

## A Nod is As Good As a Wink to a Blind Horse



In Vitro fertilization (IVF) is offered to couples that undergo infertility treatment when all the other measures to achieve pregnancy fail. The success of IVF, as a treatment modality, has gradually improved over the last 4 decades, due to scientific and technological advances. Nonetheless the resulting pregnancy rate has been modest and seems to have plateaued in the recent past. So additional steps have been taken to improve these results.

One of them is Preimplantation Genetic Screening (PGS), a technique that requires biopsy of the resulting embryos and assessment of the embryos chromosomal complement, in other words if all the chromosomes are present and intact. This procedure will eliminate any embryos that under the microscope look normal but they have an abnormality, such as a Down syndrome. Even after this step, the transfer of a chromosomally normal embryo does not guaranteed a pregnancy and in the instance that a pregnancy occurs a miscarriage could take place.

Over twenty seven (27) other measures to improve the outcome of IVF, also called "adjuvant therapies", have been implemented but none of

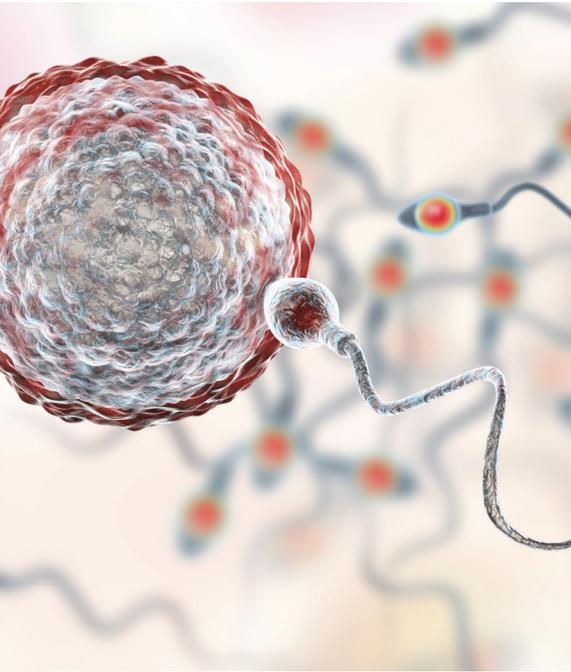
them had a proven benefit or added an improvement to the IVF outcome. One of these adjuvant therapies, the endometrial "scratch", has been extensively offered to the patient undergoing IVF despite the questionable results from studies that had a small number of participating patients or did not have the proper design.

The premise of this treatment is that endometrial injury may facilitate embryo implantation due to the resulting inflammation and immunological response especially for those patients that had repeat embryo implantation failures. Four years ago two large clinical trials found no improvement from endometrial "scratch", instead they found **a decrease in the implantation rate for those that received it**. A recent publication in the New England Journal of Medicine last month confirmed

that there is no benefit to the patient and no improvement of either the implantation or the ongoing pregnancy rate for those patient that received endometrial "scratch" as compare to those that did not. Therefore an additional procedure and cost should be eliminated as unnecessary, if not frivolous.

Evers J.L.H. Hum Reprod 2014;29:2355  
Yeung T.W., et al. Hum Reprod 2014;29:2855-6  
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## Made to order



A recent article in the "Washington Post" questioned the safety of fertility drugs. The question though is generic; are the drugs safe? Obviously the drugs are not safe or unsafe, they are useful when needed. When they are prescribed by those who are authorized and they have experience in their administration they can be beneficial. Drugs have side effects and can be even lethal! They are administered at different doses for different durations. Almost all the drugs are removed from the body by the liver enzymes that work at a certain rate. The current dose of medications are appropriate for 75% of the population, while 15% will have side effects because the liver enzymes remove them too slow and they rise into the body at a higher that intended level. For the remaining 10% of the patients the drugs have no therapeutic effect since the same enzymes remove them from the body very fast and the therapeutic dose is never achieved.

★ during fertility treatment especially with the use of gonadotropins and has issued recommendations for their safe use. Treatment with gonadotropins is responsible for the occurrence of multiple pregnancies and in turn this can cause severe problems to both the fetus and the mother.

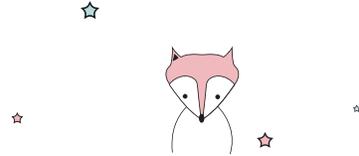
Measures were taken in the recent past and during IVF the single embryo transfer, has increased from 35% to 42%, the singleton pregnancy after an IVF treatment has also increased from 80.5% to 84%. The twin pregnancies decreased from 19% to 16%. Gonadotropins can cause severe Ovarian Hyper stimulation Syndrome ( OHSS), therefore judicial use is in order and it is suggested that treatment should start at a daily dose of 37.5 International Units (IU) and after 7 days the daily dose could be increased gradually, not to exceed 225 IU per day.

## What is the problem?

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A nationwide survey that included 40 states, 1,000 hospitals and over 8 million hospital admissions for a period of 10 years found over 11,000 admissions due to OHSS. All the admitted patients were pregnant and one out of five (1/5) had a preexisting medical condition, such as diabetes, high blood pressure, anemia, hypothyroidism, obesity and others. Women over 40 years of age had 3.5 times a

higher risk to develop OHSS and be hospitalized. The risk was twice as high for African American patients. The ASRM found that approximately one out of ten (1/10) women undergoing IVF experiences mild to severe OHSS and another study covering a period of 10 years found that seven out of a hundred women (7/100) undergoing this procedure spends at least 1 night in the hospital because of OHSS.

## What can be done?



Selecting the appropriate daily dose of gonadotropin for patient infertility treatment is necessary. Several infertility practices implement standard controlled ovarian stimulation (COH) protocols that the caretakers and patients follow. These standard protocols reflect an average daily dose of gonadotropins that has yielded favorable results. Unfortunately not "one size fits all", with the resulting OHSS and patient hospitalizations. In response, a "low dose IVF regimen" is offered by several centers in an attempt to remedy these untoward events, but in essence a "one size fits all" at a "no OHSS" level is offered instead. There is no high or low gonadotropin dose for the patient, there is just the right dose.

When it comes to infertility treatment the decision on the right gonadotropin dose requires clinical experience that is acquired over time, by safely treating patients who have different requirements and they respond differently to the medication. In reality "cookie cutter" protocols cannot replace the effectiveness of clinical experience.

The patients need to be monitored with ultrasounds and blood tests every 2 to 3 days. Ovarian stimulation should be tapered or the treatment aborted if signs of excessive ovarian response is predicted.

- ☆ Upon completion of the ovarian stimulation a lower dose of Human Chorionic Gonadotropin (HCG) or a GnRH trigger, Lupron injection, should be considered. A meticulous aspiration of the developed ovarian cysts, follicles, should take place with care taken to aspirate even the smallest of them.
- ☆ Embryo transfer can be postponed for a later time, after the risk of OHSS subsides. Instead the resulting embryos could be cryopreserved.

We should not forget that a lot of the patients that were hospitalized had preexisting medical conditions. These medical problems must be addressed prior to initiation of any infertility treatment and in particular prior to starting an IVF cycle and should be brought under tight control and monitored thereafter. At Delaware Valley Institute of Fertility & Genetics (DVIF&G) all of these steps are implemented and no OHSS or patient hospitalization has occurred for decades. At the same time we maintain a competitive pregnancy success rate at the lowest cost to the patients. This is not only due to a long clinical experience but also the result of a well-trained and performing team.