

*From the Physicians of the Diamond Institute*

*Arie Birkenfeld, MD, Jesse Hade, MD, and  
Matan Yemini, MD*

*Dear Patients, Physicians, Staff  
Members, and Friends of the Diamond  
Institute*

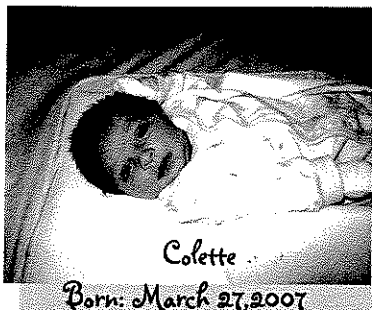
The physicians and staff at the Diamond Institute are pleased to present our 39<sup>th</sup> anniversary newsletter. In this issue we discuss several topics pertaining to women in all stages of fertility treatment.

We would like to congratulate all of our patients who have achieved their dream of having a baby and wish quick resolution to our current patients. The perseverance and courage to endure emotional distress and disappointment, when fraught with infertility, gives our patients hope and strength when on the road to parenthood. The following excerpt is a note from a patient that says it all:

*...I wanted to write you a letter to say Thank You! I was your patient from August 2005 to August 2006. If you recall, I came to you after several operations, 2 miscarriages and 6 unsuccessful treatments (from a local infertility center). My first attempt at IVF with you failed, and my FSH was very elevated (35!!!). I then achieved another pregnancy by IVF with you in December 2005, but sadly lost that baby too. ...but something in my heart told me not to give up. When you did my DeC (from the miscarriage) in January of 2006, I will never forget your kind words. My mother was sad and was crying because this was my third miscarriage and DeC. I told her not to be sad. You said to me, "Someday, you will have a daughter, and when you do, you will understand the pain your mother is feeling right now to see her daughter suffer." I believed you, and your words stuck with me. Those words gave me the extra encouragement I needed in my time of pain.*

*...It took me over 6 years, and I am so overjoyed to report I gave birth to a beautiful healthy BABY GIRL... Collette! She is our tiny little miracle!!! I hope you share my story with patients who may have begun to lose hope, and let them know that miracles do happen!*

We hope you enjoy this newsletter and feel free to share with us your questions or concerns. We wish all our friends a happy and healthy year.



*Colette*

*Born: March 27, 2007*

## Repeated IVF Failure(RIF)

Repeated IVF failure (RIF) is defined as failure to achieve pregnancy following the transfer of more than ten good embryos or after completing two or more IVF cycles without conception. For most patients even one unsuccessful IVF cycle is too much to endure. RIF can be due to poor embryo quality, decreased uterine receptivity, and other pelvic factors including hydrosalpinx (dilated fallopian tubes), and endometriosis. (continued on Page 2)

## A Note on the Endometrium

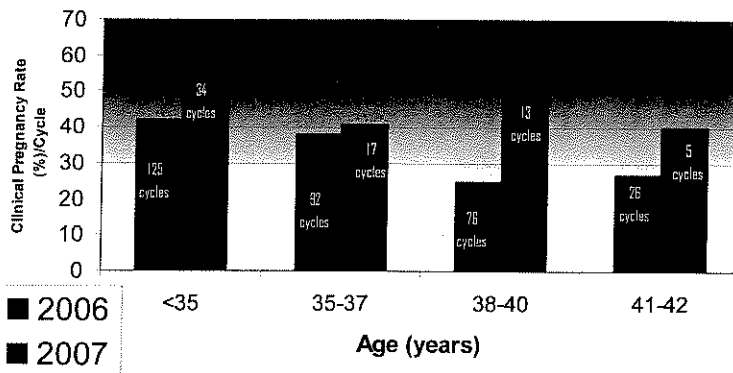
The human endometrium undergoes cyclical transformation during the menstrual cycle. These changes are induced by the ovarian steroid hormones estrogen and progesterone. Estrogen induces proliferation of the endometrium. Progesterone induces secretory transformations which occur in the stroma, supporting tissue, and the glands as well as in the vascular architecture. (continued on Page 2)

## Recurrent Pregnancy Loss

Approximately 15% of all couples who visit the Diamond Institute suffer from recurrent pregnancy loss. Although there are various reasons for why a woman miscarries, approximately 60% of the time an identifiable and treatable problem can be demonstrated.

Patients with habitual pregnancy loss are traditionally defined as women who have had three or more consecutive miscarriages before 28 weeks gestational age. However (continued on Page 2)

**Outcomes of IVF Cycle Using Fresh Nondonor Eggs  
2006 & First Quarter 2007**



\* A comparison of facility success rates may not be meaningful because patient medical characteristics and treatment approaches may vary from facility to facility  
\*\* Pregnancy is defined as an intrauterine sac on ultrasound

**Estrogen and Progesterone  
Use In the  
Peri and Postmenopausal  
Woman**

In March 2007, *The North American Menopause Society* published a position statement on Estrogen and Progesterone Use In Peri and Postmenopausal Women. Menopause: 14;168-182 2007. For your review here are the highlights:

**Vasomotor Symptoms**

Treatment of moderate to severe vasomotor symptoms (i.e., hot flashes and night sweats) remain the primary indication for systemic ET and EPT.

**Vaginal Symptoms**

Almost all systemic and vaginal ET/EPT products are government approved for treating moderate to severe symptoms of vulvar and vaginal atrophy, such as vaginal dryness, dyspareunia and atrophic vaginitis.

**Coronary Heart Disease**

The majority of observational and preclinical studies support the potential benefits of systemic ET/EPT in reducing coronary heart disease (CHD) risk. Most RCT's have not. Emerging data suggest that these disparities in findings may be related to the timing of initiation of ET/EPT in relation to the proximity of menopause. Neither ET nor EPT reduced overall CHD incidence in the Women's Health Initiative (WHI) study.

**Venous Thromboembolism**

Observational studies and RCT'S have found a significant increase in the risk of venous thromboembolism (VTE) in postmenopausal women using systemic ET/EPT.

**Stroke**

Both ET and EPT appear to increase the risk

of ischemic stroke in postmenopausal women, but RCT data have not been fully consistent in this regard. There were 8 additional strokes per 10,000 women per year in the WHI EPT arm and 12 additional strokes per 10,000 women per year in the WHI ET arm.

**Diabetes Mellitus**

Large RCT's suggest that hormone therapy reduces new onset of diabetes mellitus (DM).

**Breast Cancer**

Breast cancer risk increases with EPT use beyond 5 years. In absolute terms, this increased risk was rare in the WHI, being 4 to 6 additional invasive cancers per 10,000 women per year who used EPT for 5 or more years. Studies have not clarified whether the risk differs between continuous or sequential use of progestational agents. Women in the ET arm of the WHI demonstrated no increase in risk of breast cancer after an average of 7.1 years of use, with 8 fewer cases of invasive breast cancer per 10,000 women per year of ET use.

**Osteoporosis**

There is strong evidence of the efficacy of ET/EPT in reducing the risk of postmenopausal osteoporotic fracture. Many ET/EPT products are government approved for prevention of postmenopausal osteoporosis through long-term treatment.

**Depression**

Two small RCT's supported the antidepressant efficacy of short-term ET in depressed perimenopausal women, whereas one RCT failed to demonstrate an antidepressant efficacy of ET in depressed older postmenopausal women.

**Dementia and Cognitive Decline**

Initiating EPT after 65 years should not be recommended for primary prevention of dementia or cognitive decline as it may increase the risk of dementia during the ensuing 5 years in this population.

**Repeated IVF Failure (continued from Page 1)**

Treatments for RIF include hysteroscopy for the diagnosis and removal of intrauterine pathologies such as polyps, submucosa myomas, and scar tissue. This can improve conception after IVF embryo transfer cycles. Injury of the uterine endometrium (the inside lining where implantation occurs) by either curettage or endometrial biopsy, can increase embryo implantation and ultimately pregnancy and birth rates. Some studies have suggested that low-dose aspirin can be used to increase blood flow and improve endometrial thickness. Another option is to freeze all embryos when the endometrium is found to be too thin, then transfer them during a high-dose or prolonged estrogen cycle. Immunotherapy using intravenous immunoglobulin (IVIG), steroids injection with the partner's leukocytes, as well as, assisted hatching were all introduced empirically but not shown to affect RIF. Preimplantation Genetic Screening (PGS) has been found to

**A Note on the Endometrium (continued from Page 1)**

Fundamental reproductive issues still remain unanswered and are the focus of research and speculation. First, is the decline in pregnancy rates observed with age are related to a decline in egg and embryo quality, endometrial receptivity, or both? Secondly, are we inducing adverse endometrial effects while using "fertility drugs" for the purpose of controlled ovarian stimulation (COS) thus compromising conception rates? Finally, what are the best criteria to assess endometrial function and receptivity, and how can we prevent or reverse undesirable affects?

Subclinical, or early embryonic loss in normal cycles is hard to detect and is estimated to range between 20-30% and increases with age. Unknown numbers of embryos are wasted prior to implantation and biochemical recognition. In Vitro Fertilization (IVF) and Embryo Transfer (ET) provides a unique model to evaluate pre-implantation

**Recurrent Pregnancy Loss (continued from Page 1)**

most experts begin evaluation and treatment following two first trimester miscarriages or one second trimester loss. Common causes of recurrent miscarriage include genetic, chromosomal, anatomic, and thrombophilic abnormalities.

Evaluation traditionally begins with blood-work to evaluate the chromosomal make-up of both partners. It has been estimated that 3-4% of the population harbors a specific rearrangement of their chromosomes which increases the probability of miscarriage. Advanced techniques which incorporate in-vitro fertilization (IVF) and embryo biopsy using preimplantation genetic diagnosis (PGD) can reduce miscarriages resulting from chromosomal and genetic problems by nearly 50%.

In addition, the blood of the female partner can be evaluated for specific disorders, which contribute to excessive blood clotting. Thrombophilic abnormalities of the blood predispose a small subset

**Gestational Carrier**

Pregnancy is a result of a complex chain of events, and infertility can result from one or more problems that occur within this complicated process. A woman, who, for various reasons, (including genetic absence or abnormalities, prior hysterectomy, medical contraindications, etc) has no functional uterus or is unable to carry a pregnancy, can turn to the help of a surrogate.

A surrogate is a woman who carries a pregnancy for another couple or woman. Typically there are two types of surrogacy: *traditional surrogacy* in which the surrogate donates her own egg and uterus and is inseminated with the sperm from the male, or donor sperm, and *gestational carrier* (or gestational surrogacy) in which the surrogate carries a pregnancy created by a transferred embryo produced by the intended parents or donor egg or donor sperm.

Surrogacy is not a simple arrangement. There are many legal agreements made prior to the procedures. Traditional surrogacy carries more legal risk therefore, the greater part of surrogacy performed in the United States consist of the use of a gestational carrier.

**Managed Care**

The following is a list of only some of the insurance plans the Diamond Institute accepts. Please call to see if your insurance carrier is included in our comprehensive list.

- \*AETNA \*AMERIHALTH \*BEECH STREET \*CIGNA \*EMPIRE \*GUARDIAN
- \*HEALTHNET \*INDEX/DEVON
- \*HORIZON/BLUE CROSS BLUE SHIELD \*MAGNACARE \*MASTERCARE
- \*MEDICHOICE \*MULTIPLAN \*ONE HEALTH PLAN \*OXFORD \*PHCS \*QUALCARE
- \*ST BARNABAS \*UNITED HEALTHCARE \*WELLCHOICE \*INDEX/DEVON

significantly increase implantation and conception in young women with RIF in select cases. However, there is no strong data to support the routine use of PGS to treat RIF. Transfer of blastocyst stage embryos after RIF showed higher live birth rates thus, should be offered as a treatment for RIF.

Additionally, removal of large myomas within the muscle of the uterus or removal of damaged fallopian tubes, as well as treatment of endometriosis with medications are all found to improve conception and delivery rates. Others have tried to treat RIF with individual or group psychotherapy to reduce anxiety and enhance conception, but there is no evidence to support their benefit.

Because the causes of RIF are numerous and diverse, there is no single treatment or solution for this problem. Thus, an individual treatment and protocol needs to be formulated for every couple faced with this issue.

and early post-implantation loss. Following IVF/ET, most embryos are lost prior to chemical recognition and, therefore, probably fail to implant. Slightly more than 10% are defined as chemical pregnancies and therefore implant but fail to reach clinical detection. Thus, with normal physiologic conception, even embryos of lesser quality may implant but later fail to progress while, on the other hand, following IVF, even better quality embryos probably fail to implant. In addition, pregnancy rates following ET of embryos after IVF of donated eggs are significantly higher than IVF results with own eggs even for the younger age groups. Therefore, based upon these observations, endometrial receptivity following COS may be an important factor affecting conception rates. To date, only ultrasonographic and histological (microscopic evaluation) of the endometrium are available to determine the adequacy of the endometrium and its receptivity and synchronization. In the future we may have more specific markers for the determination of endometrial preparedness and receptivity to the embryo.

of women to over clotting of their blood during pregnancy. However, this condition can often be treated with blood thinning medications such as baby aspirin and Heparin. When treated effectively, many women improve their capability of having a full term pregnancy.

Anatomic problems of the uterus are commonly found during a hysterosalpingogram (HSG), which is a special type of X-Ray of the uterus. Additional testing not involving the use of X-Rays includes sonohysterography and hysteroscopic videography. All of these tests are useful in determining if the uterus harbors an anatomic problem increasing the chance for pregnancy loss. Commonly, intrauterine polyps, myomas (fibroids) and congenital developmental abnormalities of the uterus are factors responsible for recurrent pregnancy loss. Luckily, the majority of these problems can be corrected during a minimally invasive hysteroscopic procedure.

At the Diamond Institute, we aggressively diagnosis and treat all identifiable problems related to recurrent pregnancy loss and have yielded promising results for our patients.

Gestational carriers may be known to the intended parents or they may remain anonymous. Known carriers are ordinarily relatives or friends who have agreed to carry the pregnancy. Anonymous carriers are contacted through surrogate agencies or fertility centers. Regardless of the type of carrier, all carriers are evaluated medically and emotionally before being considered a surrogate. Also, the intended parents undergo extensive medical and psychological tests. It is only after all tests and legal and financial agreements have been made that the medical procedures begin.

A gestational carrier program is an extension of in vitro fertilization. While the intended parents begin stimulation, the carrier uses medication to prepare her uterus for implantation. The developing embryo is transferred into the uterus of the carrier. When a pregnancy is achieved the carrier will be followed for about 8-10 weeks then discharged to her obstetrician for continued prenatal care.

While using a Gestational Carrier is clearly not for everyone, it does provide a solution for many couples or singles struggling to have their baby. As the use of gestational carriers grows the understanding of the moral, ethical, and legal issues grows as well. This allows the process to move along effortlessly and delivering the ultimate goal of a healthy baby.

## BEFORE BEGINNING A TREATMENT CYCLE

Infertility treatment can be a very exciting and also very stressful process to begin. Patients may feel overwhelmed and confused about all of the necessary steps. By the time a patient is ready to start treatment, all basic testing should be completed. This generally includes STD's for both partners, Day 3 Hormones, an ultrasound, and a semen analysis.

What patients may not aware of is that there are some other things to consider before beginning the cycle which are also very important. To help ease patients into the treatment cycle, here are three major points to review:

### ✓ BE FAMILIAR WITH YOUR INSURANCE

We recognize it is not easy to sort out health insurance provider needs, therefore, at the Diamond Institute, you will have a dedicated insurance coordinator who specializes in your specific health insurance provider requirements. Your insurance coordinator will verify your benefits for you after your first appointment and is always available to answer any of your questions.

However, before the beginning of your treatment cycle, it would be beneficial to contact your insurance provider to confirm if one or more of the following will be required: predetermination letter, statement of coverage letter, referral, and/or any authorizations.

### ✓ SCHEDULE MEDICATION INSTRUCTION CLASS WITH A NURSES.

During the medication instruction class your nurse will familiarize you and your partner with the medications you will be using. Your nurse will discuss the uses for each medication, possible side effects, and the methods of administration.

Our nurses understand this is an unfamiliar territory for most patients, for this reason our medication class is performed privately and one on one, and although we provide plenty of reference materials, we encourage our patients to ask questions.

### ✓ PRE-ORDER MEDICATIONS

The medications prescribed by your doctor are available at most pharmacies; however there are specialty pharmacies that your doctor will advise you fill your prescriptions. These fertility specialty pharmacies are familiar with your doctors and have the medications readily available. They may also have a nurse on call to assist you with any questions as well. Your insurance company may require you to obtain your medications from the specialty pharmacy associated with the insurance provider.

The Diamond's doctors and nurses will gladly answer any questions about your medications and recommend the pharmacy that will best suit your needs.

**Clinical Pregnancy Rate  
2006 Frozen Embryo Transfer Cycle**

