

The Evolution of a Revolution: How Traditional Chinese Medicine Brings IVF into Modern Times

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China's Cultural Revolution marked a move from the past into a new plan for the future. A small paper published in 2002 in *Fertility & Sterility* by Paulus WE, et al.¹ showed a similar, though relatively silent revolution. The research suggested that adding acupuncture under a strict protocol to patients undergoing *in vitro* fertilization (IVF) demonstrated improvements in reproductive outcomes, i.e., more pregnancies. The impact of this small study was not fully realized for several years. However, its results prompted Diane K. Cridennda, LAc to challenge Paul C. Magarelli, MD, PhD to question how he could help his patients by stretching for solutions outside the realm of allopathic medicine.

Cridennda met with Magarelli in 2002 to discuss her belief that by adding Traditional Chinese Medicine (TCM) in the form of acupuncture, more patients could get and stay pregnant. Magarelli's position was that any medical treatment must ethically have scientific basis before subjecting patients to it. He asked her to provide data to support her position. She returned with the paper by Paulus WE, et al.¹ and added a new study by Stener-Victorin's group discussing a favorable physiologic change in blood flow [pulsatility index (PI)] through the uterine artery in IVF patients treated with acupuncture.²

ACUPUNCTURE PHYSIOLOGY

Acupuncture is the placement of fine needles into specific acupoints along the pathways of energy in the body. Acupoints relieve blockages and restore the flow of "Qi", pronounced [CHEE] or energy, encouraging the body's natural ability to heal itself. When Qi is balanced and organs are "nourished," the body will be able to function at their capacity and, in this case, for procreation.

This process works by sending messages to the brain almost like programming a computer. Qi is conducted through protein molecules giving us energy and life. Qi moves by way of meridians—a web or network of channels, which sets up communication between every organ in the body. TCM practitioners have mapped these channels out over the course of thousands of years of experimentation and observation. The insertion of fine needles into the acupoints along the meridians produces measurable effects on different parts of the body. This is how acupuncture can affect abdominal organs, such as the kidneys, liver and uterus by placing needles in the arms and legs. There are specific acupuncture points which relate to fertility, but the single most important theory is this: When Qi flows through the body in the correct direction at the right time, the body will return to health.

ACUPUNCTURE AND IVF: RESEARCH PROTOCOLS

Over the next year, IVF patients with poor prognosis for success—including having previous IVF failures, being older than 35 years of age, or having severe male factor or poor ovarian reserve as measured by day 3 follicle stimulating hormone (FSH) levels, were told that a local acupuncturist experienced some success in improving IVF outcomes and could treat them with acupuncture if interested. Many patients decided to see Cridennda for acupuncture treatments and some returned to Magarelli’s clinic for treatment for IVF only. Upon observation, more patients were getting pregnant. In response to these results, Magarelli, Cridennda and Cohen decided to create research protocols to prove or disprove the efficacy of acupuncture treatment in IVF patients.

The authors have published a chapter in a Western textbook on reproductive endocrinology and infertility in which they lay out the foundations of their research. Excerpts are below:³

Background

Assisted reproductive technologies (ART) provide reproductive services to infertile couples throughout the world in the form of IVF. The process of IVF began with the *Birth of Louise Brown* in 1978 by Edwards and Steptoe.⁴ The process has evolved significantly over the years. Like the first heart transplant, IVF has gone from medical wonder to “standard of care.” Today over 1 million IVF cycles⁵ are performed each year around the world for a population of 6 billion men and women. Most estimates of infertility when calculated, represent 15 percent of married/bonded couples. This would predict many more couples in need of reproductive care who are not able to create the family they have dreamed of, probably due to the expenses associated with the complexity of care required.

Part of the problem of poor utilization of IVF is cost and access to care. Others include the depersonalization of the process and resistance on the part of the couples themselves. Fertility is a personal matter, which is publicly monitored. It is in the nature of a community to “require”

reproduction for survival. The peak of human fertility is at 25 years of age, allowing for a 25 percent chance to conceive each month. For most couples, this hovers at 10 percent since they may not even start thinking of having children until after education is complete, jobs are intact and houses are purchased. By this time, most couples are nearing 30 years of age and just beginning to consider having a baby.⁶

After months of trying to conceive, issues of personal identity, frustration, guilt and losing faith in their body sets in. Most couples lose a sense of freedom as they no longer have intercourse for the reasons of love and true intimacy. Intercourse now turns into a job, timed at best. Couples begin to lose sight of the reason for having a child together as they experience sorrow and frustration month after month when the menses occurs, despite the vigorous attempts to achieve pregnancy. Technology may be able to help, but at a price.

Historical Perspective

In the United States, IVF programs started in the 1980s, proliferated during the mid to late 90s, and have grown to represent over 150,000 treatment cycles in the early part of the 21st century. IVF programs, according to the Centers for Disease Control and Prevention, have reported reproductive outcomes from 1986 to 2005. The average improvement each year represents 1 percent to 2 percent gain per treatment in positive outcomes, pregnancy or babies, from 1985 to 2001. After 2001, no improvement—but only a modest decrease in outcomes (34 percent to 33 percent) has been seen. Although the current results are laudable, Cridennda sought to enhance the rate of improvement by challenging Western treatments for IVF.

Magarelli, Cridennda and Cohen, encouraged by the above background and historic perspective, developed a study protocol, published as the Cridennda/Magarelli TCM protocol. This later served as the basis for all subsequent studies they reported. Key elements are shown in Table 1.

Table 1. Key Elements of the Cridennda/Magarelli TCM Protocol

KEY ELEMENTS	REASONING
Recruitment was prospective.	Eliminates historical comparisons and strengthens study applicability.
Recruitment for acupuncture was hidden or “blinded” to the physician.	Reduces physician bias.
IVF treatment protocols were hidden or “blinded” to the acupuncturist.	Reduces acupuncturist bias.
Only “standardized” acupuncture treatments were allowed (no differentiation of syndromes as a basis of treatments were done).	Eliminates treatment selection bias.
All data was collected by a third party, Mel Cohen, PhD, and kept from the physician and acupuncturist for three years.	Reduces investigator bias.
Contracts were written and signed by all TCM practitioners to follow the prescribed protocols for treatments.	Eliminates treatment variability.
TCM practitioners agreed to provide coverage for patients in the study 24/7. For example, embryo transfers occurred on weekends and holidays and patients needed to access their acupuncturist.	Reduces timing or convenience bias.
Patients, without coercion, selected whether or not to participate.	Does NOT eliminate selection bias (a weakness of most TCM studies).
No monetary gain was provided to participate.	Reduces selection bias for monetary gain.
No reduction in IVF fees for participation in the study was given.	Reduces treatment bias based on monetary gain.
No reduction in TCM treatment fees for participation in the study was given.	Reduces treatment bias based on monetary gain.
Most study data collected from 2002 were reviewed in 2005.	Reduces impact of positive outcomes on patient choice to perform acupuncture.
Study of cortisol/prolactin ^a	Although not randomized, the study was blinded to the acupuncturists, physicians and statistician until analyzed.

^aMagarelli PC, Cridennda DK, Cohen M. Changes in serum cortisol and prolactin associated with acupuncture during controlled ovarian hyperstimulation in women undergoing in vitro fertilization-embryo transfer treatment. *Fertil Steril.* 2009;92(6):1870-1879.

The Cridennda/Magarelli TCM protocol has been used to analyze more than 800 IVF cycles since 2002. The protocol's data set may be the largest in the world correlating a specific TCM protocol's impact on IVF outcomes. Research using the protocol was categorized by patient type and scientific principal in the studies shown in Table 2:

Table 2. Categories Studied Using Cridennda/Magarelli TCM Protocol

1	Poor prognosis ⁷	<ul style="list-style-type: none"> Elevated FSH Severe sperm factor Advanced maternal age Poor PI (i.e., uterine artery blood flow)
2	Improved prognosis ⁸	Anything not listed in "poor prognosis" section above
3	All IVF patients ⁹	Regardless of prognosis
4	Number of acupuncture treatments ¹⁰	Ideal number of needed for favorable outcome (i.e., pregnancy)
5	Embryology and eggs ¹¹	Impact of TCM
6	Demographics and patient infertility diagnosis ¹²	<ul style="list-style-type: none"> Effects regarding pregnancies, miscarriages, ectopics, multiples and live births Impact of patient infertility diagnosis on effects of TCM
7	Cortisol/prolactin ¹³	Mechanism of action responsible for impact of TCM treatment (i.e., changes in stress hormones cortisol or prolactin)

Outcomes Data Revealed Per Category

1. Poor Prognosis Category (Figure 1)

Key Points

- Improvements in reproductive outcomes were demonstrated when poor prognosis patients received acupuncture treatments before, during and after their IVF treatments.
- A "standardized" acupuncture treatment protocol in lieu of treatments utilizing differentiation of syndromes can be used to improve reproductive outcomes (i.e., pregnancy and live birth).

Conclusion

Poor prognosis predictions of outcomes could be "corrected" and outcomes could be created closer to and in some cases to surpass "improved prognosis" patient outcomes for pregnancy and especially live birth.

2. Improved Prognosis Category

Key Points

- Pregnancy outcomes were equal between the acupuncture group and the nonacupuncture group, not unlike the Poor Prognosis category.
- Birth outcomes were improved between the acupuncture group and the nonacupuncture group.
- Improved pregnancy outcomes for all patients
- Improved pregnancy outcomes for pregnant patients
- Significantly fewer spontaneous abortions
- Significantly fewer ectopic pregnancies

Conclusion

Even given the Good Prognosis category, patients treated with the Cridennda/Magarelli TCM protocol benefited with improved outcomes.

FIGURE 1. IMPACT OF ACUPUNCTURE ON IVF POOR RESPONDER PATIENTS

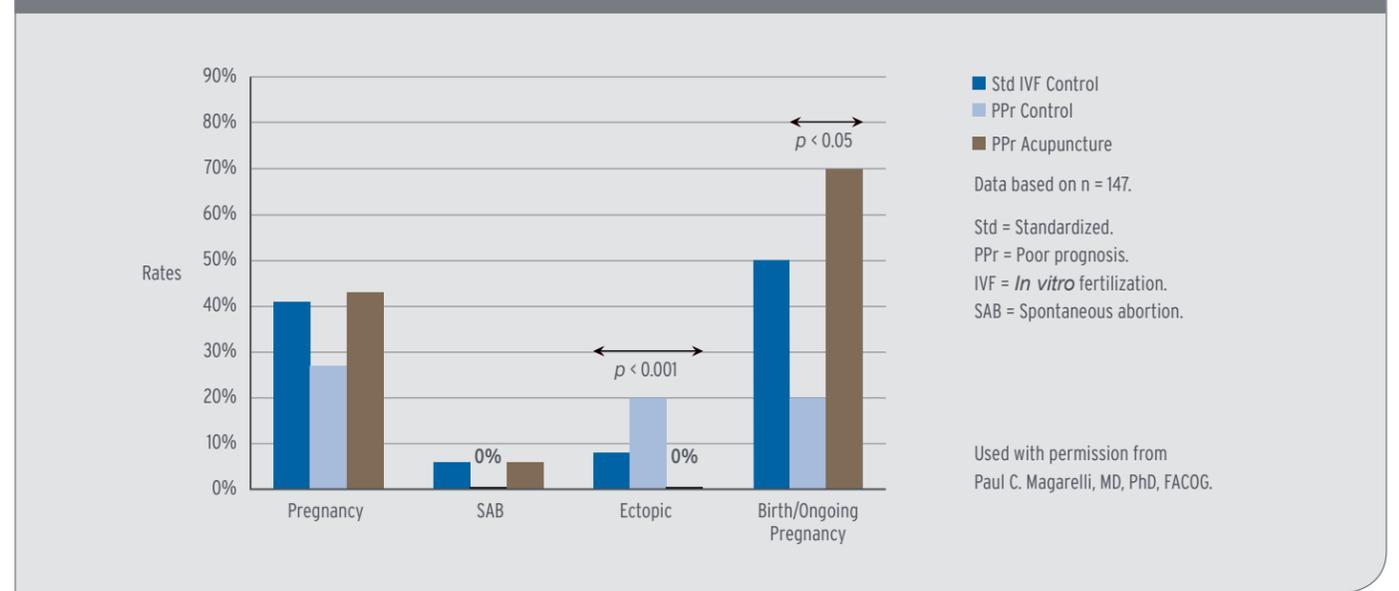
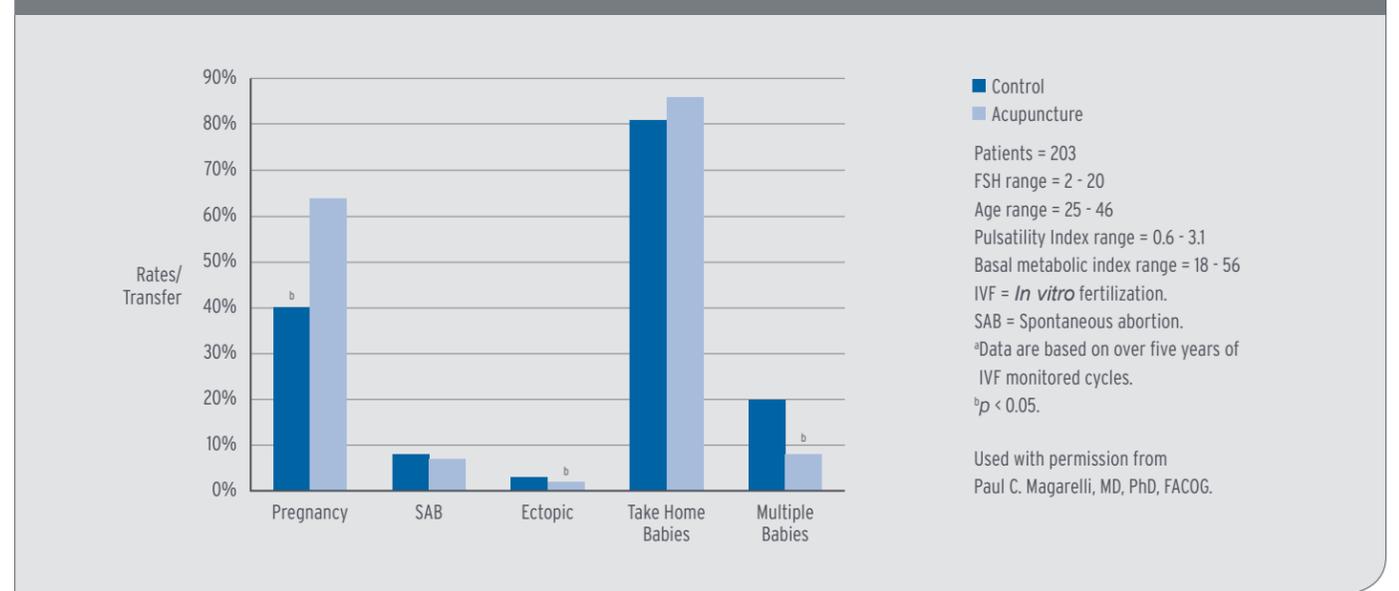


FIGURE 2. IMPACT OF ACUPUNCTURE ON IVF PATIENTS^a



3. All IVF Patients Category (Figure 2)

Key Points

- Pregnancy outcomes were superior in the acupuncture group vs. nonacupuncture group ($p < 0.05$).
- Significantly more pregnancies ($p < 0.05$)
- Birth outcomes were improved between the acupuncture group and the nonacupuncture group
- Improved pregnancy outcomes for pregnant patients
- Fewer miscarriages
- Significantly fewer ectopic pregnancies ($p < 0.05$)
- Significantly fewer multiple pregnancies ($p < 0.05$)

Conclusion

Acupuncture, even if given to all-comers, will benefit the IVF practice by improving reproductive outcomes.

4. Number of Acupuncture Treatments Category

Key Points

- The Stener-Victorin protocol of eight acupuncture treatments underestimates—by one treatment—the “ideal” number needed for improvements in pregnancy rates using the protocol.
- Acupuncture without regard to PI was believed to improve pregnancy outcome if nine or more electrostimulation treatments (where pairs of acupuncture needles are attached to a device that generates continuous electric pulses between them) are provided.
- Diazepam does not appear to alter the effects of the Paulus WE, et al. protocol on IVF outcomes based on uterine quiescence.

Conclusion

As in Western medicine, it is dose, duration and type of treatment that contribute to efficacy. The Cridennda/Magarelli TCM protocol was demonstrated to have an ideal number of treatments for improved outcomes.

5. Embryology and Eggs Category

Key Points

- Acupuncture contributes to improved reproductive outcomes in the following ways:
 - Improved pregnancy rates
 - Reduced miscarriage rates
 - Significantly reduced ectopic pregnancy rates
 - More take-home babies
- The mechanism for the effects of acupuncture is not based on objective embryology characteristics such as:
 - Number of eggs:
 - Retrieved
 - Fertilized normally
 - Implanted
 - Frozen
 - Number of:
 - Embryos transferred
 - Days of transfer
 - Previous IVF cycles

Conclusion

Changes in eggs or embryo quality were ruled out. Change was attributed to the “host” that was influenced by acupuncture.

6. Demographics and Patient Infertility

Diagnosis Category

Key Points

- Acupuncture supports pregnancy outcomes for IVF patients
- This study segregates which IVF patients would best benefit from acupuncture. They are those with:
 - Advanced ages
 - Polycystic ovarian syndrome
 - Male factor
 - Tubal factor

Conclusion

Patients with the highest opportunity for success with IVF, including those who are younger and with good prognosis, may NOT be helped as much by acupuncture.

7. Cortisol/Prolactin Category (Figures 3 and 4)

Key Points

- IVF treatments appear to create nonphysiologic changes in prolactin and cortisol levels through the stimulation phase of the IVF cycle.
- Acupuncture appears to reverse this nonphysiologic change and return IVF patient’s hormone profiles to more physiologic/reproductive levels.
- One mechanism of action of acupuncture on IVF outcomes may be the “normalization” of cortisol and prolactin during the stimulation phase of the IVF cycle.

Conclusion

The December 2009 study by Magarelli, Cridennda and Cohen¹³ in *Fertility & Sterility* provides a road map for a revolution in the integration of Western and Eastern medical practices. The authors were able to reduce bias to a minimum by utilizing serum levels of cortisol and prolactin that were collected in a blinded fashion, over a protracted period of time. This was done without knowledge of the types of fertility treatments, including acupuncture. The results demonstrated that by using the Cridennda/Magarelli acupuncture protocol, TCM reported that more pregnancies could be explained by beneficial changes in serum levels of cortisol and prolactin, which mimicked normal pregnancy menstrual cycles.

Figures 3 and 4 on the following page, show the changes in serum levels of prolactin and cortisol associated with acupuncture (solid diamonds) in women undergoing controlled ovarian hyperstimulation for IVF-embryo transfer. Acupuncture was associated with significant increase in prolactin levels (solid diamonds) on stimulation days 4, 5, 6 and 7. However, cortisol levels were significantly higher on stimulation days 7, 8, 9, 11, 12 and 13 in association with the acupuncture treated group.

FIGURE 3. PROLACTIN LEVELS IN CONTROLLED OVARIAN HYPERSTIMULATION FOR IVF-ET

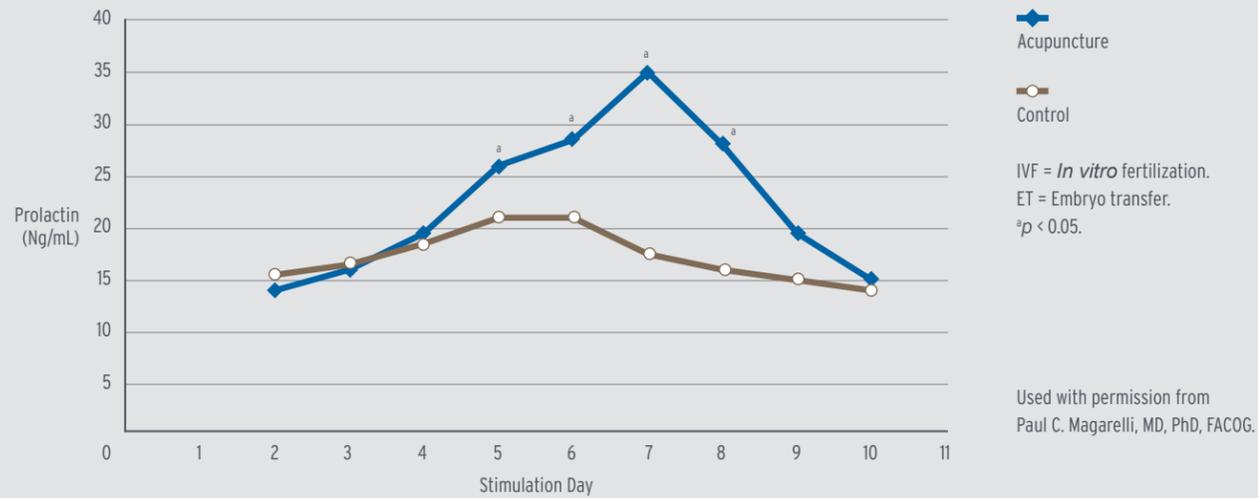
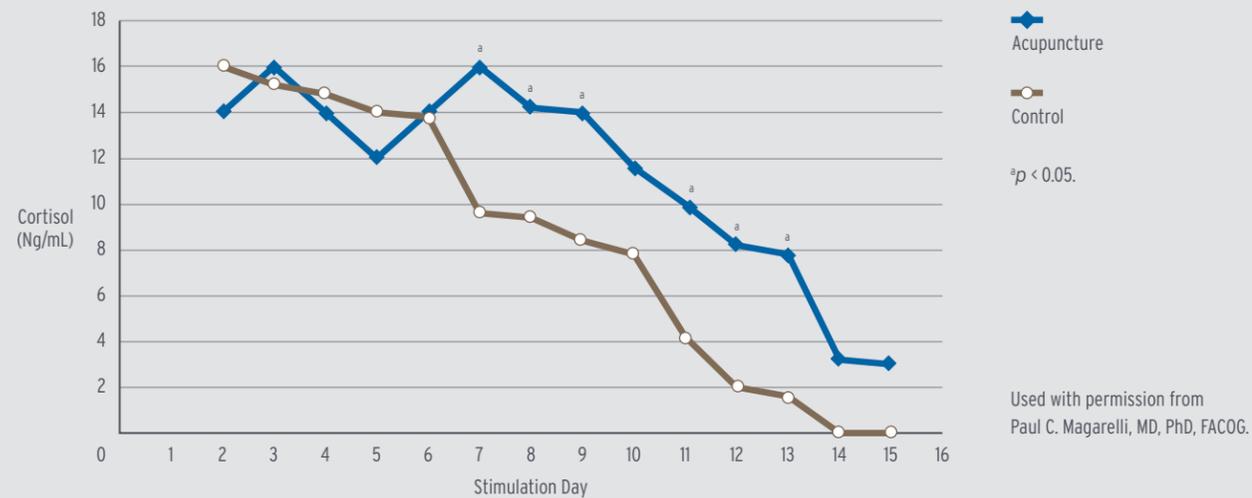


FIGURE 4. CORTISOL LEVELS IN CONTROLLED OVARIAN HYPERSTIMULATION



EVOLUTION OF A REVOLUTION

IVF outcomes demonstrated by studies from Magarelli, Cridennda and Cohen are compared on several reputable sites on the World Wide Web and serve as resources for news reporting agencies and regulatory bodies. These studies strive for patient safety and efficacy of ART.

Over 3,000,000 babies have been born because of ART. Issues related to multiple and ectopic pregnancies, miscarriages and costs for care can affect patient decisions to proceed with seeking out infertility treatment. Although Eastern medicine has proven successful for these IVF patients for thousands of years, many Western medical professionals may struggle to understand how it works. Magarelli, Cridennda and Cohen, as well as others, have demonstrated that acupuncture for IVF improves pregnancy outcomes when added to IVF protocols. The Cridennda/Magarelli TCM protocol was designed from its inception to meet the null hypothesis of “Acupuncture does NOT help.” That null hypothesis was proven incorrect, as was explained by the cortisol and prolactin data. Magarelli, Cridennda and Cohen hope their primitive work stimulates universities and the National Institutes of Health to investigate the link and confirm their data.

About the author:

Paul C. Magarelli, MD, PhD, FACOG is board certified in reproductive endocrinology and infertility (REI) in the state of Colorado and has been in practice since 1998. He is founder and medical director of Reproductive Medicine & Fertility Centers in both Colorado and New Mexico and is nationally recognized for his expertise in REI and the development of cost-effective plans for fertility care. These plans include Planning 4 Pregnancy™ and High Tech with a Personal Touch™. Dr. Magarelli is also applauded for his ground-breaking research integrating Eastern (Traditional Chinese Medicine, including acupuncture) and Western medical treatments for infertility. He has presented numerous lectures at organizations such as the American Association of Medical Acupuncturists, Society for Acupuncture Research and American Association of Acupuncture & Oriental Medicine. He has also published several works on the subject including the first Eastern medicine chapter in a Western medical textbook on reproductive medicine (Infertility and Assisted Reproduction). Dr. Magarelli is currently an advisor to the American Board of Oriental Reproductive Medicine and is a member of the American Society for Reproductive Medicine, Society of Assisted Reproductive Technologies and Pacific Coast Fertility Society.

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