P.A.R.E.S. *Postings*

Philadelphia Area Reproductive Endocrine Society
308 Rolling Creek Road, Swarthmore, PA 19081

www.paresociety.org
P: 484.343.8199 E: pares.office@yahoo.com

APRIL 2017

President's Greeting

John J. Orris, DO, MBA

Hello and Happy Spring,

I am particularly looking forward to our April 20th meeting. Dr. Claudio Benadiva will be our speaker.

Dr. Claudio Benadiva is the Director of the IVF Laboratory at The Center for Advanced Reproductive Services at the University of Connecticut. In addition to being a Clinical Professor of Obstetrics & Gynecology at the University of Connecticut, he is a Fellow of the American College of Ob/Gyn, and is Board Certified in Obstetrics & Gynecology and Reproductive Endocrinology and Infertility.

Dr. Benadiva is among the very few physicians who are certified by the American Board of Bioanalysis as a high complexity laboratory director, making him uniquely suited to integrate both clinical and laboratory protocols in an IVF program.

Dr. Benadiva graduated from the University of Buenos Aires in 1981 and completed his residency in Ob/Gyn at the University of Connecticut Health Center. He completed fellowships at the University of Pennsylvania School of Medicine and The New York Hospital-Cornell Medical Center.

Dr. Benadiva has done extensive research in Reproductive Biology and Endocrinology since 1986. He lectures nationally and internationally, with a special interest in ovulation induction for IVF, PGD, and methods for prevention of ovarian hyperstimulation syndrome.

Looking forward to seeing all of you at the April Meeting!

With warmest personal regards,

John J. Orris, DO, MBA

CONTENT

The Philadelphia Area Reproductive Endocrinology Society

Cordially invites you to our next meeting

GnRHa Trigger

Where we are we in 2017?

Speaker: Claudio Benadiva, M.D., H.C.L.D.
The Center for Advanced Reproductive Services.

Thursday, April 20, 2017
Cocktails 5:30 – 6:00 PM
Dinner & Lecture followed by Q&A – 6:00 PM
Venue: Top of the Tower, 1717 Arch Street, Philadelphia, PA

Payment by check or online at www.paresociety.org

We cannot accept payments at the door.
(If paying by check, please detach and return to our office with your check.)

Members & Staff - $70.00 Non-members - $80.00

____ number attending x $70.00/$80.00 = $_____ Amount enclosed

RSVP's are due no later than Tuesday, April 11th.

Please make your check payable to P.A.R.E.S. and mail it to
308 Rolling Creek Road, Swarthmore, PA 19081.

I will attend the program featuring Claudio Benadiva, M.D., H.C.L.D. on Thursday, April 20, 2017.

Attendee names _____

_____

P.A.R.E.S. Philadelphia Area Reproductive Endocrine Society
c/o Executive Director, Teri Wiseley, CMM, CPM
308 Rolling Creek Road, Swarthmore, PA 19081
Telephone: 484-343-8199 Email address: pares.office@yahoo.com

PARES JANUARY MEETING

Drs. Kelly, Schillings and Derman

Lou Null, Drs Orris and Brasile and Wally Zebi (Natera)

Teri Wiseley and Dr. Emelia Bachman

Speaker, Mark Umbarger, PhD and John Orris, DO

Drs. Sawin and Kelly

Dr. Feinberg, Eileen Davies and Dr. Orris

PARES JANUARY MEETING

Teresa Robinson, Dr. Orris and Sandy Saldan

Tiffany Stankewicz, Milena Jakubowska, Dr. Orris, Janice Gilchrist and Jan Kozak

Jennifer Jones and Dr. Kelly

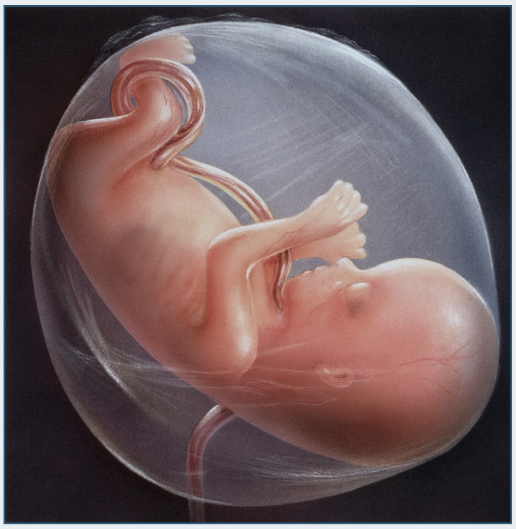
Tiffany Stankewicz, Milena Jakubowska , Janice Gilchrist, and Jennifer Jones

Olimpia Sabol, Kathi Gaffney, Dr. Umbarger and Dr. Orris

Drs Feinberg, Brasile and Eileen Davies

Proposed Federal Legislation Threatens the Future of IVF in the United States

There are now two bills in committee in the US House of Representatives that would give quasi human status to embryos. HR 681, "Life at Conception Act", declares that the right to life guaranteed by the Constitution is vested in each human being at all stages of life, including the moment of fertilization, cloning, or other moment at which an individual comes into being. HR 586, "Sanctity of Human Life Act", declares that: (1) the right to life guaranteed by the Constitution is vested in each human and is a person's most fundamental right; (2) each human life begins with fertilization, cloning, or its equivalent, at which time every human has all the legal and constitutional attributes and privileges of personhood; and (3) Congress, each state, the District of Columbia, and each U.S. territory have the authority to protect all human lives.



These bills are referred to as "Personhood Legislation". If enacted, these laws will change how a person is defined. Essentially an embryo shall legally be a person. As a result, undeveloped embryos would be entitled to a series of protections under Federal law, including the right to life, liberty, and the pursuit of happiness. Simply stated, abortion would not be permitted for any reason, including rape or incest. If "person" were defined as proposed under the Sanctity of Human Life Act, a woman choosing to have an abortion could be prosecuted and charged with the crime of murder. Women's bodies, rights, and health would be subordinated to the protection of the embryo. Additionally, certain forms of birth control, such as the "morning after" pill would no longer be available and stem cell treatments for patients with Parkinson's, Lou Gehrig's disease and cancers like leukemia would likely be discontinued.

Supporters of the Personhood Legislation point to language in the majority opinion written by Justice Harry Blackmun in the landmark 1973 case of Roe v. Wade, (410 U.S. 113) to support their stance. Many of us can recall, and others have since learned the facts of this case which involved a single, pregnant, Texas woman, under the fictional name of Jane Roe, who challenged anti-abortion laws by stating that they violated her rights under the Constitution. Ultimately, the case was presented before the Supreme Court which decided that a fetus is not a person but "potential life," and thus does not have constitutional rights of its own. Roe's claim was upheld and her right to privacy entitled her to an abortion.

While the Supreme Court ruling provided for abortion rights, Justice Blackmun who wrote the majority opinion noted, "The appellee (State of Texas) and certain amici [pro-lifers] argue that the fetus is a 'person' within the language and meaning of the Fourteenth Amendment. In support of this, they outline at length and in detail the well-known facts of fetal development. If this suggestion of personhood is established, the appellant's case, of course, collapses, for the fetus' right to life would then be guaranteed specifically by the Amendment."

Supporters of Personhood Legislation rely on this language to contend that during Blackmun's time, the "well-known facts of fetal development" were a far cry from what is known today. Ultrasounds and DNA testing were not yet invented. In 1973, it was commonly believed that "life" began at "quickening," or when a woman first felt movement of the baby in the womb somewhere between 18 to 24 weeks. Supporters argue that in 1973 technology was unable to prove that a fully human and unique individual existed at the moment of fertilization and continued to grow through various stages of development until natural death from old age. Their position is that scientific evidence has advanced tremendously, and can now establish the humanity of the pre-born child. As a result, legal protections of personhood should be restored to the pre-born child.

While Personhood Legislation would have an obvious effect on abortion and a woman's right to choose, there are other potential and perhaps unintended effects that could be far reaching and could tremendously impact the services performed at IVF clinics. Since more than one egg is harvested and fertilized to achieve a successful IVF pregnancy, making all the embryos "persons" under these federal laws would make it difficult, if not impossible to continue offering IVF treatment within the United States. When embryos are created and frozen as a part of reproductive fertility treatments,

these embryos would legally be "persons" and consequently will have all the rights due persons. The problems resulting from this change would not only be many, but illogical as well. For example, if embryos are to be defined as persons, would the freezing of embryos be considered child abuse? If one of these embryos "dies" in some part of the in vitro fertilization process, will a criminal investigation be conducted? Would physicians if faced with the choice of saving a woman's life or refusing to harm an embryo be sued for malpractice no matter what choice was made? Would stored embryos be given names (non-birth certificates)?

What about the several references to "person" currently found in federal and state laws which are inconsistent or incompatible with the Personhood Legislation? If passed, does it mean that embryos would have property or inheritance rights? Are Termination of Parental Rights laws applied to these embryos? Adoption laws? If more than five unrelated embryos are housed in a single building, will it have to be licensed as a child residential care home? It's ludicrous, yet the list could go on and on.

The Personhood Legislation has called into question not only a woman's right to choose, but also stem cell research and treatment, and accepted infertility treatments designed to assist couples in creating and sustaining birth, which ironically is the stated goal of its proponents.

The concept that a person exists from the moment of "fertilization, cloning or the functional equivalent thereof" stems from religious beliefs. People have many different ideas and theories about when human life begins. Personhood is an attempt to impose one particular theory, the theory that life begins at fertilization. But what about those who believe otherwise? Why should they be forced to accept and live by this one theory? Religious ideology is not an appropriate foundation for the law in this country.

Melissa B. Brisman is an attorney who practices exclusively in the field of reproductive law and is considered by her peers to be a leader in her profession. Ms. Brisman's experience and qualifications are unparalleled. She employs an experienced and qualified staff of legal and administrative professionals and is licensed to practice law in Massachusetts, New Jersey, New York and Pennsylvania. Ms. Brisman has a practice, Melissa B. Brisman, Esq., LLC, located in Montvale, New Jersey, offering a full range of legal services in connection with gestational carrier arrangements, ovum, sperm, and embryo donation, and adoption. In addition, Ms. Brisman is sole owner of Reproductive Possibilities, LLC, an agency that facilitates gestational carrier arrangements, and Surrogate Fund Management, LLC, a company that manages escrow in connection with reproductive arrangements. Ms. Brisman can be reached at info@reproductivelawyer.com.

Pre-pregnancy progesterone helps women with recurrent pregnancy loss

Top News in Obstetrics & Gynecology

- University of Illinois Hospital & Health Sciences System

Women who have had two or more unexplained miscarriages can benefit from natural progesterone treatment before pregnancy, a new a study shows.

Progesterone has been used for infertility for more than 50 years because it helps stabilize the endometrium, the inner lining of the uterus. But the hormone's use has not been well–studied in women who become pregnant easily but have difficulty maintaining pregnancy.

Dr. Mary Stephenson, chief of the Department of Obstetrics & Gynecology and director of the Recurrent Pregnancy Loss Program at UI Health, led the new study. She says recurrent pregnancy loss is common, but very few evidence–based treatment options are available.

Stephenson and her colleagues see more than 200 women each year who suffer from recurrent pregnancy loss, making UI Health one of the largest subspecialty centers in the U.S. for helping women struggling to maintain pregnancy.

Unlike previous studies, the new, prospective study of progesterone supplementation looked at a large and specific group of patients – 116 women who had a history of recurrent pregnancy loss.

Recent evidence has suggested that endometrial glands may play a larger role in early pregnancy than previously thought, so Stephenson

worked with Dr. Harvey Kliman, director of the reproductive and placental research unit at the Yale University School of Medicine, who specializes in the endometrium, to identify women with abnormal endometrial development by examining the expression of nuclear cyclin E, or nCyclinE.

Women with abnormal levels of nCyclinE, a molecular marker for the health of the endometrium, were prescribed progesterone during the second half of their menstrual cycle, when the uterine lining matures in preparation for a possible pregnancy.

The researchers found that natural progesterone, administered vaginally, led to a higher birth rate. Over two–thirds of pregnancies were successful in women who received progesterone, compared to barely half in women who did not receive the hormone.

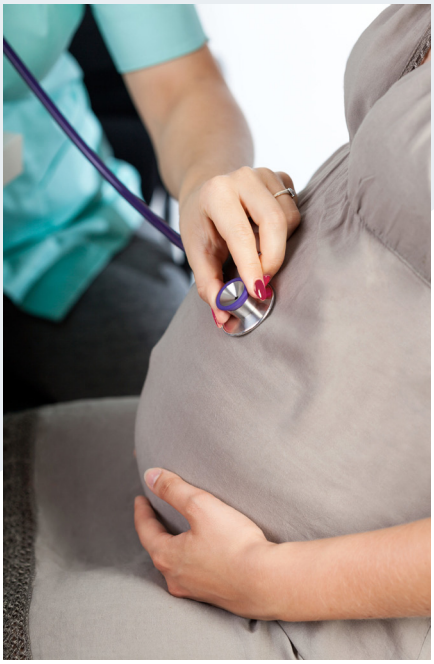
The results were published in the journal *Fertility and Sterility.*

The positive results suggest a prospective randomized trial is needed to validate the findings, Stephenson said. The results also indicate that molecular markers like nCyclinE could help doctors determine which patients would benefit from progesterone, and at what dose.

Stephenson suggests that women who have experienced recurrent pregnancy loss should discuss possible progesterone supplementation with their doctor, but she strongly recommends "a thorough evaluation of known factors associated with pregnancy loss" before making a treatment decision.

COMMENTARY...

The original research study by Stephenson, et al brings a new light to a common issue in realm of Infertility management. This prospective observational cohort study addresses multiple aspects of the issue of recurrent pregnancy loss. Not only does it address the concept of endometrial glandular activity deficiency contributing the RPL, but also it further contributes to our understanding of vaginal micronized progesterone as a treatment strategy in RPL. While progesterone has commonly been used empirically in the treatment of RPL, these authors suggest that previous studies have many limitations. They have had heterogeneous cohorts, included variable routes of P administration, and have investigated variable start times of P treatment. Although this study has its own limitations, it has attempted to address the shortcomings of prior research by narrowing its population of interest and attempting to control for confounders in the initial data analyses.



In summary, this study utilized a Database of patients with recurrent pregnancy loss to create a cohort of patients with two or more unexplained pregnancy losses less than 10 weeks in size. The study also had strict necessary criteria including: a negative RPL evaluation (TSH, PRL, cytogenetic analysis, antiphospholipid antibodies, normal hysteroscopy), a normal endometrial biopsy 9-11 days following LH surge, and at least one subsequent pregnancy achieved without fertility drugs. This study then used the endometrial expression of nCyclinE, an endometrial molecular marker of development to stratify the cohort into 2 groups. Those with elevated nCyclinE were treated with commercially available vaginal micronized P from 3 days following LH surge to 10 weeks of gestation. These women were compared to women with normal nCyclin E who did not use vaginal P. Interestingly, there was a subset of women with normal nCyclinE that insisted upon using vaginal P. Ultimately, the hypothesis was that if nCylinE is abnormally elevated in the luteal phase of a cohort of women with RPL, then vaginal micronized P starting 3 days following the LH surge may be effective in improving subsequent pregnancy outcomes.

Of the 116 women and resulting 499 pregnancies included in the study, pregnancy success in the 49% of those with elevated nCyclinE improved from 6% to 69% with vaginal micronized P treatment. Pregnancy success in subsequent pregnancies was overall improved in women given vaginal micronized P when compared to controls (68% vs 51%). There was no statistically significant improvement in pregnancy rates noted for those women with normal nCyclin E who insisted upon vaginal P usage. The aforementioned improvements remained significant even when controlled for age, BMI, race, and concomitant factors associated with RPL. Overall, the number of women needed to treat with P to achieve one additional pregnancy success was only six. Interesting, the secondary measure of the prevalence of abnormal nCyclinE among women with RPL revealed worthwhile results. In the study, those women with previously abnormal nCyclinE expression undergoing vaginal P treatment were offered repeat EMB. In those who underwent repeat biopsy, 84% had a decrease or normalization of nCyclinE expression. Additionally, a stepwise increase in pregnancy success was noted with decreased or normalization of nCyclinE expression.

While this study does add support for the benefit of using vaginal micronized P in the RPL patient, it also brings up a few important points and questions. Firstly, the study addresses the potential unreliability of nCyclinE alone given that there are

other molecular markers that play into endometrial activity. Although the authors suggest further study of other molecular markers, the inclusion of nCyclinE itself is a unique and important aspect of the current study. While prior research has largely relied on empiric use of Progesterone treatment, this study sheds light on a potential mechanism of use and future strategies to better target its application to RPL patients.

Although this study has many positives, the authors gloss over a large potential confounder – the potential effect of close monitoring and supportive care on future pregnancy outcome. The lack of a placebo control in the current study design is an unfortunate limitation. Additionally, while the current study is designed to be prospective, much of the data from prior pregnancy outcomes was obtained by retrospective chart review. Although much of the data from the RPL Database may have been collected in real-time and, therefore, may not have been prone to recall bias, it is possible that aspects of patient history may have been obtained retrospectively.

Ultimately, despite its limitations, this study does provide further evidence to recommend the empiric use of luteal start vaginal micronized progesterone in women with RPL. While future research regarding endometrial development, molecular markers of the endometrium, and the psychosocial component of RPL care should be developed, the overall safety and affordability of vaginal micronized progesterone should not serve as a deterrent for its current use.

Samara Rutenberg, MD, BS

PGY-2, Hahnemann University Hospital/ Drexel University College of Medicine

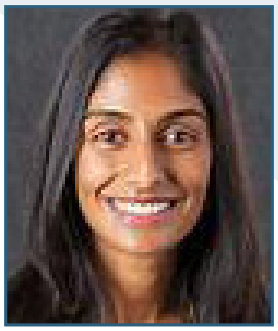
Meet the Board

John J. Orris, D.O, M.B.A.
President

Maureen Kelly, M.D.
President-Elect

Emelia Bachman, M.D.
Secretary-Treasuer

Jay Schinfeld, M.D.
Secretary-Treasurer Elect



Divya Shah, M.D., M.M.E.
Director at Large

Scott Edwards, M.D.
Immediate Past President