follicle to be aspirated. A suction machine is used to remove the eggs through the needle and as each egg is retrieved, it is immediately passed into the laboratory for inspection and later insemination. Some follicles may not contain eggs; therefore, the number of follicles may not be the same as the number of eggs retrieved. You will be notified of the number of eggs retrieved at the conclusion of the retrieval. **Risks of vaginal ultrasound guided retrieval include bleeding, risks of the anesthesia or pain medication that is used, infection, sterility and injury to blood vessels, bladder or bowel (any of which could require a laparotomy).** All of these complications are considered to be extremely rare.

During the retrieval, your spouse/significant other will be able to wait in a private waiting room located near the retrieval room. You may bring in compact discs to listen to during the
retrieval and transfer if you wish. Discharge from the medical center will be approximately 1 hour after the procedure. You will need transportation home following the retrieval as you will not be allowed to drive after the IV sedation. Spouse/partner is able to view retrieval on a monitor.

Once you are home, you may resume your normal diet. If you are nauseated, we recommend clear liquids (i.e. jello or soup broth).

If you experience cramping or pain, take regular strength Tylenol, 2 tablets, every 6 hours. If pain persists, contact our staff person “on call” by calling our office at (763) 494-7700. If you need emergency care after hours, report to North Memorial Health Care’s emergency room or West Health emergency room.
PROCEDURE DAY INFORMATION

DAY OF RETRIEVAL

Retrieval time: ______

1. Nothing to eat 6-8 hours prior to procedure. Last opportunity to eat: ______
2. Drink 16 ounces of clear, decaffeinated liquids 3 hours prior to procedure. Then nothing to drink until after procedure. Time: ______
3. No perfume, cologne or scented lotion to the office for patient or spouse.
4. No contact lenses. You may wear your glasses.
5. No jewelry, including body piercings.
6. No fingernail polish.
7. No medications/pills prior to your retrieval.
8. You will need a ride to and from your procedure. You will not be able to drive.
9. Tylenol every 6 hours post procedure can be used if needed for discomfort post procedure.
10. Mild cramping can be expected for a few days following your retrieval.
11. You may advance your diet as tolerated following your procedure.
12. Please continue to check your IVF voicemail daily for updates re: your embryo transfer.
13. In an effort to be sensitive to all of our patients, we ask that children do not attend appointments.

DAY OF EMBRYO TRANSFER

1. No perfume, cologne or scented lotion to the office for patient or spouse.
2. No dietary restrictions.
3. Remain on all medications as directed.
4. You will be instructed to take 600mg of Ibuprofen 30 min. prior to your procedure, please bring this with you.
5. You may engage in light activity and resume normal activity the following day.
6. Tylenol every 6 hours post procedures can be used if needed post procedure.
7. Please continue to check your IVF voicemail for any updates from the embryology lab.
8. In an effort to be sensitive to all of our patients, we ask that children do not attend appointments.
INSEMINATION, FERTILIZATION AND CULTURE OF SPERM & EGGS

When the semen sample is delivered to the laboratory prior to egg retrieval, the sample will be immediately evaluated for how many sperm are present and how healthy they appear. The sperm will be isolated from the semen and held until the time of insemination of the oocytes. Depending upon how many sperm are present, how healthy they appear, and past history of the male, the number of sperm to be incubated with the oocytes and type of insemination will be determined.

After egg retrieval, the oocytes will be evaluated as to their maturity. Based upon this evaluation, a time for insemination with the sperm will be determined. Once in culture together, the sperm and oocytes will not be disturbed for approximately 16-20 hours.

Fertilization Evaluation
After 16-20 hours, the oocytes will be evaluated for evidence of fertilization. Some oocytes may not fertilize. When fertilized, the oocyte breaks the sperm down and reconfigures the male chromosomes into a structure called the male pronucleus. At the same time, the oocyte reconfigures its own chromosomes into the female pronucleus. These two pronuclei are very prominent and easily recognizable under the microscope. Also at this time, if more than one sperm gained entry into any oocyte (polyspermy), that embryo will be discarded as it resulted from abnormal fertilization. Embryos of this type can be identified by the fact that they contain more than 2 pronuclei. Normally fertilized oocytes will be returned to culture for an additional 1 to 4 days.

Embryo Culture
During the following days, the embryos are cultured in a Petri dish containing medium that will support cell division and growth. Two days after the retrieval, the embryos should be at the 2-4 cell stage. Three days after the retrieval, the embryos should be at the 6-8 cell stage. Five and six days after retrieval, the embryos should be at the blastocyst stage. Following fertilization, it is not unusual for some normally fertilized oocytes to cease cell division and degenerate and/or are of too poor quality to support embryo cryopreservation. Embryos of this type will be discarded.

In vitro-fertilization (IVF) procedures require collaboration between physicians, nursing staff and lab staff for each patient’s case. The IVF team members are hard at work maximizing your success. No news is good news! If things progress appropriately, the lab embryologist will update you when you arrive for your transfer with the number of eggs that fertilized, the number of embryos in culture and how many embryos are candidates for transfer and/or possible freezing. At the time of transfer you will also be finalizing your decision about how many embryos to transfer (1 or 2). We understand this is a big day with a lot of information and want to have a face to face update with you. The final update on how many, if any, embryos are frozen commonly happens via voicemail from the nursing staff after your transfer. We understand that waiting may be hard and want to reassure you that the lab staff is growing and caring for your embryos. We wish you the best of luck and can’t wait to see you in a few days!
LUTEAL PHASE SUPPORT

Progesterone is a hormone that is naturally produced by the corpus luteum (ruptured follicle) during the second half of the menstrual cycle. The placenta will take over progesterone production at around 8-9 weeks of pregnancy. Natural progesterone is prescribed by most fertility specialists and is especially prescribed for those patients undergoing a variety of the assisted technology procedures. This natural source of progesterone will optimize implantation and continue through 12 weeks unless directed otherwise by your physician.

The package insert that accompanies the medication may include advice against its use in pregnancy. This is because both synthetic progestins and natural progestins are grouped together by the FDA. Synthetic progestins have been associated with a slight increase in birth defects if taken during early pregnancy. To date, there is no evidence that supports this when using natural progesterone and the benefits of this medication outweigh any potential risks.

- Refer to your individualized patient medication outline

Progesterone Options:

- **Progesterone Suppositories** contain natural progesterone. This medication is usually suspended in glycerin base; therefore, it will dissolve and the medication is absorbed. We recommend that you wear a pantyliner or pad when using these suppositories as discharge is common.

- **Endometrin** is a vaginal insert that contains 100 mg of natural progesterone in each tablet. Each Endometrin insert comes with its own individually wrapped, disposable applicator. Once inserted, Endometrin dissolves rapidly with minimal discharge.

Potential side effects of progesterone include lethargy, nausea, breast tenderness, water retention, weight gain, increased sensitivity to sunlight, delayed menses or decrease in flow during menses. Worsening of pre-existing depression, migraine headaches, epilepsy, asthma, heart disease or kidney disease may occur and should be discussed if present in your medical history prior to beginning this medication.

**Midwest Center staff will provide instruction regarding the progesterone option(s) and dosage appropriate for your treatment.** Progesterone will continue daily until the second pregnancy test, even if vaginal bleeding or spotting occurs. If your pregnancy test is positive, progesterone will be continued through 12 weeks unless instructed otherwise.
Section VIII
Embryo Transfer
EMBRYO EVALUATION / UTERINE EMBRYO TRANSFER

On the morning of the embryo transfer, all embryos that were placed in culture will be evaluated. This is in an attempt to identify embryos that are most likely to continue development once transferred back to the uterus. You will be provided with information regarding the number of your embryos the day of the transfer. After you review the information, the number of embryos to be transferred will be discussed with you prior to the procedure. The embryos that appear most likely to result in a pregnancy will be transferred. As a general guide, 1-2 embryos will be transferred.

- The following will be used to determine the number of embryos to be transferred:
  - Patient age
  - Total number of embryos
  - How the couple feels about the possibility of a multiple pregnancy and multi-fetal reduction

- The embryo transfer is performed two to five days following egg retrieval. The nurses will inform you regarding the transfer date once the embryologist reviews fertilization.

- There are no dietary restrictions on the day of transfer. Regular eating/dietary habits recommended.

- It is requested that patients and partners do not wear cologne, perfume, or scented hygiene products the day of embryo transfer.

- Patients will take Ibuprofen, 600 mg, one 1/2 hour before the embryo transfer. Please bring your own medication

- You will need to check in at MCRH at the time designated by MCRH staff, and you will then be taken to the transfer suite. After lying down on the table, the physician will place a speculum in the vagina to visualize and cleanse the cervix. The embryologist will place the embryos into the catheter. The physician will pass the catheter through the cervix into the uterine cavity. The embryos are then placed in the appropriate portion of the uterus to optimize implantation.

- You may bring your own CD’s to listen to during your transfer, or one can be chosen from MCRH’s supply.

- After the transfer, you will recover in transfer room for 5-10 minutes. You may rest or you may want to bring reading material or a tape player.

- Following transfer, you can engage in light activity and resume normal activity the following day.

- If you experience pain or cramping, take regular strength Tylenol, 2 tablets, every 6 hours.

- Potential risks associated with embryo transfer include uterine cramping, bleeding, infection, sterility, multiple pregnancies, and ectopic pregnancy which may require major surgery for treatment.
EMBRYO STATUS REPORT

Below please find an example of the information you will be given at the time of embryo transfer. This information will provide you with the number of your embryo(s). Please review this information in advance of your procedure in order to prepare yourselves for meeting with the embryologist. When meeting with the embryologist, you will sign off on how many embryos you wish to transfer and what you wish to do with any remaining or “extra” viable embryos. Most often couples elect to culture any remaining embryos for possible cryopreservation. If for some reason you are electing not to cryopreserve your embryos, please communicate this to your IVF coordinators. A consultation with Dr. Corfman is required for this election prior to oocyte retrieval.

Embryo Status Report

The following information is being provided to you in preparation for your upcoming transfer.

- Number of embryos to transfer:
  1-2 is optimal

- Multifetal Reduction:
  Do not transfer more than you are willing to take home
  There is a rare chance of getting more than you transfer (identical twins)

There are medical/surgical conditions that may indicate fewer embryos should be transferred. These conditions are typically reviewed with the physician during your initial consultation.

Date __________

_____ # of oocytes retrieved

ICSI? Yes No

_____ # of oocytes ICSI’d

_____ # of oocytes fertilized

_____ # of viable embryos
LOW DOSE ASPIRIN

Patients may be instructed to take low dose aspirin (81mg) orally **beginning the day of transfer** if they fall into any one or more of the following categories:

- Equal to or greater than 38 years old
- History of previous pregnancy loss
- History of severe endometriosis
- History of chlamydia
- Immunological indications

The role of the immune system in implantation and prolongation of pregnancy is not well understood. It is thought, however, that if an immunologic imbalance is present, the woman who has received embryos may develop antibodies that “attack” the placenta, inducing blood clots to form, thereby reducing transfer of nutrients from the mother to the fetus. This might jeopardize the pregnancy. Low dose aspirin, taken orally, has been used to treat such at risk individuals by lowering the likelihood of blood clot formation at the placenta.

Patients will continue low dose aspirin through 12 weeks of pregnancy unless otherwise instructed by their primary physician.

Low-dose aspirin can be taken any time of the day you choose, but keep that chosen time consistent.
LOVENOX/HEPARIN

Patients may be instructed to administer Lovenox/Heparin subcutaneously, if indicated by your physician, to treat immunological disorders or a history of recurrent pregnancy loss.

The role of the immune system in implantation and prolongation of pregnancy is not well understood. It is thought, however, that if an immunologic imbalance is present, the woman who has received embryos may develop antibodies that “attack” the placenta, inducing blood clots to form, thereby reducing transfer of nutrients from the mother to the fetus. This might jeopardize the pregnancy. Lovenox/Heparin, administered subcutaneously, has been used to treat such at risk individuals by lowering the likelihood of blood clot formation at the placenta.

Lovenox/Heparin injections will begin when notified and should be administered subcutaneously every 12 hours as instructed.

Risks of Lovenox/Heparin include bleeding, but the risk is small with proper monitoring.

This medication should not be taken in conjunction with other aspirin products unless otherwise instructed.
PREPARATION OF HEPARIN

Heparin will either be packaged in a prefilled syringe or a multi-dose vial. If using a prefilled syringe, uncap the needle and follow the injection instructions on the following page. If using a multi-dose vial, please follow these instructions.

1. Clean the work surface that will be used to prepare the injection with soap and water, or swab with alcohol, and wash your hands thoroughly.

2. Assemble the necessary materials: Heparin, syringe and needle, alcohol wipes, and disposal container. The needles and syringes are intended for one time use only.

3. Check medication label for proper type of medication and expiration date (medication should be clear and free of particles).

4. Using your thumb, remove flip top cap from Heparin bottle. The medication does not need to be recapped after use.

5. Wipe top of vial with an alcohol swab and allow alcohol to dry. Do not touch the rubber stopper after it is wiped.

6. Remove syringe from packaging and draw air into the syringe by pulling plunger back to amount prescribed.

7. Insert needle straight down through the center circle of the rubber stopper of the vial.

8. Inject air into the Heparin vial equal to or greater than the amount of medication to be withdrawn.

9. Without removing the needle, turn the bottle upside down. Slowly pull back the plunger filling the syringe to slightly more than the prescribed dose and then adjust the plunger to your prescribed dose to clear away air bubbles. Make sure the tip of the needle remains in the medication to avoid withdrawing large amounts of air. It may be necessary to back the needle out of the vial to ensure the needle tip remains below the level of medication.

10. Inject excess medicine and air bubbles back into Heparin bottle.

11. Once the plunger is set at your prescribed dose, remove the syringe needle from the vial.

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1. Make yourself comfortable by sitting or lying down.

2. Choose an injection site (abdomen, thigh, or upper arm).

3. Clean the injection site with an alcohol swab and allow it to air dry.

4. Carefully uncap the needle by pulling the needle cap from the syringe.

5. Holding the syringe in one hand, use the other hand to pinch a fold of skin at the prepared injection site.

6. Holding the syringe like a pencil, quickly insert the entire length of the needle into the skin at a 90° angle.

7. Inject prescribed amount of Lovenox/Heparin into the subcutaneous tissue by slowly and steadily depressing the plunger. Be careful **not** to move the syringe and needle while you are injecting.

8. After injecting all the medication, leave needle in place for 10 seconds after the injection and then release the pinch.

9. Gently withdraw the needle.

10. Dispose of the syringe and needle safely. Please check with your individual disposal company for specific information regarding disposal. Pharmacies will generally supply Sharps containers or you may dispose of the needle and syringe by placing them in an empty plastic liter bottle. For safety reasons, please do not bring to the office for disposal.

11. Place a tissue or gauze over the skin where you gave the injection. If any bleeding occurs, apply gentle pressure for 10-15 seconds.

12. Do not massage the injection site.

13. Alternate injection sites to help minimize bruising.
PREGNANCY TESTS AND FOLLOW-UP

- It is **normal** to experience some mild cramping and bloating throughout stimulation and while waiting for blood test results. If this interferes with your normal activities, please contact our office.

- Some bleeding may occur with or without pregnancy. If you experience bleeding prior to your pregnancy test, be sure to continue your prescribed progesterone until pregnancy test results are known and you have received instructions from MCRH staff.

- BhCG (quantitative) pregnancy tests will be drawn approximately 14 and 16 days from embryo transfer. The BhCG tests are to be drawn on the specific dates given to you. They need to be drawn prior to 8:45 a.m. for patients having the test at The Midwest Center. These results will be reported the same day. **Please call (763) 494-7700 to schedule.**

  If you have your BhCG drawn elsewhere, please be aware that results may not be reported until the following business day. A message will be left on your voicemail by Midwest Center staff upon receipt of the result.

- If done at an outside facility, please obtain a quantitative (BhCG) pregnancy test. These arrangements can be made through your local physician and/or nurse. All interpretation of these results and recommendations must be made by your physician/staff at MCRH.

- It is a requirement that all patients have the first quantitative BhCG drawn to confirm the pregnancy outcome even if bleeding begins prior to your scheduled pregnancy test. Results of the first pregnancy test may or may not indicate outcome.

- If a **positive** pregnancy test is obtained, prenatal instructions will be provided. An **ultrasound should be scheduled** for approximately 2 to 3 weeks after the positive blood test. Arrangements should be made for this ultrasound to be done at The Midwest Center or by your primary care physician. **It is required that you abstain from intercourse until fetal heart motion is identified.**

- If the first BhCG is **negative**, you have the option to decline the second test. Your progesterone will be discontinued and a menses should begin within one week. If no menses occurs, contact our office at (763) 494-7726.

- If the pregnancy test result is negative, you will be instructed to schedule a follow up consultation via telephone or office visit to summarize your treatment cycle, discuss future treatment options and recommendations at no additional charge.

- **Refer to individualized patient medication outline.**
SELECTIVE (MULTI-FETAL) REDUCTION

Transferring several embryos back into the uterus can increase the potential for a pregnancy but can also increase the chance of multiple gestation. It is estimated that 40% of the pregnancies achieved may result in pregnancies with two or more fetuses. Several considerations to reduce multiple gestations, however not eliminate them, include limiting the number of embryos transferred (and cryopreserving the remaining embryos for later transfer) and selective reduction during early pregnancy. These measures would also reduce the risk of preterm infants and complications associated with them.

Selective reduction requires attention when a pregnancy occurs and more than 2 gestational sacs are seen on ultrasound. These pregnancies are considered “high-risk” and have potential for complications. OB/GYN physicians often refer patients in this situation to a perinatologist, an OB/GYN physician who specializes in high risk pregnancies. The perinatologist would provide counsel regarding selective reduction and perform the procedure, if desired.

You will be provided with information regarding the number of embryos the day of the transfer. After you review the information, the number of embryos to be transferred will be discussed with you prior to the procedure. This decision is partly based on your feelings about selective reduction.
Section IX

ART Options
ASSISTED ZONA HATCHING (AZH)

Your physician may recommend that you have a procedure called assisted zona hatching performed on your embryo(s). With this procedure, a small hole is created in the shell (zona pellucida) that surrounds the embryo. By creating this hole artificially, it appears that the embryos are better able to escape the zona; therefore, it increases the chance of implantation and pregnancy. Embryo transfer for patients undergoing AZH occurs two to three days after egg retrieval unless otherwise instructed.

There is a small possibility of embryo damage occurring with this procedure. If the embryo quality is poor, then this risk is increased. Long-term follow-up of infants born as a result of this technique is not available. Further study will be required before a final determination can be made.

Women undergoing this procedure will be prescribed a medication (steroid) called Methylprednisolone. It is believed that this medication can help prevent rejection of the embryos and does not cause adverse effects which are associated with long term steroid use.
INTRACYTOPLASMIC SPERM INJECTION (ICSI)

ICSI is a technique which involves injecting a single sperm into the egg using micromanipulation techniques. It may be used in cases where there is severe male factor (low sperm quantity or quality), and for patients that have previously undergone IVF with no fertilization using routine fertilization methods. The use of ICSI can markedly increase the chance of achieving fertilization in male factor infertility. The physician and embryologist will decide which patients are good candidates for ICSI based on medical history and semen parameters.

Some drawbacks may exist with this technique. For example, damage may result to some of the oocytes during ICSI which can cause the egg to lose viability. Secondly, while sperm entry into the egg is ensured with ICSI, fertilization is a complex process. Simply injecting a sperm into the oocyte does not ensure that fertilization will be completed and an embryo will be produced. Lastly, because men with severe male factor infertility are known to produce higher percentage of sperm that have an abnormal number of chromosomes, sex chromosome abnormalities (SCA) rate of offspring born through the use of ICSI is about 3 times higher than the general population. However, the rate of sex chromosome abnormalities in ICSI is still very low at less than 1%.

In approximately 5% of patients with normal pre-IVF semen analysis, the semen sample on the day of egg retrieval is not adequate for insemination. In order to avoid a failed fertilization, ICSI will be performed.
What is intracytoplasmic sperm injection (ICSI)?

Before a man’s sperm can fertilize a woman’s egg, the head of the sperm must attach to the outside of the egg. Once attached, the sperm pushes through the outer layer to the inside of the egg (cytoplasm), where fertilization takes place.

Sometimes the sperm cannot penetrate the outer layer, for a variety of reasons. The egg’s outer layer may be thick or hard to penetrate or the sperm may be unable to swim. In these cases, a procedure called intracytoplasmic sperm injection (ICSI) can be done along with in vitro fertilization (IVF) to help fertilize the egg. During ICSI, a single sperm is injected directly into the cytoplasm the egg.

How does ICSI work?
There are two ways that an egg may be fertilized by IVF: traditional and ICSI. In traditional IVF, 50,000 or more swimming sperm are placed next to the egg in a laboratory dish. Fertilization occurs when one of the sperm enters into the cytoplasm of the egg. In the ICSI process, a tiny needle, called a micropipette, is used to inject a single sperm into the center of the egg. With either traditional IVF or ICSI, once fertilization occurs, the fertilized egg (now called an embryo) grows in a laboratory for 1 to 5 days before it is transferred to the woman’s uterus (womb).

Why would I need ICSI?
ICSI helps to overcome fertility problems, such as:
- The male partner produces too few sperm to do artificial insemination (intrauterine insemination [IUI]) or IVF.
- The sperm may not move in a normal fashion.
- The sperm may have trouble attaching to the egg.
- A blockage in the male reproductive tract may keep sperm from getting out.
- Eggs have not fertilized by traditional IVF, regardless of the condition of the sperm.
- In vitro matured eggs are being used.
- Previously frozen eggs are being used.

Will ICSI work?
ICSI fertilizes 50% to 80% of eggs. But the following problems may occur during or after the ICSI process:
- Some or all of the eggs may be damaged.
- The egg might not grow into an embryo even after it is injected with sperm.
- The embryo may stop growing.

Once fertilization takes place, a couple’s chance of giving birth to a single baby, twins, or triplets is the same if they have IVF with or without ICSI.

Can ICSI affect a baby's development?
If a woman gets pregnant naturally, there is a 1.5% to 3% chance that the baby will have a major birth defect. The chance of birth defects associated with ICSI is similar to IVF, but slightly higher than in natural conception.

The slightly higher risk of birth defects may actually be due to the infertility and not the treatments used to overcome the infertility.

Certain conditions have been associated with the use of ICSI, such as Beckwith-Wiedemann syndrome, Angelman syndrome, hypospadias, or sex chromosome abnormalities. They are thought to occur in far less than 1% of children conceived using this technique.

Some of the problems that cause infertility may be genetic. For example, male children conceived with the use of ICSI may have the same infertility issues as their fathers.

Revised 2014

For more information on this and other reproductive health topics, visit www.ReproductiveFacts.org
PATIENT FACT SHEET
Intracytoplasmic Sperm Injection (ICSI)

Before a man's sperm can fertilize a woman's egg, the head of the sperm has to attach to the outside of the egg. Then it pushes through the outer layer of the egg to the inside of the egg (cytoplasm). Sometimes the sperm cannot penetrate the outer layer. A procedure called intracytoplasmic sperm injection (ICSI) can help fertilize the egg by injecting the sperm directly into the egg.

How does ICSI work?
In traditional IVF, the sperm are mixed with the woman's egg in a laboratory. If ICSI is needed, a small needle is used to inject a sperm into the center of the egg. The fertilized egg grows in a laboratory for one to five days, then it is placed in the woman's uterus (womb).

Why would I need ICSI?
ICSI helps to overcome a man's fertility problems, for instance:
• He may produce too few sperm
• His sperm may be not be shaped correctly or move in a normal fashion
• The sperm may have trouble attaching to the egg
• A blockage in his reproductive tract may keep sperm from getting out

ICSI can also be used when the use of traditional IVF has not produced fertilization, regardless of the condition of the sperm.

Will ICSI work?
ICSI fertilizes 50% to 80% of eggs. But the following may occur after the use of ICSI:
• The ICSI procedure might damage some eggs
• The egg might not grow into an embryo even after it is injected with sperm
• The embryo may stop growing

Once fertilization takes place, a couple's chance of giving birth to a single baby, twins, or triplets is the same if they have IVF with or without ICSI.

Can ICSI affect a baby's development?
If a woman gets pregnant naturally, there is a 1.5% to 3% chance that the baby will have a major birth defect. The chance of birth defects after ICSI are rare. Certain conditions that have been associated with the use of ICSI (Beckwith-Wiedemann syndrome, Angelman syndrome, hypospadias, or sex chromosome abnormalities) are thought to occur in far less than 1% of children conceived using this technique.

Some of the problems that caused your infertility may be genetic. Therefore, boys conceived with the use of ICSI may have infertility issues as adults.
RESCUE INTRACYTOPLASMIC SPERM INJECTION (RICSI)

RICSI is a technique which involves injecting a single sperm into the egg using micromanipulation techniques. RICSI is only used in the event none of the eggs fertilize with regular insemination on the day of egg retrieval. The use of this treatment option is unknown until the day after egg retrieval, and the chance for establishing a pregnancy is low (less than 10%). Similar to ICSI, there may be risks associated with RISCI, including sex chromosome abnormalities.
SEX CHROMOSOME ABNORMALITY (SCA)

During normal sperm production, each sperm receives either an X or Y chromosome (the sex chromosomes). In men with abnormal sperm production, the percentage of sperm with just an X or Y is reduced due to errors in spermatogenesis. While the number of normal sperm is still typically greater than 90%, the higher rate of abnormal sperm increases the chance that an offspring will have a sex chromosome abnormality.

The incidence of sex chromosome abnormalities in the general population is approximately 0.2%. The most comprehensive study of ICSI offspring found a 0.6% incidence of sex chromosome abnormality, or 3 fold higher than non–ICSI babies. While the risk is higher for ICSI babies, it is still relatively low.

There are several variants of SCA, with the female Turner’s syndrome (XO) and the male Klinefelter’s syndrome (XXY) being the most characterized. In both syndromes, affected individuals may have learning disabilities, though intelligence is not affected in all cases.

Turner’s syndrome is usually caused by a missing X chromosome. There are many manifestations of this syndrome but the main features are short stature, webbing of the skin of the neck, absent or retarded development of secondary sexual characteristics, absence of menstruation, narrowing of the aorta, and abnormalities of the eyes and bones. The condition is either diagnosed at birth because of the associated anomalies, or at puberty when there is absent or delayed menses and delayed development of normal secondary sexual characteristics.

Klinefelter’s syndrome is caused by an extra X chromosome and affects only males. An infant appears normal at birth, but the defect usually becomes apparent at puberty when secondary sexual characteristics fail or are late to develop, and testicular changes occur that eventually result in infertility in the majority of those affected. Some mild cases may go undetected with no abnormalities present except infertility.
PREIMPLANTATION GENETIC DIAGNOSIS (PGD) FOR ANEUPLOIDY

The purpose of PGD is to select and transfer to the uterus those embryos that appear chromosomally balanced.

Chromosomes are structures found in the center or nucleus of cells. A human typically has 46 chromosomes or 23 pairs. An embryo receives 23 chromosomes from the sperm and 23 from the egg. Chromosomes are made of genes, which contain the information that instructs the body how to function. Having extra or missing chromosome(s) (called aneuploidy) can result in lack of implantation of an embryo, pregnancy loss, and other conditions such as infertility and Down’s syndrome.

PGD of aneuploidy is being offered to patients undergoing in-vitro fertilization (IVF) who are at increased risk of miscarriage or birth defects. PGD may reduce these risks. PGD of aneuploidy may also assist the embryologists to select embryos more likely to result in a pregnancy. PGD of aneuploidy may also be used for patients of all ages who have unexplained failure to conceive despite several IVF cycles. Other patients who may benefit are patients with a history of miscarriages, especially when testing reveals no clear explanation. Patients who have had an aneuploid pregnancy in the past may also want to consider PGD of aneuploidy.

The procedure consists of five different steps, usually performed by a team of experts in multiple laboratories. (i) The first part is in vitro Fertilization (IVF) by which embryos are produced. This part occurs at The Midwest Center for Reproductive Health, P.A. (ii) The second part is embryo biopsy, by which cells of the embryo are removed to be analyzed. This is done at The Midwest Center for Reproductive Health, P.A. by the embryology staff or a contracted embryologist. (iii) The processing of the cell is performed at The Midwest Center for Reproductive Health, P.A. by the embryology staff or a contracted embryologist. (iv) The analysis of the cell is performed by a reference laboratory. (v) The final step, the transfer of the embryos to the patient, is done by the physician at The Midwest Center for Reproductive Health, P.A.

If PGD is of interest to you, please contact MCRH for more information.
PREIMPLANTATION GENETIC DIAGNOSIS (PGD) FOR SINGLE GENE DISORDER

Currently, the only way to determine whether or not an embryo is affected by a genetic disorder is to wait until pregnancy has begun and then perform a prenatal test, such as chronic villus sampling (CVS) or amniocentesis. These procedures involve sampling fetal cells from within the womb during the first trimester or second trimester of pregnancy, respectively. The cells are then analyzed to determine whether an inherited disorder is present in the developing fetus. If a disorder is detected, parents face the difficult choice of whether to continue or terminate the pregnancy.

The purpose of preimplantation genetic diagnosis (PGD) is to identify affected embryos at a very early stage and prevent them from implanting in the womb. The effect of such a procedure is to increase the probability that embryos that implant and form a pregnancy will be unaffected by the specific disease tested. Preimplantation analysis is not yet considered to be a standard technique and consequently we strongly recommend that patients who become pregnant undergo prenatal testing using CVS or amniocentesis. Prenatal testing will reveal whether the preimplantation genetic analysis was correct, and confirm whether or not the fetus has been affected by the genetic disease tested.

The procedure consists of five different steps, usually performed by different experts and laboratories. (i) The first part is in vitro Fertilization (IVF) by which embryos are produced. This part occurs in The Midwest Center for Reproductive Health, P.A. (ii) The second part is embryo biopsy, by which cells of the embryo are removed to be analyzed. This is done by The Midwest Center for Reproductive Health, P.A. (iii) The processing of the cell is performed by The Midwest Center for Reproductive Health, P.A. (iv) The analysis of the cell is performed by an outside reference laboratory. (v) The final step, the transfer of the embryos to the female patient, is done by the physicians at The Midwest Center for Reproductive Health, P.A.

If PGD for an identified genetic diagnosis is of interest to you, please contact MCRH for more information.
EMBRYO CRYOPRESERVATION

Embryo cryopreservation is a process whereby embryos are frozen and then maintained in a frozen state. The procedure eliminates the need to surgically remove fresh eggs from the female’s ovaries each time a pregnancy is attempted. We strongly recommend freezing extra embryos because of their inherent potential and the significant effort you will extend to create them. This is an additional fee. The “extra” embryos will be stored in a frozen state until it is determined that appropriate conditions exist in the woman’s uterus to achieve pregnancy. Approximately 50% of our patients have freezable embryos. If you elect to not cryopreserve embryos, you will need a mandatory consultation with Dr. Corfman to discuss risks/benefits. Please let us know in advance so we can schedule that appointment prior to egg retrieval.

It is important to recognize that use of cryopreserved embryos might, in specific instances, represent the most effective means of gaining a pregnancy. For example, it is our belief that the uterine environment in a fresh IVF cycle may be somewhat compromised because of relatively high levels of estrogen associated with the ovarian stimulation. This relatively high estrogen level may impair the endometrium’s ability to receive an embryo; therefore, all embryos would be cryopreserved. In contrast, the endometrium of a cryopreserved-thawed cycle is artificially manipulated to closely mimic a normal, unstimulated cycle. This results in a nearly ideal environment with which to gain implantation. Given our inability to predict if the endometrial environment of a fresh cycle is compromised, it is reassuring to have cryopreserved embryos for subsequent use. In addition, a frozen embryo transfer (FET) cycle costs less and is less invasive than a fresh cycle.

Risks associated with embryo cryopreservation include possible failure of the equipment or mechanical support system, possible damage to the embryos during the freezing and thawing processes, and risks to the woman’s uterus during the transfer. The degree of these risks is unknown at the present time. Extensive investigations of cryopreserved animal embryos have not demonstrated a significant increased risk of obstetric complications or fetal abnormalities. The rate of congenital abnormalities or malformations in the offspring of IVF cryopreserved pregnancies is the same as that of the general population. Long-term follow-up of infants born as a result of this technique is not available.

MCRH is not a long-term storage facility. If you wish to have embryos frozen, you must complete the appropriate consent forms by the testing deadline of your IVF cycle to have your embryos frozen and transferred to ReproTech Limited (RTL) for storage. RTL is a local, long-term storage facility that specializes in providing safe, efficient and effective maintenance of frozen specimens. Your completed RTL consent forms need to be returned directly to RTL at the following address:

ReproTech, Ltd.
33 Fifth Avenue NW, Suite 900
St. Paul, MN 55112
Fax 651-489-0442

At the conclusion of your fresh cycle, if it is determined that you have frozen embryos, they will set up an account in your name. Your embryos will be automatically transferred to RTL following your cycle, and they will notify you by mail upon receipt of your embryos.
DONOR SPERM

Your physician may recommend the use of donor sperm, especially if there are findings significantly outside of normal semen parameters. Other conditions that may require the use of donor sperm are patients who have had a vasectomy, previous radiation or chemotherapy treatment, and hereditary or genetic disorders. Also, single women who desire pregnancy may request donor insemination.

Consent forms specific to using donor sperm will require signatures from both patient and spouse/partner (when applicable).
DONOR OOCYTE (EGG)

Oocyte (egg) donation is the removal of eggs from the ovary/ovaries of a donor, following ovarian stimulation, and transferring the embryo(s) to the uterus of the recipient or gestational carrier. The transfer, in most cases, will take place after sperm from the recipient’s husband/partner has fertilized the donor’s egg(s). The patients who benefit from oocyte donation are those with:

- premature ovarian failure (POF)
- limited ovarian function
- previous surgery, radiation, chemotherapy
- inaccessible ovaries for egg retrieval
- genetic disorders
- advanced maternal age
- unexplained repeated pregnancy loss
- repeated unsuccessful IVF/ART cycles

Medications will be given to both the donor and recipient and their cycles will be synchronized so the endometrium (the uterine lining) of the recipient is optimal when the embryos are ready for transfer.

The donation can be non-anonymous/known, generally using donated oocytes from a relative or friend, or anonymous, which would utilize donated oocytes from an unknown donor. Currently, oocyte donation is one of the most successful fertility treatments. Pregnancy rates are quoted as high as 60% with a very low incidence of miscarriage.
FROZEN EMBRYO TRANSFER (FET)

Frozen embryo transfer is the transfer of cryopreserved embryos that were obtained during a previous IVF cycle. Frozen embryo transfer is a fairly simple procedure and since stimulation of the ovaries is not required, no stimulation medications are prescribed. The procedure is performed in the same manner as the embryo transfer utilized during IVF cycles and is performed only during our “uptimes”.

Specific instructions are given with regard to medication and a consultation will take place with the physician/embryologist to discuss the number of frozen embryos that should be thawed and examined. If it appears that one or more are medically appropriate for transfer, the transfer will occur.

Down regulation, similar to that used in fresh cycles, is necessary as is hormone replacement of the uterine lining with estrogen. An estrogen preparation, Estrace (oral) or Estradiol Transdermal Patch, is taken and when the lining appears to be optimal for embryo implantation, the transfer will be scheduled.

Risks associated with a frozen embryo transfer include embryos of poor quality which have a significantly decreased chance of implantation and contamination of embryos which might increase the chance of infection.

If you wish to proceed with a frozen embryo transfer, you will need to contact the IVF Coordinator (763-494-7702) two to three months prior to your desired series to initiate treatment.
Section X

Risks and Complications
RISKS AND COMPLICATIONS

OVARIAN STIMULATION/POST EMBRYO TRANSFER

- **Ovarian Hyperstimulation Syndrome (OHSS)** is a condition in which the ovaries enlarge and secrete fluid producing a distended abdomen, abdominal discomfort, respiratory distress and weight gain. This occurs as a result of elevated estrogen levels and increased follicular response. These symptoms are uncommon, but they can occur together or separately. Hyperstimulation generally occurs between the time of embryo transfer and the pregnancy tests.

Should you experience severe bloating, nausea, constipation, difficulty urinating, or troubled breathing, please notify the nurses at (763) 494-7726. Treatment of OHSS may require medications, hospitalization, IV fluids and removal of the abdominal fluid.

If preventative measures are taken, OHSS rarely leads to further complications that could include thrombosis, heart attack, stroke, and/or kidney failure. Close observation of the patient’s symptoms and careful monitoring (ultrasounds and estradiols) of ovarian response during the stimulation cycle will minimize the risk of this occurring. In some cases, an IVF cycle may be cancelled or all embryos may be frozen to prevent hyperstimulation.

- **Ovarian Torsion**
  The risk of ovarian torsion, although rare, exists with gonadotropin use. It occurs when the weight and/or size of the enlarged ovary causes the ovary to twist, cutting off the blood supply to that ovary. You are asked not to participate in activities that require bouncing or twisting, such as running and aerobics during your treatment cycle as these activities could cause ovarian torsion. Surgery is required to untwist and in some cases remove the ovary.

- **Medication Side Effects**
  Side effects of fertility medications include soreness at the injection site, dizziness, nausea, hot flashes, bloating, left or right side cramping, breast tenderness, blurred vision, mood swings, headaches and fluid retention. These side effects are uncommon, but they can occur together or separately. Should you experience severe side effects, please notify the nursing staff at (763) 494-7726.

- **Cancellation** of a cycle is uncommon, but does occur in approximately 15-20% of cycles due to one of the following circumstances:

  The ovarian response from the medications may be vigorous resulting in a high level of estrogen and excessive follicle development. If this should occur, hCG (Pregnyl/Novarel) may not be given and you will be asked to abstain from intercourse. In some cases, hCG may be given and retrieval performed with cryopreservation of all embryos for a subsequent frozen embryo transfer.

  The ovarian response may be less than optimal resulting in a low level of estrogen and/or poor follicle development. If you have open fallopian tubes, you may be instructed to proceed with an intrauterine insemination and medications may be altered with a future attempt.

- **Ovarian Cancer**
  There has been discussion regarding the association between fertility medication use and the risk of ovarian cancer. The results from studies have produced inconclusive data regarding this issue. The long-term effects are unknown due to the limited time frame of use. The main risk factor relevant to your treatment is a family history of ovarian cancer.
OOCYTE (EGG) RETRIEVAL

- Risks of vaginal ultrasound guided retrieval include bleeding, risks of the anesthesia or pain medication that is used, infection, sterility and injury to blood vessels, bladder or bowel (any of which could require a laparotomy).

- All of these complications are considered to be extremely rare.

- It is also important to remember that eggs will be retrieved from approximately 80% of the follicles and approximately 80% of those will fertilize.

EMBRYO TRANSFER

- Introducing embryos into the uterus could potentially result in an infection; however, it is rare. As a preventative measure, you will take an antibiotic called **Doxycycline**. Patients begin this medication as instructed before the retrieval and continue it for a total of 5 days. An aseptic technique of cleansing the vagina will also be used at the time of retrieval.

PREGNANCY/DELIVERY

- Approximately 1% of people who achieve a pregnancy will unfortunately experience an **ectopic** (tubal) pregnancy. An ectopic pregnancy is not viable and may require medical or surgical intervention.

- As with pregnancies that are achieved naturally, the risk of **miscarriage** also exists. Factors affecting this include patient age and previous reproductive history.

- Transferring several embryos back into the uterus can increase the potential for a pregnancy but can also increase the chance of **multiple gestation**. It is estimated that 40% of the pregnancies achieved may result in pregnancies with two or more fetuses. The potential that a developing embryo may split into **identical twins** is **less than 0.5%**. Multiple pregnancies are complicated by an increased risk of premature labor and delivery, maternal hemorrhage, Cesarean delivery, pregnancy-induced high blood pressure and gestational diabetes. Several considerations to reduce multiple gestations, however not eliminate them, include limiting the number of embryos transferred (and cryopreserving the remaining embryos for later transfer) and **multi-fetal reduction** during early pregnancy. These measures would also reduce the risk of preterm infants and complications associated with them.

- As with naturally conceived and born children, there is a possibility of complications of childbirth, stillbirth or miscarriage, or birth of an abnormal child/children.

BIRTH DEFECTS

Two studies published in November 2005 (Fertility and Sterility) have indicated that in vitro fertilization is associated with a slightly higher rate of major birth defects in conjunction with naturally conceived children.

Based on the evidence, infertility is one risk factor for this increased birth defect incident. More research is needed to ascertain whether factors associated with ART treatment are directly related to the increased risk.
In vitro fertilization (IVF): what are the risks?

IVF is a method of assisted reproduction in which a man's sperm and a woman's eggs are combined outside the body in a laboratory dish. One or more fertilized eggs (embryos) may be transferred into the woman's uterus, where they may implant in the uterine lining and develop. Serious complications from IVF medications and procedures are rare. As with all medical treatments, however, there are some risks. This document discusses the most common risks.

What kind of side effects can occur with IVF medications?

Usually, injectable fertility medications (gonadotropins) are used for an IVF cycle. These medications help stimulate a number of follicles with eggs to grow in the ovaries. A more detailed discussion of fertility medications can be found in the ASRM booklet, Medications for inducing ovulation.

Possible side effects of injectable fertility medicines include:

- Mild bruising and soreness at the injection site (using different sites for the injections can help)
- Nausea and, occasionally, vomiting
- Temporary allergic reactions, such as skin reddening and/or itching at the injection site
- Breast tenderness and increased vaginal discharge
- Mood swings and fatigue
- Ovarian hyperstimulation syndrome (OHSS)

Most symptoms of OHSS (nausea, bloating, ovarian discomfort) are mild. They usually go away without treatment within a few days after the egg collection. In severe cases, OHSS can cause large amounts of fluid to build up in the abdomen (belly) and lungs. This can cause very enlarged ovaries, dehydration, trouble breathing, and severe abdominal pain. Very rarely (in less than 1% of women having egg retrieval for IVF), OHSS can lead to blood clots and kidney failure. For more information about OHSS, see the ASRM fact sheet Ovarian hyperstimulation syndrome (OHSS).

Earlier reports from several decades ago suggested a link between ovarian cancer and the use of fertility medicines. However, more recent and well-designed studies no longer show clear associations between ovarian cancer and the use of fertility medications.

What are the risks of the egg retrieval?

During the egg retrieval, your doctor uses vaginal ultrasound to guide the insertion of a long, thin needle through your vagina into the ovary and then into each follicle to retrieve eggs. Possible risks for this procedure include:

- Mild to moderate pelvic and abdominal pain (during or after). In most cases, the pain disappears within a day or two and can be managed with over-the-counter pain medications.
- Injury to organs near the ovaries, such as the bladder, bowel, or blood vessels. Very rarely, bowel or blood vessel injury can require emergency surgery and, occasionally, blood transfusions.
- Pelvic infection (mild to severe). Pelvic infections following egg retrieval or embryo transfer are now uncommon because antibiotic medicines are usually given at the time of egg collection. Severe infection may require hospitalization and/or treatment with intravenous antibiotics.
- Rarely, to manage a severe infection, surgery may be required to remove one or both of the ovaries and tubes and/or uterus. Women who have had pelvic infections or endometriosis involving the ovaries are more likely to get IVF-related infections.

What are the risks associated with the embryo transfer?

A catheter containing the embryos is used to gently place them into the uterus (womb). Women may feel mild cramping when the catheter is inserted through the cervix or they may have vaginal spotting (slight bleeding) afterward. Very rarely, an infection may develop, which can usually be treated with antibiotics.

If I conceive with IVF, will my pregnancy be more complicated (than if I conceived on my own)?

Having a multiple pregnancy (pregnancy with more than one baby) is more likely with IVF, particularly when more than one embryo is transferred. These pregnancies carry significant risks, including:

- Preterm labor and/or delivery: premature babies (regardless of whether or not they were stillborn) are more likely to be delivered before 37 weeks' gestation. Higher rates of stillbirth are also common.
- Inutero death of one or both twins
- Birth defects
- Increased risk of serious problems for the mother, such as placenta previa and preeclampsia
- Maternal hemorrhage

The more embryos that are transferred into the uterus, the greater the risk. Your doctor should transfer the minimum number of embryos necessary to provide a high likelihood of pregnancy with the lowest risk of multiple pregnancy. For more information about multiple pregnancy, see the ASRM booklet titled Multiple pregnancy and birth: twins, triplets and high-order multiples. One way to avoid multiple pregnancy is to choose to transfer only one embryo at a time. More information about this, see the ASRM fact sheet Single embryo transfer.

Will IVF increase the risk of my child having a birth defect?

The risk of birth defects in the general population is 2%-3%, and is slightly higher among infertile patients. Most of this risk is due to delayed conception and the underlying cause of infertility. Whether or not IVF alone is responsible for birth defects remains under debate and study. However, when intracytoplasmic sperm injection (ICSI) is done along with IVF, there may be an increased risk of birth defects.

In addition, there may be a slightly increased risk of sex chromosome (X or Y chromosome) abnormalities with ICSI. However, it is uncertain if these risks are due to the ICSI procedure itself or to problems with the sperm themselves. Men with sperm defects are more likely to have chromosomal abnormalities, which can be transmitted to their children. However, these disorders are extremely rare. Rare genetic syndromes called imprinting disorders may be slightly increased with IVF.

Miscarriage and ectopic pregnancy

The rate of miscarriage after IVF is similar to the rate following natural conception, with the risk going up with the mother's age. The rate of miscarriage may be as low as 16% for women in their 20s to more than 50% for women in their 40s.

There is a small risk (1%) of an ectopic (tubal) pregnancy with IVF; however, this rate is similar to women with a history of infertility. If an ectopic pregnancy occurs, a woman may be given medicines to end the pregnancy or surgery to remove it. If you are pregnant and experience a sharp, stabbing pain; vaginal spotting or bleeding; dizziness or fainting; lower back pain; or low blood pressure (from blood loss), and have not had an ultrasound confirming that the pregnancy is in the uterus, call your doctor immediately. These are all signs of a possible ectopic pregnancy. There is a 1% risk for a heterotopic pregnancy after IVF. This is when an embryo implants and grows in the uterus while another embryo implants in the tube, leading to a simultaneous ectopic pregnancy. Heterotopic pregnancies usually require surgery (to remove the ectopic pregnancy). In most cases, the pregnancy in the womb can continue to develop and grow safely after the tubal pregnancy is removed.

Revised 2015

For more information on this and other reproductive health topics, visit www.ReproductiveFacts.org
Side effects of injectable fertility drugs (gonadotropins)

What are gonadotropins?
Gonadotropins are fertility medications given by injection that contain follicle-stimulating hormone (FSH) alone or combined with luteinizing hormone (LH). During a regularly occurring menstrual cycle, both FSH and LH are produced by the pituitary gland in the brain to naturally stimulate the ovaries to make a single egg each month. When FSH (with or without LH) is given as an injection, it works directly on the ovaries to make multiple follicles (cysts containing eggs). Other fertility medications, such as clomiphene citrate, stimulate the ovaries by working in conjunction with the brain.

How are these medications used?
Gonadotropins usually are used during fertility treatments such as intrauterine insemination (IUI) or in vitro fertilization (IVF). Injections of gonadotropins are started early in the menstrual cycle to cause multiple eggs to grow to a mature size. Human chorionic gonadotropin (hCG), another injectable medication, is then used to trigger the release of the eggs when they are mature. Close monitoring of patients with ultrasound who are using these medications is advised in order to minimize the side effects and risks.

What are some of the potential side effects of gonadotropins?
- **Ovarian Hyperstimulation Syndrome (OHSS).** OHSS is characterized by enlarged ovaries and fluid accumulation in the abdomen after stimulation by gonadotropins and after ovulation occurs. A mild form occurs in 10% to 20% of cycles and results in some discomfort but usually resolves quickly without complications. The severe form occurs approximately 1% of the time. The chance of OHSS is increased in women with polycystic ovary syndrome and in women who become pregnant during the cycle in which gonadotropins are given. When severe, OHSS can result in nausea, vomiting, rapid weight gain, dehydration, blood clots, kidney dysfunction, twisting of an ovary (torsion), fluid collections in the chest and abdomen, and, rarely, even death. In severe cases, hospitalization is often required for monitoring. The condition is temporary, usually lasting only a week or two. Several strategies exist to prevent or minimize symptoms, including withholding further gonadotropin stimulation, delaying hCG administration until hormone levels plateau or decline, or even withholding hCG to prevent ovulation. In IVF cycles in which OHSS is felt likely to develop, an oral medication, cabergoline, may be given to lessen the severity of these symptoms. Another way to shorten the time that a patient may have OHSS symptoms is to consider delaying the embryo transfer in IVF couples by freezing (cryopreserving) the embryos and transferring at a later date when the OHSS symptoms are completely resolved.
- **Multiple Gestation.** When using injectable gonadotropins alone or with IUI, up to 30% of pregnancies are associated with multiple implantations (twins or more), which only occur in 1% to 2% of naturally occurring pregnancies. The increased risk of multiples is due to the number of eggs that are stimulated during an ovulation induction cycle or due to the number of embryos transferred in an IVF cycle. While most multiple pregnancies are twins, up to 5% are triplets or higher. When a woman has twins or more, she is at higher risk of miscarriage, preterm delivery, infant abnormalities, handicap due to the consequences of preterm delivery, pregnancy-induced hypertension, bleeding, and other significant maternal complications. The risk of severe complications increases as the number of fetuses that implant in the uterus goes up.
- **Ectopic (Tubal) Pregnancies.** While ectopic pregnancies occur in 1% to 2% of naturally occurring pregnancies, in gonadotropin cycles the rate is slightly increased. Ectopic pregnancies can be life threatening and require treatment with medication or surgery. Occasionally a tubal pregnancy can occur at the same time as an intrauterine pregnancy (heterotopic pregnancy) and requires surgery to remove the ectopic pregnancy while not harming the pregnancy inside the uterus.
- **Adnexal Torsion (Ovarian Twisting).** In less than 2% of gonadotropin cycles the stimulated ovary can twist on itself since the ovary is heavier from more follicles. This twisting can cut off the blood supply. Therefore, surgery is required to untwist the ovary, or in severe cases, to remove the ovary.
- **Gonadotropins and Cancer.** Although early studies suggested that the risk of ovarian or other cancers of the female genital tract might be increased when exposed to medications for ovulation induction, current studies have shown no increase in any cancers with the use of fertility medications.
- **Local or Generalized Reactions.** In some women, the injection may cause a local skin irritation. It is extremely rare to have an actual allergy to medication. Some women may experience breast tenderness, headaches, or mood swings from the gonadotropins.

Revised 2012

For more information on this and other reproductive health topics, visit www.ReproductiveFacts.org
Fertility drugs and the risk of multiple births

Infertility treatments that cause multiple eggs to develop make it more likely that you will become pregnant with twins, triplets, or more. This is called multiple gestation. You might think it would be nice to have many babies at once, but this may not be good for the health of you or your babies.

How likely is multiple gestation?
Very possible. Depending on the type of fertility treatment used, if more than one follicle is produced, the risk of multiple gestation can be as much as 1 out of 3 women who become pregnant.

What could happen to the babies?
The babies could be born too early, which is called premature birth. Half of all twins and 90% of all triplets are born prematurely. Babies born prematurely may have many health problems. Their lungs might not be strong enough, so they might have trouble breathing. The blood vessels in their brains might bleed easily. Many other birth defects are associated with multiple births as well. The babies will probably be underweight and may get sick or even die.

Before birth, the babies might not get all the nutrition that is carried by the blood from their mother. This is particularly true if they share a placenta, the tissue that carries nutrients from the mother to the baby. The babies may not grow as fast as normal. If the multiple babies share important blood vessels through a common placenta, they may develop heart problems or die.

Twins, triplets, and other multiples are more likely to have problems with their brain development and nerves if they are born early. One of the more common problems is cerebral palsy, an abnormality of the brain. Other problems associated with multiple births may not become known for many years after delivery.

What could happen to the mom?
If you are pregnant with more than one baby, you may experience problems during pregnancy. These potential problems could include high blood pressure, diabetes, anemia (low blood count), or too much or too little amniotic fluid (the fluid that surrounds the baby during a pregnancy). Too much amniotic fluid can be a problem because it can cause premature labor, while too little fluid can cause a problem with the baby’s development. You may need to stay in bed or the hospital for weeks before delivery. This is especially likely if you go into labor early.

Also, you may have problems delivering your babies. There is a higher likelihood of undergoing a Cesarean section, which is when the babies are delivered through a surgical opening in your belly.

What can I do to reduce the risk of multiple births?
During a fertility treatment cycle when fertility drugs are used with timed intercourse or insemination, your doctor will monitor your cycle very carefully. The use of fertility medications makes it more likely that one or more eggs will be fertilized. However, if it appears that too many eggs are developing, your doctor may cancel your cycle and tell you not to have an insemination or intercourse to eliminate your risk of multiple births.

In vitro fertilization (IVF) means that your egg and your partner’s sperm are joined (fertilized) in the laboratory and the doctor places the fertilized eggs (embryos) into your womb. It is much less likely that you will become pregnant with triplets or more if only one or two embryos are placed in your womb. Before the placement of these embryos (embryo transfer), you and your doctor will decide how many embryos to place in your womb. ASRM has published guidelines on the number of embryos to transfer when undergoing an IVF cycle. These guidelines can be found at www.asrm.org.

If three or more embryos implant inside your uterus, your doctor may suggest that you undergo a procedure called selective reduction. Selective reduction allows you and your doctor to reduce the number of fetuses to one or two. Usually the procedure is done early in the pregnancy to increase the chance of a healthy and successful pregnancy. Choosing to do this procedure is difficult. Couples who are thinking about this option should talk to a counselor.

Revised 2012

For more information on this and other reproductive health topics, visit www.ReproductiveFacts.org
Complications and Problems associated with Multiple Births

Women who can get pregnant without fertility drugs or medical procedures usually have only one baby. Women who need fertility treatment are at higher risk to get pregnant with twins, and rarely with triplets or more. This is called multiple gestation. Multiple gestation can increase the risk of pregnancy for the mother and for all the babies.

What could happen to me and the babies?
Multiple gestation is risky for the babies. Because there are too many babies in the womb, you may have a miscarriage. A miscarriage occurs when your pregnancy ends without the birth of any infants that can survive, before the 20th week of pregnancy. Or you could have a premature delivery when the babies may be born too early (but after 20 weeks of pregnancy) and have problems with lungs, stomach, or intestinal tract. They may have bleeding in the brain, which can cause problems with the baby's brain, nervous system, and hamper its development. If the babies are born very early, they will probably be very small and may even die.

Twins, triplets, and other multiples are more likely to have problems with their brain development and nerves if they are born early. One of the more common problems is cerebral palsy, a condition that affects movement. Other problems associated with multiple births may not be sent for many years after delivery.

The mother might have health problems, too. Your blood pressure may get too high (called pre-eclampsia, pregnancy induced hypertension, or toxemia) and you may develop diabetes (high blood sugar). During the first 12 weeks of pregnancy, you may have more nausea and vomiting than a woman with one baby in her uterus. You also may have gastrointestinal problems and constipation. You could have problems with bleeding before or after delivery.

What can I do if I have a multiple gestation pregnancy?
You have options that you can talk about with your partner and your doctor. You may decide to continue the pregnancy, end the pregnancy, or reduce the number of fetuses. Reducing the number of fetuses is called multifetal pregnancy reduction. Multifetal pregnancy reduction is done to increase the chance of a healthy and successful pregnancy.

Sometimes this happens naturally: in 1 out of 3 pregnancies with multiple gestation, the woman's body naturally reduces the number of fetuses.

You may also consider multifetal pregnancy reduction if you have a health condition that will make your pregnancy risky.

How is multifetal pregnancy reduction done?
Multifetal pregnancy reduction usually takes place early in the pregnancy, within the first 12 weeks. A specialist performs the process and you can go home the day of the procedure.

At 12 weeks in the pregnancy, the fetus is enclosed in a fluid-filled pouch, called a gestational sac. The specialist will inject a needle filled with a liquid, frequently potassium chloride, into the gestational sac of the target fetus. The liquid will stop fetal heart motion.

After this procedure, 4% to 5% of women may miscarry all the fetuses. You are very unlikely to have an infection after this procedure. Even if you have multifetal pregnancy reduction, you are still at risk of going into labor and giving birth too early.

Making a tough decision
It's hard for most couples to decide to have multifetal pregnancy reduction, especially if you've tried hard to get pregnant in the first place. If you are thinking about having this procedure, you and your partner should talk to your doctor who may recommend a visit with a maternal-fetal medicine specialist or get professional counseling before the procedure. Both partners need to be comfortable with their decision and may need emotional support prior to and immediately following the procedure.

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Revised 2008
Multiple problems
The dangers and costs of multiple births

By Randle S. Corfman, Ph.D., M.D.

First there were the seven McCaughhey babies, born to a couple in rural Iowa. More recently, there were the Chukwu births in Houston — the first known set of surviving octuplets, weighing less than two pounds each. Between those two incidents, there have been countless multiple births across the nation, in numbers of three, four, five and six. Although many in the news media glorify and sensationalize multiple births, the facts tell a very different story.

The fact is that a reputable fertility clinic tries at all costs to reduce the risk of multiple births. Multiple births (meaning triplets and more) cause a wide variety of stresses, including familial and marital stress, as well as financial and economic strains on families and on the health care system in general. Divorce rates for couples with multiples are much higher than for their counterparts who had single or double births. Let’s face it — in our busy world it is difficult enough to raise one child at a time, much less three or more. Unlike the McCaughneys, most couples who have four, five, or six children will not have the luxury of a town that enlists around-the-clock baby sitters, national companies that build them a new house and a state school that ensures seven college educations. Where will the town be when there are seven McCaughhey 12-year-olds that need special attention? Babies are fun to hold and watch — puberty-striken adolescents are a different thing altogether.

Another issue with bringing multiples into the world is cost — not only to the family, but to society in general. Our health care and insurance systems cannot support the astronomical costs those frail, little lives bring with them. For example, seven of the eight babies born in Houston were on ventilators after birth to help them breathe. When babies such as those are able to breathe on their own, they still are at great risk for brain, heart, lung, metabolic, vision and infection complications. It has been estimated that the hospital will spend at least $2 million to care for the Houston octuplets, which by no means ensures their survival or addresses the health problems they may encounter later because of their extremely premature births.

In an article published in the New England Journal of Medicine in July 1994, researchers compared costs incurred from singleton, twin and triplet pregnancies. Costs incurred from singleton births amounted to $9,845; twin births amounted to $37,947 ($18,974 per baby); triplet births were $109,765 ($36,588 per baby). Those results are staggering, especially considering the frequent high-order, multiple gestations around the country. The author suggests that “more attention be paid to approaches to infertility that reduce the likelihood of multiple gestation.” I concur wholeheartedly.

Medical risks
Besides the obvious risks to the health of the children, the mother is also at great medical risk when she carries and delivers more than three children from one pregnancy. With a multiple birth comes a risk of cardiac problems, hemorrhage or the loss of the uterus. In fact, the mother of the Houston octuplets required surgery after labor to stop internal bleeding from her abdominal wall. Raising multiple children without the help, support and love of a mother is an almost impossible responsibility, but one that every multiple-birth scenario places in the realm of reality.

Another multiples issue that fertility clinics and patients must consider is multifetal pregnancy reduction (MFPR), the abortion of one or more of the fetuses in order to create a better chance of survival for the remaining fetuses. MFPR still has its opponents in both the moral and scientific worlds. In the April 1999 issue of Contemporary Ob/Gyn, Sabrina D. Craig, M.D., discusses the use of MFPR with triplets in order to increase the survival rate for the remaining (reduced twin) fetuses. She concludes
that though MFPR may be beneficial in increasing survival rates for high-order multiple gestations, the benefits with triplets are not so cut and dried. In fact, no clear improvement in overall survival or long-term outcome for the surviving twins was shown. The only apparent benefits were higher birth weights and lower admission rates to the NICU — at the cost of the deliberate demise of one of the three fetuses, as well as emotional pain and distress for the parents.

MFPR is a practice that both the McCaughneys and the Chukwus morally opposed — and one that many Catholic medical institutions will not perform. The fact that MFPR puts the pregnancy in an 8 percent risk of complete failure worries many couples, especially those that went through ART (assisted reproductive technology) in getting pregnant. And many couples encounter emotional distress and depression if they are forced into a decision regarding MFPR. Reputable fertility clinics prevent patients from having to make the MFPR decision at all.

At my clinic, we look upon multiple births as a worst-case scenario and do everything possible to prevent them from occurring. In our minds, a singleton or twin birth is ideal, because it places the least amount of stress on the babies, on the expecting couple and on our system as a whole. We believe that fertility doctors must look at the issue from both a micro and macro perspective. Every clinic should have a strategy for the prevention of multiple births.

Our strategy to prevent multiple births is relatively simple. The crucial dilemma in fertility-drug treatment comes after the stage at which hormones are administered to cause the follicles to mature. That is when doctors must decide whether too many follicles have matured to permit the use of a second drug that triggers the release of eggs — or, in the case of in-vitro procedures, how many embryos to replace in the womb. We stop fertility-drug treatment if more than five follicles have ripened at one time, and we do not implant more than three embryos in the womb. Normally, we implant two eggs for women younger than 30 and three eggs for women older than 30. Since our strategy was implemented in 1996, our pregnancy rates have not been compromised.

**Insurance coverage**

Sadly, along with the health threats to multiple children and mothers, as well as the astronomical costs of caring for the frail babies at birth and afterwards, another issue exists in the world of fertility. It is one that, for many people, threatens the very existence of fertility treatment itself. It is the availability of insurance coverage for the often-expensive fertility treatments — and the continued coverage of pregnancy costs under insurance programs. If fertility clinics do not start getting a handle on multiple-to-single birth ratios, insurance companies will continue to forgo coverage of fertility treatments. Insurers might even begin to write in clauses covering themselves in the case of multiple births — or covering themselves in general against pregnancies conceived through fertility programs. Such measures work toward one unfortunate reality: Some people will be able to afford to have children and some will not.

A myriad of considerations are swirling in the debate over multiple births: insurance issues, divorce rates and familial strains, and financial, economic and moral issues. But during the heated debate, let’s not forget the most important issue of all: the well-being of the child, mother and family. It is very rare that after a septuplet birth, one will see a happy, healthy family like the McCaughneys. It is more likely that the family, like the Chukwus, still may be watching their babies from behind hospital glass after a year, without all of them to hold.

Randle S. Corfman, Ph.D., M.D., is a reproductive endocrinologist at the Midwest Center for Reproductive Health in Minneapolis.
Section XI

Questions and Answers
ASSISTED REPRODUCTIVE TECHNOLOGY

QUESTIONS AND ANSWERS

Q: Do Assisted Reproductive Technologies (ART) damage the ovaries?
A: There is no evidence to suggest that egg retrieval damages the ovaries. There are even some reports in the literature suggesting that after ovarian biopsy, pregnancies occur in couples with long-standing, unexplained infertility. In fact, on occasion, patients have become pregnant during the spontaneous cycle immediately following their ART cycle.

Q: Is there a possibility of multiple births from ART?
A: Yes, any time more than one embryo is transferred, the chance for multiple pregnancy exists. In fact, many twin births have resulted from ART at The Midwest Center, with fewer triplets and quadruplets. Although we do not directly offer it, multi-fetal reduction is available through referral for couples who achieve a multiple pregnancy.

Q: Is there an increased chance of birth defects if I become pregnant through ART?
A: A review article in the January 1991 edition of Fertility and Sterility reported no increased risk of congenital anomalies in children conceived through routine ART compared to those conceived in the general population. However, when Intracytoplasmic Sperm Injection (ICSI) is used in conjunction with the ARTs, the situation is less clear. Details of these possibilities are listed in the "ART Options" section. As of January 2001, the consensus remains that IVF does not present an increased risk of birth defects.

Q: I had my tubes tied (tubal ligation) several years ago. Would I be a candidate for IVF?
A: Although surgical reversal of tubal sterilization may be a better option, IVF is still a consideration. The success rate may be greater for ligation reversal than for IVF. However, if ligation reversal has been attempted and has failed, IVF represents the best option. In addition, cost and other factors involved in surgical reversal must be considered when making this decision.

Q: Does insurance cover the procedure?
A: Insurance companies in the state of Minnesota vary considerably regarding their infertility benefits. Although most insurance carriers do not cover IVF/ART, we urge verification prior to beginning treatment.

Q: How many days does the entire procedure take?
A: The entire procedure takes approximately six weeks. However, we only need to see you intensively at MCRH over a 4-5 day period.

Q: Can we have intercourse while attempting pregnancy through ART?
A: You must use barrier contraception upon initiation of the birth control pill and abstain from intercourse after the start of stimulation medications. Your ovaries will be markedly enlarged and tender, and intercourse could possibly cause a premature LH surge inducing ovulation or decreased blood supply to your ovaries. This latter condition is called “ovarian torsion” and is an emergency situation.
Q: **What if I ovulate before retrieval?**
A: Once ovulation has occurred, it is difficult to retrieve the eggs. On the day of hCG or day before retrieval, an ultrasound may be performed to make sure the follicles are still intact. If they are, it can be assumed that ovulation has not occurred and egg retrieval will be attempted. The medications Leuprolide Acetate (Lupron) and Ganirelex Acetate also help to ensure that ovulation does not occur before egg retrieval has been performed. If, however, ovulation has truly occurred prior to retrieval, the cycle would be canceled.

Q: **Will scar tissue around my ovaries make it impossible to retrieve oocytes?**
A: No, oocytes can usually be retrieved by transvaginal aspiration even when the ovaries are covered with scar tissue.

Q: **When can I go back to work after the retrieval?**
A: Since IV narcotics will be given to you during your procedure, you should not return to work afterwards. Most patients feel able to return to work the day after retrieval.

Q: **How much activity is recommended after Embryo Transfer (ET)?**
A: We recommend light activity for 24 hours after ET. Thereafter, most patients resume their normal routines. Strenuous exercises should be avoided until a pregnancy test has been performed.

Q: **After Embryo Transfer (ET) takes place, how long must we wait until we have intercourse?**
A: Nobody really knows how long one should wait. Theoretically, uterine contractions resulting from intercourse could impair implantation. We recommend that you abstain from intercourse until after the pregnancy test. If the pregnancy test is positive, please abstain until the fetus’ heartbeat is seen on ultrasound (2-3 weeks after pregnancy test).

Q: **What options do we have if the ART cycle results in a higher number of multiples (i.e. triplets or quadruplets)?**
A: In cases of high order multiple pregnancies, you will be counseled regarding your options by the staff at Midwest Center and your referring physician. One option includes multifetal reduction, a procedure by which the number of fetuses is reduced, under ultrasound guidance. The procedure is performed by a perinatologist (high-risk obstetrician) upon referral. Risks with that procedure include a small chance of total loss of the pregnancy (4-7% chance of total loss per embryo reduced). Since spontaneous reductions (i.e. from 3 to 2) can occur in early pregnancy, the procedure is performed after that may have occurred, typically at 10 weeks.

Q: **Are drop-in childcare services available when I undergo my procedure(s)?**
A: The Midwest Center does not offer on-site childcare services. Kinder Care Learning Center, a daycare center in Maple Grove, does offer this drop-in service. They would like to receive a one week notice, but they are willing to work with patients. Their address and contact information is the following:

KinderCare Learning Center
13380 Grove Drive
Maple Grove, MN 55369
(763) 420-9200
Section XII

Frozen Embryo Transfer
FROZEN EMBRYO TRANSFER

Frozen embryo transfer (FET) is the transfer of cryopreserved embryos that were obtained during a previous IVF cycle. FET is a fairly simple procedure and since stimulation of the ovaries is not required, no stimulation medications are prescribed. The procedure is performed in the same manner as the embryo transfer utilized during IVF cycles and is performed only during our “uptimes”.

Specific instructions are given with regard to medication and a consultation will take place with the physician/embryologist to discuss the number of frozen embryos that should be thawed and examined. If it appears that one or more are medically appropriate for transfer, the transfer will occur.

Down regulation with Leuprolide Acetate (Lupron), similar to that used in fresh cycles, is necessary as is hormone replacement of the uterine lining with estrogen. An estrogen preparation, Estrace (oral) or Estradiol Transdermal Patch is taken, and when the lining appears to be optimal for embryo implantation, the transfer will be scheduled.

Risks associated with a frozen embryo transfer include embryos of poor quality which have a significantly decreased chance of implantation and contamination of embryos which might increase the chance of infection.

If you wish to proceed with a frozen embryo transfer, you will need to contact the IVF Coordinator (763-494-7702) two to three months prior to your desired series to initiate treatment.
FROZEN EMBRYO TRANSFER OVERVIEW

Preparation

Clinical / Laboratory Requirements
- Rubella/Varicella
- Lupus Anticoagulant and Anticardiolipin Antibody (if indicated)
- Sonohysterogram/Uterine Profile, (if indicated)
- If no previous tubal evaluation, Hysterosalpingogram (HSG) or Laparoscopy

Team Member Interaction
- IVF Coordinator: informs of and reviews screening requirements and consents
- MD: FET review, sonohysterogram and uterine profile, if more than 1 yr. since last cycle
  - per patient need or pregnancy loss has occurred
- MD/Embryologist: thawing process / outcomes and freezing technique
- Nursing: coordinate patient care and prescriptions and medication outline
- IVF information update and injection technique review – per patient need
- Business office: financial arrangements – per patient need

Down Regulation
- Birth control pills: one tablet once daily as directed
- Norethindrone Acetate (Aygestin) one tablet once daily for 10-20 days
- Pituitary desensitization: GnRH agonist (Leuprolide Acetate (Lupron), subcutaneous injection) for a minimum of 10 days or until down regulation has been achieved
- Ultrasound and Estradiol (E2)
- * All ultrasound and estradiol (E2) results must be received in our office by 12:00 p.m. CST/CDT.

Hormone Replacement Therapy
- Estrace (oral) or Estrogen Patch
- Ultrasound and Estradiol (E2) when indicated
- Progesterone suppositories
- Progesterone in oil (intramuscular injection)
- Methylprednisolone (oral), if indicated

Thawing of embryos

Assisted Zona Hatching (AZH) variable

Embryo Transfer

BhCG level
- (approximately 14 - 16 days from embryo transfer)

Ultrasound confirmation
- Intrauterine Pregnancy
  - (2-3 weeks from positive BhCG level)
- Delivery
  - (33 weeks)

Clinical Pregnancy per transfer

Risks and Complications
- Ectopic Pregnancy
- Multiple Births
- Multi-fetal reduction
This form is an example of the checklist completed by Midwest Center staff and filed in your chart.

THE MIDWEST CENTER FOR REPRODUCTIVE HEALTH, P.A.
FROZEN EMBRYO TRANSFER MEDICATION OUTLINE

PATIENT NAME:_________________________ PARTNER NAME:_________________________

Date prepped:__________________ By:__________________ Series:________

___ Answering Machine/Voicemail System
___ Medication Outline
___ Kardex Monitoring Sheet
___ Copy of Previous ART Monitoring Sheet
___ Injection experience discussed/direction provided re: training

___ Current Medications__________________________________________________
___ Zika virus travel restrictions/risks discussed with patient

Prescriptions
___ Norethindrone 5mg tablets, #____, refills x 1
___ Leuprolide Acetate (Lupron) 2.8 ml vial, #_____, refills x 2.
___ Estrace 1 mg, #200, refills x 4 or _____ Estradiol Valerate 10 mg/ml (10 ml vial), #1, refills x 2
___ Estradiol Transdermal Patch 0.1mg Qty # 48 with 3 refills
___ Prenatal Plus Vitamins #100, refills x 1
___ Doxycycline 100mg tablets, #10, refills x 1
___ Progesterone in Oil 50 mg/ml (10ml vial), #4, refills x 4
___ Methylprednisolone 4 mg tablets, #16, refills x 1
___ Lovenox 30mg SQ BID, 2 week supply, refills x 4
___ Glucophage (Metformin), 500 mg tablets, #120, refills x 2
___ Metformin XR 750mg tablets, #120, refills x 2
___ Vaginal Progesterone Suppositories 200 mg, #80, refills x 4
___ Endometrin 100 mg, #90, refills x 4

If Satellite
___ Satellite Location:____________________ Contact Person:____________________
___ Monitoring sheet/orders faxed by________________________Date __________
___ Monitoring requirements reviewed with patient.

___ Informed to call business office with any questions.
___ Informed to contact educators with injection questions.

______ Patient verbalizes understanding of information presented.
______ Above instructed by ____________________ Date:

____________________ Units:________

By phone:       Y           N

Ivf/medoutlines/fetcklis/0615

12-3
CYCLE PREPARATION AND TESTING

In attempts to provide information for patients, complete testing, and alleviate some of the stresses involved with your treatment cycle, you will receive extensive education regarding the frozen embryo transfer process. Throughout your treatment, detailed instruction will be provided by staff members outlining your individualized treatment plan.

The physician may also perform a “sonohysterogram/uterine profile” (if not performed within the last year or if pregnancy loss has occurred), which is a measurement of the uterine cavity. This will aid in the future uterine embryo transfer by assuring proper placement of the embryos within the uterus.

Female Testing

For a detailed description of the following required procedures and blood tests, please refer to Section IV – Program/Testing requirements.

**Procedures:**
- Sonohysterogram/Uterine profile (within one year of a FET cycle unless a pregnancy loss has occurred)

*If an evaluation of the fallopian tubes has never been performed:*
- Hysterosalpingogram (HSG)
  - OR
- Laparoscopy

*May be indicated by Dr. Corfman as a pre-screening requirement:*
- Mammogram
- Electrocardiogram (EKG) (age 42 y/o or >)
- BMI ≤ 30

**Blood Tests:**
- Rubella Immune Status
- Varicella Immune Status
- Blood type with Rh factor (done once in a lifetime)
- HIV I and II
- Hepatitis B and C if never completed prior to a previous IVF cycle
- Varicella Immune Status
- TSH/Prolactin (if indicated)

**Immune System Evaluation:**
- Anticardiolipin Antibody (ACA)
- Lupus Anticoagulant (LAC)
- Antichlamydial Antibody
- Factor V Leiden
Male Testing

Although your husband/partner will not need to provide a semen sample for a frozen embryo cycle, the following blood tests are still necessary due to the fact that these infections can spread by having intercourse; therefore, testing is required of both partners. For a detailed description of the following required blood tests, please refer to Section IV – Program/Testing requirements.

**Blood Tests:**
- **Blood type with Rh factor** (done once in a lifetime)
- **HIV I and II**
- **Hepatitis B and C** if never completed prior to a previous IVF cycle
INITIATING TREATMENT AND DOWN REGULATION

Preparation for Treatment

To allow planning for your FET cycle, our center currently has “uptimes” approximately 5 times a year (2-3 weeks in length). It is during this time that your transfer will be performed. However, testing and medications will begin 1-2 months prior to your frozen embryo transfer.

Once medications are initiated, subsequent office visits are needed for the ultrasound monitoring of your response to these medications, as well as blood tests. Due to the number of visits in this 2-3 week period of treatment, flexibility in your schedule is needed. In an effort to provide you with timely information, please access your private voicemail system daily between 3:00 p.m. and 4:00 p.m. CST/CDT during your treatment cycle. Patients can expect to receive messages on all monitoring days regarding test results and future treatment plans and occasionally, there may be other communications left for patients throughout their treatment cycle. If you have not received an anticipated message by 4:00 p.m. CST/CDT, please contact the nurses. Questions may then be answered during office hours for your convenience. We require that you have an answering machine/voice mail where we can leave detailed messages regarding medication and monitoring instructions as a backup to the confidential phone system.

The monitoring of hormone replacement therapy is performed either at MCRH or one of our satellite clinics. Your embryo transfer will be performed at MCRH in Maple Grove, a northwestern suburb of Minneapolis, Minnesota.

To Begin FET Cycle

Please recognize there will be references made to three different types of days.

| Cycle Day | Relating to the day of your menstrual cycle |
| Down Regulation | Relating to the days on the birth control pill, Norethindrone Acetate (Aygestin) and Leuprolide Acetate (Lupron) for ovarian suppression |
| Hormone Replacement Therapy | Relating to the days on Leuprolide Acetate (Lupron) and medications to enhance endometrial lining |

- Call the IVF Coordinator at (763) 494-7702 with the onset of menses 2-3 cycles prior to your planned FET cycle.
- Since the adverse effects of these medications on a possible pregnancy are unknown, **barrier contraception or abstinence is required** upon starting the birth control pill. Patients are to **abstain from vaginal intercourse after the start of hormone replacement therapy medications until documentation of fetal heart motion**.
- Fill prescription(s) for the down regulation medications at least 2 weeks prior to initiating treatment.

You will be given your individualized medication outline prior to initiating treatment.
**Down Regulation Medications**
For a detailed description of the down regulation medications and their side effects, please refer to Section V – Initiating Treatment and Down Regulation.

- Oral Contraception
- Norethindrone Acetate (Aygestin)
- Leuprolide Acetate (Lupron)

**Preparation and Administration of Leuprolide Acetate (Lupron)**
For instructions regarding the preparation and administration of Leuprolide Acetate, please refer to section V – Initiating Treatment and Down Regulation.

**Prenatal Vitamin**
A prenatal vitamin is an oral vitamin given to supplement your diet by providing you with the vitamins and minerals needed for pregnancy. This vitamin contains the recommended amount of folic acid which will help to decrease the chance of birth defects in early development of the fetus.

Prenatal vitamins are formulated to optimize supplementation for an expecting mother, and it is our feeling that this is also optimal for conception. Given the wide variety of other herbs and vitamins available, and given the lack of studies demonstrating their effect upon reproduction, we ask that you **do not take other vitamins or herbal preparations** while undergoing in vitro fertilization.

**Potential Side Effects of Prenatal Vitamins**
- Constipation
- Darkening of the stools due to iron contained in the vitamins
- Nausea

You may want to drink plenty of water as well as include fiber in your diet to help counteract these effects.

Stool softeners (i.e. Metamucil, Citrucel) may be taken to treat constipation.

Begin taking one vitamin daily when hormone replacement therapy medications begin if you have not already started.
HORMONE REPLACEMENT THERAPY

**Estrace and Estradiol Patch**

Estrogen is a hormone that is naturally produced by the granulosa cells lining the follicle wall during the first half of the menstrual cycle. The purpose of this hormone is to enhance the growth of the uterine lining to optimize implantation. Patients will be instructed to begin this after down regulation has been achieved. There are two means of estrogen administration, oral medication and intramuscular injection. Patients will be given instruction regarding the mode of administration and time frame of use that your physician has prescribed.

**Estrace**

Estrace is a form of estrogen that is taken orally. Patients will be instructed on timing and dosage. If the pregnancy test is positive, Estrace will be continued through 12 weeks of pregnancy unless instructed otherwise.

**Estradiol Transdermal Patch**

Estradiol Transdermal Patch is a form of estrogen that is administered via a patch that is applied to the abdomen every other day. The patch should be applied to clean, dry skin. If you bathe or swim while wearing the patch, you may have to apply a new patch afterwards. If the pregnancy test is positive, it will be continued through 12 weeks of pregnancy unless instructed otherwise.
Estradiol Valerate Syringes, Needles and Dosages

Conversions need to be made according to the dosage you are prescribed and the medication concentration provided by your pharmacist. Outlined below is a tool to assist in making dosage modifications. When drawing up this medication, please note that 1 cc = 1 ml.

Estradiol Valerate TB (Tuberculin) Syringe and IM needle used to draw up medication. Change needle to a new IM needle for administration.

Dosage Conversions:

10 mg/mL
- .2 cc = 2 mg
- .4 cc = 4 mg
- .6 cc = 6 mg

20 mg/mL
- .1 cc = 2 mg
- .2 cc = 4 mg
- .3 cc = 6 mg
Preparation of Estradiol Valerate

1. Clean work surface that will be used to prepare the injection with soap and water, or swab with alcohol, and wash your hands thoroughly.

2. Assemble the necessary materials: medication vial, tuberculin syringe and needle, 22 G 1 ½” needle, alcohol wipes and disposal container.

3. Remove flip top from vial. Wipe top of vial with alcohol and allow to dry.

4. Remove tuberculin needle from syringe and replace with intramuscular (22 G 1 ½”) needle.

5. Remove cover from the needle.

6. Draw prescribed number of cc's (or ml's) of air into the tuberculin syringe. Insert needle into vial and inject the air. Please refer to your individualized patient medication outline.

7. Draw prescribed number of cc's (or ml's) of Estradiol Valerate into the syringe. Please refer to your patient medication outline.

8. Replace the needle cap and twist needle off. Attach a new, intramuscular (22 G 1 ½”) needle to the tuberculin syringe prior to administering injection.

9. Check for air bubbles. If any are visible, invert the syringe and needle, tap lightly to collect any air bubbles into the top of the syringe, and then gently press the plunger to expel the air.

10. This medication is injected intramuscularly. Refer to intramuscular injection administration instructions.
**Luteal Phase Support**

**Progesterone** is a hormone that is naturally produced by the corpus luteum (ruptured follicle) during the second half of the menstrual cycle. The placenta will take over progesterone production at around 8-9 weeks of pregnancy. Natural progesterone is prescribed by most fertility specialists and is especially prescribed for those patients undergoing a variety of the assisted technology procedures. This natural source of progesterone will optimize implantation and continue for approximately 12 weeks unless directed otherwise by your physician.

The package insert that accompanies the medication may include advice against its use in pregnancy. This is because both synthetic progestins and natural progestins are grouped together by the FDA. Synthetic progestins have been associated with a slight increase in birth defects if taken during early pregnancy. To date, there is no evidence that supports this when using natural progesterone and the benefits of this medication outweigh any potential risks.

**Refer to your individualized patient medication outline**

**Progesterone Options**

For a detailed description regarding your progesterone options and their potential side effects, please refer to the Luteal Phase Support information located in Section VII – Oocyte Retrieval and Fertilization.

- **Progesterone Suppositories** contain natural progesterone. This medication is usually suspended in glycerin base; therefore, it will dissolve and the medication is absorbed. We recommend that you wear a panty liner or pad when using these suppositories as discharge is common.

- **Progesterone in Oil** is a medication that is administered by intramuscular injection. It is normal to have muscle soreness around the injection site. However, if the sites become red or hard, please notify the nurses at (763) 494-7726. Warm, moist packs at the site may help to alleviate discomfort; however, hot tub baths are not recommended.

- **Endometrin** is a vaginal insert that contains 100 mg of natural progesterone in each tablet. Each Endometrin insert comes with its own individually wrapped, disposable applicator. Once inserted, Endometrin dissolves rapidly with minimal discharge.

Potential side effects of progesterone include lethargy, nausea, breast tenderness, water retention, weight gain, pain or swelling at the intramuscular injection site for Progesterone in Oil injections, increased sensitivity to sunlight, delayed menses or decrease in flow during menses. Worsening of pre-existing depression, migraine headaches, epilepsy, asthma, heart disease or kidney disease may occur and should be discussed if present in your medical history prior to beginning this medication.

**Midwest Center staff will provide instruction regarding the progesterone option(s) and dosage appropriate for your treatment.** Progesterone will continue daily until the second pregnancy test, even if vaginal spotting occurs. If your pregnancy test is positive, progesterone will be continued through 12 weeks unless instructed otherwise.

**Intramuscular Injection Administration**

For instructions regarding the intramuscular injection administration of Estradiol Valerate, please refer to Section VI – Ovarian Stimulation.
PREPARATION OF PROGESTERONE IN OIL

Preparing the Injection

1. Clean the work surface that will be used to prepare the injection with soap and water, or swab with alcohol, and wash your hands thoroughly.

2. Assemble the necessary materials: medication vial, syringe and 22 G 1 ½” needle, alcohol wipes, and disposal container.

3. Attach needle to syringe.

4. Remove flip top from vial. Wipe top of vial with alcohol and allow to dry.

5. Remove cover from the needle.

6. Draw prescribed number of cc’s (or ml’s) of air into the syringe. Insert needle into vial and inject the air. Please refer to your individualized patient medication outline.

7. Draw prescribed number of cc’s (or ml’s) of the progesterone into the syringe. Please refer to your patient medication outline.

8. Replace the needle cap and twist needle off. Attach a new, intramuscular (22 G 1 ½”) needle to the syringe prior to administering injection.

9. Remove any air bubbles.

10. This medication is injected intramuscularly. Refer to intramuscular injection administration instructions.

11. Progesterone is oil-based and will take longer to draw up into the syringe and to inject.

* If you touch the needle, if you blow on the needle, or if it comes in contact with any surface, it is considered contaminated. In the event this occurs, recap and remove the contaminated needle. Attach a sterile needle to the syringe and continue preparation.

* When drawing this medication, please note that 1 cc = 1 ml.
EMBRYO STATUS REPORT

Below is an example of the information you will be given at the time of embryo transfer. This information will provide you with the number of embryo(s). Please review this information in advance of your procedure in order to prepare yourselves for meeting with the embryologist.

Embryo Status Report
(Frozen Embryo Transfer)

The following information is being provided to you in preparation for your upcoming transfer.

- **Number of embryos to transfer:**
  
  1-2 is optimal

- **Multifetal Reduction:**
  
  Do not transfer more than you are willing to take home
  
  There is a rare chance of getting more than you transfer (identical twins)

There are medical/surgical conditions that may indicate fewer embryos should be transferred. These conditions are typically reviewed with the physician during your initial consultation.

Date __________

____ # of embryos thawed

____ # of viable embryos

____ # of remaining frozen embryos
EMBRYO TRANSFER

**Doxycycline**
Introducing embryos into the uterus could potentially result in an infection; however, it is rare. **Doxycycline**, an oral antibiotic, is used as a preventative measure. You will begin this medication prior to embryo transfer and continue it for a total of 5 days (one tablet in the a.m. and p.m.).

**Potential Side Effects:**
- Nausea—take with meals or light snack
- Sun sensitivity—limit exposure to the sun and tanning devices. If exposure is unavoidable, sunscreen of 30 SPF is recommended.

- Refer to your individualized patient medication outline

**Transfer/Post Transfer**
For detailed information regarding the following, please refer to Section VIII – Embryo Transfer.

- Embryo evaluation and transfer
- Low-dose aspirin
- Lovenox/Heparin – preparation and administration
- Pregnancy tests and follow-up
- Selective (multi-fetal) reduction

**ART OPTIONS**
For a detailed description of the following micromanipulation technique, please refer to Section IX – ART Options.

- Assisted Zona Hatching (AZH)
RISKS AND COMPLICATIONS

Medication Side Effects

- Soreness at the injection site, breast tenderness, mood swings, headaches, nausea, dizziness and weight fluctuation are all side effects of these medications that can occur. These side effects are uncommon, but they can occur together or separately.

- Should you experience severe side effects, please notify the nursing staff at (763) 494-7726.

Infection

- Introducing embryos into the uterus could potentially result in an infection; however, it is rare. As a preventative measure, you will take an antibiotic called Doxycycline. Patients begin this medication as instructed before the transfer and continue it for a total of 5 days.

Pregnancy/Delivery

- Approximately 1% of people who achieve a pregnancy will unfortunately experience an ectopic (tubal) pregnancy. An ectopic pregnancy is not viable and may require medical or surgical intervention.

- As with pregnancies that are achieved naturally, the risk of miscarriage also exists. Factors affecting this include patient age and previous reproductive history.

- Transferring several embryos back into the uterus can increase the potential for a pregnancy but can also increase the chance of multiple gestation. It is estimated that 40% of the pregnancies achieved may result in pregnancies with two or more fetuses. The potential that a developing embryo may split into identical twins is less than 0.5%. Several considerations to reduce multiple gestations however not eliminate them, include limiting the number of embryos transferred and multi-fetal reduction during early pregnancy. These measures would also reduce the risk of preterm infants and complications associated with them.

- As with naturally conceived and born children, there is a possibility of complications of childbirth, stillbirth or miscarriage, or birth of an abnormal child/children.
Section XIII

Support Services
INFERTILITY SUPPORT SERVICES

MCRH will provide referrals to a variety of support services in your area upon request. These services will address the psychosocial and emotional needs of individuals and couples dealing with the stress of infertility.

We are staffed with a licensed social worker who will see patients either on-site or off-site to help people cope with the emotional effects of infertility. The social worker may be utilized before, during and/or after treatment for those whose attempt at pregnancy results in a negative outcome.

All couples and individuals receiving infertility treatment are encouraged to utilize this service. Single visits or ongoing consultations by our professionally trained social worker are available either in person or by phone.

This visit is an opportunity to learn to cope and fully understand the emotional impact of infertility. She will explore and develop with you stress management techniques and ways to implement them in daily living.

Scheduling an appointment with the social worker at her private practice office may be done by calling (952) 925-3533. There will be an additional charge for this service and will be handled directly through the social worker. These visits may or may not be reimbursed by insurance depending upon the terms of your policy.

Other support services offered through MCRH include:

- RESOLVE of the Twin Cities, Inc. This is a national infertility support group. The goal of this organization is to provide compassionate support and information to people who are experiencing infertility and to increase awareness of infertility issues through advocacy and public information. Call (651) 659-0333 for information on meetings or to get on their mailing list.

- Quest This is a Christian based support group that meets twice a year for eight sessions. This group is designed to provide spiritual and emotional support for people. Call New Life Family Services at (612) 866-7643 to receive further information about Quest.

- Referral to a specialist in massage and relaxation.

- Referral to adoption resources.

- Jeanette Truchsess, Ph.D. Psychotherapy, Mind-Body Spirit Approaches, and Infertility and Adoption Counseling Call (651) 226-4704 for information.
Infertility Counseling and Support: When and Where to Find It

Infertility is a medical condition that touches all aspects of your life. It may affect your relationships with others, your perspective on life, and how you feel about yourself. How you deal with these feelings will depend on your personality and life experiences. Most people can benefit from the support of family, friends, medical caregivers, and mental health professionals. When considering infertility treatment options such as sperm, egg, or embryo donation or gestational carriers, it may be especially helpful to gain the assistance of a fertility counselor. The following information may help you decide if you need to seek professional help in managing the emotional stresses associated with fertility treatment or need assistance regarding your treatment options.

When do I need to see an infertility counselor?
Consider counseling if you are feeling depressed, anxious, or so preoccupied with your infertility that you feel it is hard to live your life productively. You also may want to seek the assistance of a counselor if you are feeling "stuck" and need to explore your options. Signs that you might benefit from counseling include:
- persistent feelings of sadness, guilt, or worthlessness
- social isolation
- loss of interest in usual activities and relationships
- depression
- agitation and/or anxiety
- mood swings
- constant preoccupation with infertility
- marital problems
- difficulty with "scheduled" intercourse
- difficulty concentrating and/or remembering
- increased use of alcohol or drugs
- changes in appetite, weight, or sleep patterns
- thoughts about suicide or death

Where can I get support?
Support can come from many different sources. Books can offer information and understanding about the emotional aspects of infertility. Support groups and informational meetings can reduce the feeling of isolation and provide opportunities to learn and share with others experiencing infertility. Individual and couple counseling offer the chance to talk with an experienced professional to sort out your feelings, identify coping mechanisms, and work to find solutions to your difficulties. Discussions with supportive family members and friends also can be useful.

How do I find an infertility counselor or other support?
Start by asking your physician for referrals to trained mental health professionals in your area, a list of relevant books and articles, and support resources that deal with fertility-related matters. Counselors may be psychiatrists, psychologists, social workers, psychiatric nurses, or marriage and family therapists. Visit ReproductiveFacts.org and click on the button labeled "Find a Healthcare Professional" for a list of doctors and mental health professionals in your area.

Are there any specific resources available to guide individuals coping with infertility?
There are many resources included on the ASRM patient Website (ReproductiveFacts.org), including frequently asked questions, videos, fact sheets and booklets (many also in Spanish), and ASRM Practice and Ethics statements.

Below are listed several additional resources that may be helpful in addressing a variety of concerns and issues. This list is by no means exhaustive. If you require help regarding other topics, please consult the patient resources section of ReproductiveFacts.org or your healthcare professional.

- American Fertility Association (AFA): An organization created to educate the public about reproductive disease and support families during struggles with infertility and adoption, theafa.org
- Choice Moms: An organization to help single women who proactively decide to become the best mother they can, through adoption or conception, choicemoms.org
- Fertile Hope: A national LIVESTRONG initiative dedicated to providing reproductive information, support, and hope to cancer patients and survivors whose medical treatments present the risk of infertility, fertilehope.org
- Frank Talk: A peer-support Website dedicated to helping men deal with erectile dysfunction, FrankTalk.org
- InteNational Council on Fertility Information Dissemination, Inc. (INCIID), inciid.org
- North American Council on Adoptable Children: An organization committed to meeting the needs of waiting children and the families who adopt them, nacac.org
- Parents Via Egg Donation: An organization created to provide information to parents and parents-to-be and to share information about all facets of the egg donation process, parents viaeggdonation.org
- Pop Luck Club: The Pop Luck Club has evolved into a substantial voice, helping to support the growth of our wonderfully diverse LBGT community, popluckclub.org
- RESOLVE: A national infertility support organization, Resolve.org
- Single Mothers by Choice: Offering support and information to single women who are considering motherhood and to single mothers who have chosen this path to parenthood, singlemotherbychoice.org
- Magazines: Fertility Road, Fertility Magazine, Conceive Magazine, Gay Parent Magazine

Revised 2014

For more information on this and other reproductive health topics, visit www.ReproductiveFacts.org
Section XIV

Financial Arrangements
FINANCIAL INFORMATION

IVF is generally not a covered service of most insurance companies and is considered cash in advance by most infertility programs. We require payment of all professional services prior to your in vitro fertilization cycle. All other charges are due in full, within 28 days of billing.

MCRH is not in network with any insurance company for IVF, we will submit claims if you have coverage, however, no provider adjustments will be taken.

If you have any questions regarding whether or not IVF is a covered benefit under your policy, we would encourage you to contact your insurance company. We can also provide you with a pre-determination of benefits packet, giving a breakdown of fees and associated charges, to submit to your insurance.

We encourage you to call the business office at (763) 494-7736 or (800) 508-9763 option 4 with any questions you may have regarding the participating status with your insurance company or billing procedures.
PREPAYMENT
FULL STIMULATION IVF

Date:

Patient Name:

Patient Account Number or Date of Birth:

Minimum Pre-payment Amount: $ 11,735.00
-$200.00 Commitment Deposit (if previously paid for this cycle)
Total $______________
(Pre-payment does NOT include Monitoring, Medication or Variables.)

1. A check or money order for the amount of ________________ is enclosed.
   Make Payable to: The Midwest Center for Reproductive Health.

2. Please charge my credit card for amount of ________________.

   Credit Card: VISA Master Card Discover AMEX (please circle one)
   Name on Card: ____________________________________________
   Card Number: ____________________________________________
   Security Code: _______ Expiration Date: _____________________
   Address: __________ Zip Code: ________________
   Signature of Card Holder: __________________________________

All procedures will be billed through The Midwest Center for Reproductive Health; we are OUT-OF-NETWORK with ALL insurance companies.

**Following the IVF procedure, we will be billing your credit card for any remaining patient responsibility balances for Monitoring, Extended Culture and/or Cryopreservation of Embryos, etc. which were NOT included in the prepayment. Please provide the credit card information for which you would like these services charged.

REQUIRED:

Credit Card: VISA Master Card Discover AMEX (please circle one)
Name on Card: ____________________________________________
Card Number: ____________________________________________
Security Code: _______ Expiration Date: _____________________
Address: __________ Zip Code: ________________
Signature of Card Holder: __________________________________

Fee For Service: This is for One cycle using fee for service, there are no guarantees or refunds with this program.

VIP Program: You would need to notify our staff, qualify for the program, no claims would be submitted to insurance and you would have a greater prepayment.

Please call the Business Office at 763-494-7736 if you have any questions.
Please return this letter along with your payment by The Prepayment Deadline. Thank you
FULL STIMULATION IVF COSTS

Included in this packet is a price list for your upcoming IVF procedures. Please note which fees are included and/or not included in the prepayment which is due prior to the beginning of the series.

In the event that you self-cancel prior to your retrieval, the Commitment Deposit is non-refundable.

Someone from the Business Office will be available to meet with you and discuss these costs in greater detail. If you have any questions before that time, please feel free to contact our Business Office at 763-494-7736 or 1-800-508-9763 option 4. Our business hours are 8:00 am to 4:00 pm.
FULL STIMULATION IVF

I. Pre- Cycle Costs
II. Prescreening Requirement Costs
III. Monitoring*
IV. Ovum Harvest (included in pre-payment)
V. Embryo Transfer (included in pre-payment)
VI. Variable/Optional Costs
VII. Post Cycle Costs*

*May be performed by another physician.
I. **Pre-cycle Costs (Not included in prepayment)**

<table>
<thead>
<tr>
<th>Service</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sonohysterogram/UPT</td>
<td>$444.00</td>
</tr>
<tr>
<td>Physician reading of Sonohysterogram (off site)</td>
<td>$72.00</td>
</tr>
<tr>
<td>Additional consultation with physician - in office</td>
<td>$114.00 - 264.00</td>
</tr>
<tr>
<td>- by phone</td>
<td>$87.00 - 150.00</td>
</tr>
</tbody>
</table>

*Services provided by phone are less likely to be reimbursed by insurance carriers.*
II. Prescreening Requirement Costs (Not included in prepayment)

The tests listed below are shipped to Memorial Blood Centers for processing.

Standard IVF Tests for Female and Male:
- Hepatitis B $22.00
- Hepatitis C $38.00
- HIV 1 & 2 $28.00
- Anti-HTLV I/II $36.00
- Syphilis Testing (Anti-TP) $19.00
- Blood type/Rh typing $21.00
- Blood draw $19.00

Additional Tests Available Through MBC:
- Anti-HTLV I/II $36.00
- Capture CMV Total – IgM/IgG $21.00
- CMV-IgG/IgM Specific (if reactive) $164.00
- Chlamydia culture $60.00
- Gonorrhea culture $60.00

Tests Processed Through North Memorial
- Rubella Immunity $47.00
- Anticardiolipin Antibody $37.00
- Beta 2 Glycoprotein $37.00
- Lupus Panel (includes Anticardiolipin and Beta 2 Glycoprotein) $397.00
- TSH $113.00
- FSH $109.00
- Prolactin $123.00

Male Testing Through MCRH:
- Semen Analysis $186.00
- Semen Analysis with Strict Criteria $279.00
- Antisperm assay $365.00
- Cryopreservation of back up semen sample $135.00
- Transport kit for off-site semen cryopreservation collection $190.00

*These tests may be done by your primary care physician.
Please note not all testing may be required.
III. Monitoring (Not included in prepayment)

<table>
<thead>
<tr>
<th>Description</th>
<th>Estimated Quantity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood draw @ $19.00 each</td>
<td>3 - 5</td>
</tr>
<tr>
<td>Estradiol blood tests @ $147.00 each</td>
<td>3 - 5</td>
</tr>
<tr>
<td>Baseline ultrasound @ $350.00</td>
<td>1</td>
</tr>
<tr>
<td>Follicle tracking ultrasounds @ $275.00 each</td>
<td>1 - 4</td>
</tr>
</tbody>
</table>

(If monitoring at Midwest Center, this phase will range from $1123 – $2280. If monitoring is done elsewhere, one ultrasound and one estradiol with blood draw may be performed at Midwest Center prior to retrieval)

IV. Ovum Harvest**

- Retrieval by physician                                $2,770.00
- Sedation Medications, Pre/Intraprocedure/Post-op Observation, Lab fees $5,465.00

Total Retrieval Costs $8,235.00

V. Embryo Transfer**

- Extended culture of embryo(s), 4-7 days $1,200.00
- Preparation of embryo for transfer 800.00
- Transfer by Physician 1,500.00

Total Transfer Costs $3,500.00

TOTAL PREPAYMENT $11,735.00

Precycle Costs
Medication
Monitoring
Variable Costs

**Included in pre-payment amount
VI. Variable/Optional Costs (Not included in prepayment)

<table>
<thead>
<tr>
<th>Service</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>AZH (if applicable, will be billed)</td>
<td>680.00</td>
</tr>
<tr>
<td>Initial Cryopreservation (if applicable, will be billed)</td>
<td>415.00</td>
</tr>
<tr>
<td>Donor Sperm</td>
<td>400-1000.00</td>
</tr>
<tr>
<td>(When stimulation meds are initiated, specimen is ordered; this fee is non-refundable)</td>
<td></td>
</tr>
<tr>
<td>Sperm ID from testis (if testicular biopsy)</td>
<td>550.00</td>
</tr>
<tr>
<td>Thawing of cryopreserved sperm/semen (each aliquot)</td>
<td>30.00</td>
</tr>
</tbody>
</table>

VII. Post Cycle Costs* (Not included in prepayment)

<table>
<thead>
<tr>
<th>Service</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Two quantitative BhCG’s w/ blood draw</td>
<td>$ 226.00</td>
</tr>
<tr>
<td>Initial OB Ultrasound</td>
<td>0.00</td>
</tr>
<tr>
<td>Follow-up OB Ultrasound</td>
<td>190.00</td>
</tr>
</tbody>
</table>

*May be performed by another physician
IVF PAYMENT POLICY

A. The Midwest Center for Reproductive Health, P.A. accepts payment in the form of checks, cash, and credit cards (Visa/MasterCard/Discover/American Express).

B. Pre-payment of $11,735.00 is due prior to your medication stimulation. All checks should be made payable to The Midwest Center for Reproductive Health, P.A.

C. If applicable, full payment for AZH and cryopreservation of embryos is due once the procedure has occurred. This will be reflected on your monthly billing statement.

D. Letters of insurance pre-determination are not accepted in lieu of payment. Be aware that a pre-determination letter is not a guarantee of payment.

E. We will file to your insurance once the IVF cycle is complete if you have coverage for IVF.

F. All balances over 30 days old must be paid prior to starting IVF cycle.

G. Fees are subject to change without notice.

(Initial consultation with physician is not included in IVF charges.)
Date:

Patient Name:

Patient Account Number or Date of Birth:

Minimum Pre-payment Amount: $ 2,610.00

(Pre-payment does NOT include Monitoring, Medication or Variables.)

1. A check or money order for the amount of _______________ is enclosed.
   Make Payable to: The Midwest Center for Reproductive Health.

2. Please charge my credit card for amount of _______________.

   **Credit Card:** VISA Master Card Discover AMEX (please circle one)
   Name on Card: ________________________________
   Card Number: ________________________________
   Security Code: _______ Expiration Date: ________________
   Address: _________________________ Zip Code: ________________
   Signature of Card Holder: ________________________________

All procedures will be billed through The Midwest Center for Reproductive Health; we are OUT-OF-NETWORK with ALL insurance companies.

**Following the IVF procedure, we will be billing your credit card for any remaining patient responsibility balances for Monitoring, Extended Culture, Cryopreservation of Embryos, etc. which were NOT included in the prepayment. Please provide the credit card information for which you would like these services charged.

**REQUIRED:**

   **Credit Card:** VISA Master Card Discover AMEX (please circle one)
   Name on Card: ________________________________
   Card Number: ________________________________
   Security Code: _______ Expiration Date: ________________
   Address: _________________________ Zip Code: ________________
   Signature of Card Holder: ________________________________

Fee For Service: This is for One cycle using fee for service, there are no guarantees or refunds with this program.

VIP Program: You would need to notify our staff, qualify for the program, no claims would be submitted to insurance and you would have a greater prepayment.

Please call the Business Office at 763-494-7736 if you have any questions.
Please return this letter along with your payment by The Prepayment Deadline. Thank you.
FET COSTS

Included in this packet is a price list for your upcoming IVF procedures. Please note which fees are included and/or not included in the prepayment amount which is due prior to the beginning of the series.

In the event that you self-cancel prior to your transfer, the Commitment Deposit is non-refundable.

Someone from the Business Office will be available to meet with you and discuss these costs in greater detail. Feel free to contact our Business Office at 763-494-7736 or 1-800-508-9763 option 4. Our business hours are 8:00 am to 4:00 pm.
FET COSTS

Pre-cycle Costs: (Not included in prepayment)

Next Step Visit with Physician (if necessary) – in office $ 114.00 – 264.00
- by phone 87.00 – 150.00
Sonohysterogram/UPT 444.00
Estradiol 147.00
Blood Draw 19.00

The above services are billed at the time they are provided to you.

Prepayment:
Embryo Transfer 1,500.00
Preparation of Embryo(s) for transfer (any method) 800.00
Thawing of Cryopreserved Embryo(s) 310.00

Prepayment Total $ 2,610.00

Variables: (Not included in prepayment)
Baseline Ultrasound 350.00
Additional Ultrasounds 275.00
Additional Estradiol’s w/ Venipuncture 166.00
Two quantitative BhCG’s w/blood draws 226.00
AZH – Assisted Zona Hatching 680.00
Extended culture of embryo(s), 4-7 days 1200.00
Refreezing Thawed Embryos at Blastocyst 415.00

Medications are NOT included in the above fees.
IVF PAYMENT POLICY

A. The Midwest Center for Reproductive Health, P.A. accepts payment in the form of checks, cash, and credit cards (Visa/MasterCard/Discover/American Express).

B. Prepayment of $2,610.00 is due prior to your medication stimulation. All checks should be made payable to The Midwest Center for Reproductive Health, P.A.

C. If applicable, full payment for extended culture and cryopreservation of embryos is due once the procedure has occurred. This will be reflected on your monthly billing statement.

D. Letters of insurance pre-determination are not accepted in lieu of payment. Be aware that a pre-determination letter is not a guarantee of payment.

E. Itemized bills will be supplied to you following the IVF procedure. We will file to your insurance once the IVF cycle is complete if you have coverage for IVF.

F. All balances over 30 days old must be paid prior to starting IVF cycle.

G. Fees are subject to change without notice.

(Initial consultation with physician is not included in IVF charges.)
Section XV

Glossary
GLOSSARY OF MEDICAL TERMS

Aspiration
The application of light suction in the ovarian follicle to remove the eggs.

Blastocyst
An embryo formed after five to six days in culture.

Corpus Luteum
The gland that forms on the surface of the ovary at the site of ovulation and produces Progesterone during the second half of the menstrual cycle. It is necessary to prepare the uterine lining for implantation of the embryo.

Down Regulation
Use of Norethindrone Acetate (Aygestin) and Leuprolide Acetate (Lupron) to suppress the body's natural hormones.

Ectopic Pregnancy
Implantation of an embryo anywhere but in the uterine cavity (including the fallopian tube, the ovary, or the abdominal cavity).

Embryo
The early stage of fetal growth, from conception to the eighth week of pregnancy.

Embryo Transfer
Introduction of the embryo into the uterus after fertilization has occurred.

Endometrium
The lining of the uterus where the embryo implants.

Estradiol (E2)
The hormone released by the developing follicles in the ovary. Estradiol levels are used to help determine growth and maturity of the follicle during stimulation.

Fallopian Tube
The structure that carries the egg from the ovary to the uterus. This is normally where fertilization takes place.

Fertilization
The penetration of the egg by the sperm and fusion of genetic material that results in the development of an embryo.

Follicle
Fluid filled sac in the ovary that occurs during stimulation from which the egg is released during ovulation.

Follicle Stimulating Hormone (FSH)
The hormone produced and released from the pituitary gland in the brain that stimulates the ovary to prepare a follicle for ovulation.

Hormone Replacement Therapy
The use of medications to enhance the endometrium for implantation.
**Human Chorionic Gonadotropin (hCG) – Pregnyl/Novarel**
The hormone used to induce ovulation by substituting for the preovulatory surge of LH that a body produces during a normal menstrual cycle.

**Hyperstimulation Syndrome**
A syndrome which may include ovarian enlargement, gastrointestinal symptoms, nausea, vomiting, diarrhea, abdominal distention and weight gain. Severe cases may be complicated requiring hospitalization.

**Implantation**
The imbedding of the embryo in the lining of the uterus.

**Laparoscopy**
The direct visualization of the ovaries and the exterior of the fallopian tubes and uterus by inserting surgical instruments through several small incisions in the lower abdomen.

**Laparotomy**
A surgical procedure that requires an abdominal incision. This allows the physician to adequately visualize any complication that may have occurred.

**LH Surge**
The release of luteinizing hormone by the pituitary gland triggering the release of mature eggs from the follicles.

**Luteal Phase**
The phase of the menstrual cycle after ovulation has occurred. It is associated with Progesterone production.

**Ovulation**
The release of an egg from an ovarian follicle.

**Polyspermy**
This occurs when the egg has been fertilized by more than one sperm and therefore, cannot be used.

**Preimplantation Genetic Diagnosis (PGD)**
The purpose of PGD is to select and transfer to the uterus those embryos that appear chromosomally balanced.

**Progesterone**
A hormone secreted by the corpus luteum of the ovary after ovulation has occurred and is also produced by the placenta during pregnancy.

**Ultrasound**
High frequency sound waves that form an image on a monitor screen through the insertion of a probe into the vagina. There is minimal, if any, discomfort experienced by the patient. This technique is used for visualizing the follicles in the ovaries and later used to both document the presence of the fetus in the uterus and to estimate size and gestational age.

**Uterine Profile**
The placement of a small sterile catheter through the cervix to measure the length of the uterine cavity for the purpose of future embryo transfers.