

UNCOVERING THE MYSTERY OF EMBRYO IMPLANTATION

By Dr. George S. Taliadouros

An overwhelming number of advances in the treatment of infertility occurred during the last decade. Pioneering work at laborato-

ries and careful clinical implementation of these discoveries led to marked improvements in the care of infertile couples. Not only have infertile couples achieved a better pregnancy rate than ever before, but they also are able to conceive faster (saving time, emotional anguish, and money).

We have seen intracytoplasmic sperm injection (ICSI) give couples newfound hope to conceive. During this assisted fertilization procedure a single sperm is mechanically inserted into an egg so that fertilization may take place. ICSI is prescribed in cases where patients have low sperm counts, low sperm morphology (normal shape of the sperm), and previous failed normal fertilization during an in vitro fertilization (IVF) cycle.

Next came assisted hatching (AH), a form of embryo micromanipulation, where a hole is artificially made in the embryo's outer layer in order to increase

the likelihood of embryo development. Selected AH offers new hope for women age 39 or older with elevated basal FSH levels, a history of implantation failure, and embryos

having a thick zona pellucida (the layer surrounding the oocyte).

Preimplantation genetic diagnosis (PGD) has helped couples that choose IVF successfully deliver healthy babies. This new testing can identify genetic defects at two different stages, in an ovum (unfertilized egg) before fertilization or in an embryo (before implantation). Since approximately 60 percent of all reproductive losses in pregnancy are linked to a chromosomal abnormality, performing this testing may help prevent unsuccessful IVF pregnancies. In fact, a recent study found the pregnancy rate with IVF patients ages 35 to 45 increased from 16 to 30 percent when PGD was conducted.

Last, but not least, the implementation of new culture media has allowed the early embryo to develop to its final stage, the blastocyst. Only the strongest, healthiest embryos have the ability to grow into a blastocyst after five days of culturing under optimum conditions. This "natural selection" of embryos boosts the success rates of transfers and eventual healthy deliveries. Moreover, by establishing a blastocyst transfer program, fertility specialists can transfer one to two embryos on day five of culturing, and in turn, reduce the incidence of multiple births. By not being classified as "high risk," patients can then enjoy healthy and less stressful pregnancies.

All these new technologies have helped double the pregnancy rate to 50 percent via IVF. Moreover, by transferring fewer embryos, multiple births have been reduced.



Instead, the remaining non-transferred embryos are saved for future treatment attempts via cryopreservation (freezing).

Although these achievements are remarkable, scientists continue to explore new research frontiers in reproductive medicine. One of the most exciting areas of study involves implanting embryos into the uterus. This important part of the reproductive process has been a missing black box since its circumstances are so difficult to study. In humans, ethical and technical issues have made it impossible to systematically observe this complicated process step by step. Due to this fact information was collected from animal models and more recently in laboratories from cultures of endometrial cells that line the uterine cavity.

Scientists are working feverishly in this area to resolve a range of issues, including the best time for the embryos to be transferred and the type of environment that favors implantation. This knowledge also can help doctors correct the environment that hinders implantation or causes repeated miscarriages. Ultimately the goal of this knowledge will be to further increase pregnancy rates, reduce the number of embryos transferred to the uterus, reduce multiple pregnancy rates, reduce the cost of treatment, and offer several opportunities for other pregnancies by transferring cryopreserved embryos.

A Complex Picture

Implantation is a very complex procedure involving both the lining of the uterus and the embryo that undergo a litany of changes synchronized through signaling systems. A protective layer that creates a barrier to microbial infection covers the lining of the uterus and helps keep its environment the same. This barrier is selectively removed during the appropriate time for the embryo to be implanted, and it unmask a number of attachment sites where the embryo is initially anchored.

This initial attachment with the uterus begins a cascade of signals between the embryo and the lining of the uterus. There are significant changes in the lining of the uterus at the site of implantation, both in the cells that cover the surface and also in the underlying structures. The environment also changes when a number of hormones and messages are locally released so that a

wider area is created to allow better adhesion of the embryo. These local changes in the lining bring about new anchor sites that more firmly attach the embryo. By this time a number of signals are going back and forth between the embryo and the lining of the uterus. The embryo is maneuvered on a precise orientation similar to the way in which a ship coming into port is led to the dock.

By this time some of the ongoing signals initiate invasion of the embryo. This process is carefully controlled and regulated by a sequence of specific messages that guide the embryo inside the uterine lining. The mechanisms used for this interaction are not any different from those used in other parts of the body to keep the cells of the body together or, for instance, to allow the white blood cells to enter infected tissues and areas.

The only difference in the uterus is that these mechanisms are under the control of ovarian hormones that dictate the appropriate time for them to be expressed and made available to the embryo. It's nature's wisdom that permits already existing and tried mechanisms to perform a specific function by subjugating them to the control of the ovarian hormones. It also provides a large number of redundant mechanisms to secure the perpetuation of humans and other species.

The illumination of this process provides considerable potential for the proper timing of embryo transfer and guarantees higher pregnancy rates. Detection of these changes in the lining of the uterus through markers secreted in the uterine cavity or blood stream will allow us to make the right decisions. By the same token, the lack of these markers can reveal the underlying reason why embryo implantation failed and the inability of the couple to conceive. These breakthroughs should finally help us to understand unexplained infertility and to open the door for successful therapeutic measures.

It's an exciting time for the field of reproductive medicine. With better evaluation and therapies at our disposal, we can help more and more infertile couples quickly resolve their problems and conceive the children they always wanted.



George S. Taliadouros, M.D., FACOG, is the founder and president of the Delaware Valley Institute of Fertility & Genetics, one of the leading fertility practices in South Jersey.



ASK THE DOCTORS

Q: I recently became pregnant after years of trying and am thrilled, but I'm terrified of gaining 60 or 70 pounds like my sister did. Can you please give me some tips on how to stay healthy while pregnant?

A: Congratulations on your news and also for being concerned about your health during this wonderful time. Although it's normal to gain between 25 and 35 pounds during pregnancy if you're of normal weight, expectant women who pack on too many pounds are four times more likely to be obese a year later, according to a recent study.

To keep your weight gain within the acceptable range, follow these tips:

- With physician approval, do combine aerobic exercise (walking, treadmill) with muscle strengthening throughout your pregnancy.
- Don't get overheated. Drink plenty of water before, during, and after exercise.
- Do sit down for upper-body exercises. When pumping weights, for example, don't stand still for long periods of time. This can make you dizzy and slow the circulation in your legs.
- Don't do activities that increase your risk of falling, such as tennis and step class.
- To keep nausea at bay and to keep you and baby well-nourished, eat small, frequent meals (every two to three hours) and include plenty of fruits and vegetables. For an average weight gain, you only need to add 300 calories a day to your normal diet.
- Take up yoga or practice meditation every day to relieve stress.

If you need help in planning healthy meals, you may want to make an appointment with a medical nutrition therapist. We have one on our staff. A registered dietitian and Certified Diabetes Educator, Melissa Bennett can help you learn to eat healthy for both you and baby. To schedule a weight-management consultation with Melissa Bennett, RD, CDE, please call (856) 988-0072.

Q: My husband and I are trying to conceive, but he won't quit smoking cigarettes. Is it true that just by living with a smoker I can have difficulty becoming pregnant?

A: Yes, it is true. According to a recent World Health Organization (WHO) report, more and more women are experiencing health problems from passive smoking (inhaling the smoke from other people's cigarettes) than ever before.

A mixture of smoke from burning cigarettes and that exhaled by smokers, secondhand smoke exposure is widespread in the U.S. and throughout the world. A previous study published in the Journal of the American Medical Association (JAMA) found detectable levels of serum cotinine (a breakdown product of nicotine) in 9 out of every 10 nonsmokers in a large, nationally representative sample.

Day-to-day exposure to secondhand smoke has been found to double a woman's risk of heart attack and stroke, and to increase her risk of developing osteoporosis. Women who smoke or who are exposed to secondhand smoke regularly also are more likely to experience infertility, delays in conceiving, an increased risk of earlier menopause, and lower bone density, according to the WHO report. Men who smoke also have a greater likelihood of experiencing problems with sperm production, which can severely affect fertility.

Day-to-day exposure to secondhand smoke also affects children. Children of smokers are twice as likely to have asthma as children of nonsmokers, and their attacks may be more severe and frequent. Children of smokers also are at greater risk of developing upper respiratory infections. Chronic secretory otitis media, the most common cause of deafness in children, is linked to parental smoking. Exposure to secondhand smoke is also a factor in sudden infant death syndrome (SIDS).

Insurance Corner

By Carla Scott

Now is a good time to inquire about your choices in health care coverage and to make a change in your plan if you're unhappy with your current provider. Many companies have "open enrollment" in their health care benefits plans during the summer.

Set aside some time to investigate your infertility options and to plan ahead for future treatment. Most insurance companies now cover members for the diagnostic workup to determine the cause of infertility. Some insurance companies go a step further to include monitored ovulation cycles in their benefits packages, along with artificial insemination. Very few insurance carriers will cover in vitro fertilization (IVF).

When you inquire about infertility coverage, remember to ask much more specific questions than: "Is infertility covered?" Here are some questions to ask:

- Is artificial insemination covered?
- Do I have a limit of coverage based on a dollar amount or on lifetime attempts?
- Is there a certain number of treatment cycles allowed?
- Do I have injectable infertility medication coverage?
- What needs to be pre-authorized?
- Do I need referrals?
- Can the ultrasounds and labs be performed in the infertility center to ensure quicker results and better treatment outcomes?
- Is in vitro fertilization covered?
- Is surgery covered if recommended to correct medical problems related to infertility?

These tips can help you better make informed insurance coverage decisions, but I can also help answer any questions you may have regarding infertility treatment and insurance coverage. I can help you to understand the sometimes confusing and vague coverage benefits.

We do not let insurance issues interfere with patient treatment and have established good communication with participating insurance companies. Please give me a call if you have any questions regarding your insurance coverage at 856-988-0072.



Conceptions is published quarterly for a select group of OB/GYNs and their patients. To receive extra copies of the newsletter or to be placed on our mailing list, please call Carla Scott at (856) 988-0072 or e-mail her at: info@startfertility.com.

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Happy Birthday to . . .



Taylor Faith Speranza, born on November 20, 2000, to Tara and Michael Speranza.

Emma Hope Gubman, born on January 22, 2001, to Jodi and David Gubman.

Alexis Marie Santoferraro, born on April 16, 2001, to Jamie and Dale Santoferraro.

Eliza Drew Broder, born on April 21, 2001, to Meredith and Seth Broder.

Olivia Grace Coffey, born on April 27, 2001, to Kathleen and Gary Coffey.

Chole Elizabeth Lin, born on May 6, 2001 to Kathleen and Jeffrey Lin.

All the babies and parents are doing well. Thank you, DVIFG!

DVIFG Opens New Office

In June, DVIFG opened an office in the Princeton area. The office is located at 3100 Princeton Place, Building 4, Suite D, Lawrenceville, NJ 08648. To make an appointment, please call (609) 895-0088.

Thanks For Your Input

The Patient Questionnaire yielded great results! Thank you for taking the time to mail them back to us with your answers. Look for some of your ideas to be included in the next issue of *Conceptions*. If you have any story ideas or questions for "Ask the Doctors," please e-mail them to me at: christinenorris@earthlink.net



— Christine Norris, *Conceptions* Editor

*"Hope is an echo,
hope ties itself yonder,
yonder."*

— Carl Sandburg

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