

# JONES Health Watch

ADVANCES IN REPRODUCTIVE MEDICINE & INFERTILITY

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## Physicians

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*The Mason C. Andrews Professor and  
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## Services

- *Treatment of General Infertility*
- *Reproductive Surgery*
- *Endocrine Dysfunction*
- *Intrauterine Insemination*
- *In Vitro Fertilization Program*
- *Assisted Oocyte Fertilization  
(ICSI, TESA, MESA)*
- *Donor Egg Program*
- *Cryopreserved Embryo Program*
- *Pre-implantation Genetic Diagnosis  
Program*
- *Sperm Bank (CLIA Certified)*
- *Andrology Laboratory (CLIA Certified)*
- *Semen Analysis*
- *Full-Service Endocrine Laboratory  
(CLIA Certified)*
- *Contraception*
- *Menopause*



**William Gibbons, M.D.**

Dear Colleague,

I hope that you enjoy the spring issue of the Jones Institute's physician newsletter. Our goals are to provide you with important information concerning advances in reproductive medicine that could directly affect your infertility patients' care and keep you apprised of current events at the Jones Institute.

Of particular import in this issue is Dr. Oehninger's article on the 2001 in vitro fertilization success rates at the Institute. We reached an impressive 52% success rate

(presence of a gestational sac) in patients under 35 while reducing the incidence of multiples in all categories. Our cryopreserved cycle pregnancy success rates (IVF donor egg and IVF) reached 38%. This means that one stimulated cycle producing numerous embryos for cryopreservation can result in pregnancy rates as high as 55-65%. This depends on the individual patient and the number of frozen cycles attempted.

In the research arena, we are pleased to announce the appointment of Roger Gosden Ph.D. as Scientific Director of the Jones Institute. Dr. Gosden has had an outstanding career in Europe and Canada and is considered a top scientist and pioneer in the field of reproductive biology and medical science applied to assisted reproductive technologies. In fact, at the last American Society of Reproductive Medicine meeting in Orlando he was awarded the Distinguished Scientist Award. Originally from the United Kingdom, he completed his education in Cambridge and Edinburgh before moving to McGill University in Montreal, Canada.

We believe strongly that our participation in research protocols transfers directly to improved quality of patient care. Many procedures pioneered by us, such as intracytoplasmic sperm injection, are now commonly used in programs throughout the United States. Several of our scientific teams continue research in other clinical areas such as preimplantation genetic diagnosis, fertilization and embryo culture, assisted hatching, and others.

David Archer, MD, Director of the Clinical Research Center and Fellowship Program, has included information on several active research projects in women's health care including the prevention of osteoporosis, a study involving HRT and prevention of endometrial hyperplasia and a comparison study involving bazedoxifene, a selective estrogen receptor modulator/conjugated estrogen combinations in postmenopausal women. He details several other studies in contraception.

Kimberly Kinney, MSN, Women's Health Care Practitioner, discusses a multicenter trial on the treatment of male infertility by improving sperm "quality" with PROXEED® (acetyl-L-carnitine and L-carnitine) supplementation. Enrollment is now underway for this study.

We are available for phone consults with you to discuss specific cases. We believe that the best patient care is delivered when we work with you as a treatment team. I am available by telephone (757) 446-7100 or e-mail at gibbonwe@evms.edu.

Sincerely,

**William Gibbons, M.D.**

*The Mason C. Andrews Professor and  
Chairman, Obstetrics and Gynecology,  
Eastern Virginia Medical School*

## Current State-of the-ART (Assisted Reproductive Technologies) at the Jones Institute

*Sergio Oehninger, M.D.*

*Professor, Departments of Ob/Gyn and Urology*

*Director, Division of Reproductive Endocrinology and Infertility  
Eastern Virginia Medical School*

We are proud to announce the birth of ART baby number 2,700 in February of 2002! This achievement represents another milestone in our ever-growing devotion to the cause of alleviating infertility. This mission is signified in our logo: **“An Institute Founded on Science and Dedicated to Life”**.

We are thrilled that Roger Gosden, PhD, has been appointed our Scientific Director as of November 2001, bringing excellence and a tremendous scientific reputation to the Jones Institute family. The state of the Institute could therefore not be stronger, both in terms of current clinical successes and of expected scientific advances.

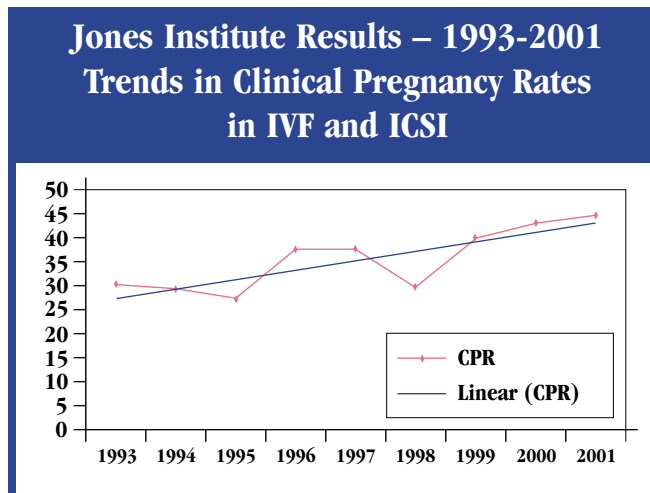
Here, it is my aim to present our present pregnancy results in our IVF and Donor Egg programs. First, I would like to share an overall historic view of ART results at the Jones Institute from 1981 through 2001 (table 1). Two decades of dedicated work in more than 12,000 ART cycles have resulted in 2,067 deliveries with 73% of births being singleton pregnancies. Although twins represent most of our multiple births, we are still concerned about higher order multiple pregnancies and we have set our goals to decrease their frequency as discussed below.

**Table 1**

Jones Institute ART Program 1981-2001	
• Number Fresh ART Cycles	10,500
• Number Cryopreserved Cycles	1,879
• Number of Babies	2,700
• Number Deliveries	2,067
– Singletons	73%
– Twins	23%
– Triplets	3%
– Quads	<1%

Figure 1 shows our IVF clinical pregnancy rates per transfer (including results of intracytoplasmic sperm injection or ICSI). ICSI is used in cases of male infertility and represents approximately 35% of all IVF

**Figure 1**



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## Assisted Reproductive Technologies

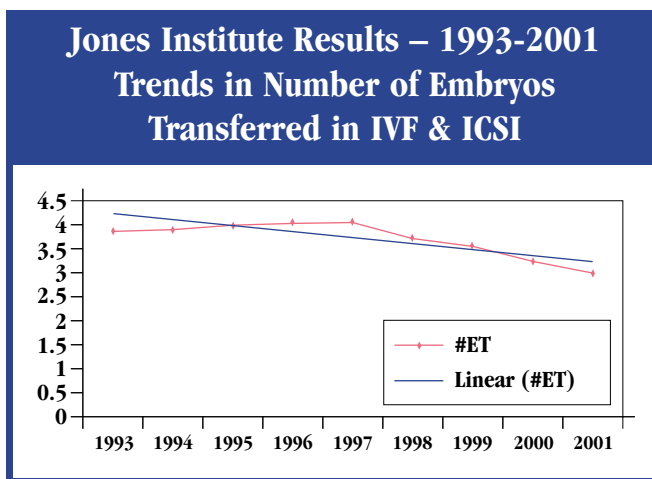
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cases. Clinical pregnancy refers to a conception confirmed by ultrasonography as demonstrated by the presence of an intrauterine gestational sac.

As observed, pregnancy outcomes have increasingly improved, with an overall 45% pregnancy rate for the year 2001 (including women of all ages and all diagnoses). The subgroup of patients <35 years of age and with a normal ovarian reserve reached an outstanding 52% pregnancy rate. These outcomes are the result of multiple factors, including the use of newer hormonal preparations, optimization of laboratory techniques for culture of gametes and embryos, and application of ultrasound-guided embryo transfers.

Importantly, the improvement in pregnancy rates occurred while there was a simultaneous decrease in the number of embryos transferred per attempt (figure 2). This is a direct reflection of our new policies aimed at decreasing multiple pregnancies.

**Figure 2**



Whereas the number of embryos transferred in the early and mid 90's was four, presently we are transferring an average of only 2.9 embryos.

Consequently, we are witnessing a lower incidence of triplet pregnancies, with virtually no higher order multiples in the last two years. This is true for both the IVF and Donor Egg programs as shown in table 2. Egg donation cycles have resulted in an excellent 53% pregnancy rate, with a mean of 2.7 embryos transferred per cycle and only 2% of pregnancies as triplets.

**Table 2**

<b>Jones Institute IVF Results 2001</b>		
	<u>IVF</u>	<u>Donor Egg</u>
Number of Embryos Transferred	<u>2.9</u>	<u>2.7</u>
Clinical Pregnancy Rate	<u>45%</u>	<u>53%</u>
Implantation Rate	<u>22%</u>	<u>25%</u>
Multiple Pregnancy Rate	<u>34%</u>	<u>31%</u>
– Triplet Rate	<u>5%</u>	<u>2%</u>

We are now freezing embryos not only as pronuclear zygotes (1-cell stage) but also at the cleaving (embryos of 6-10 cells) and blastocyst stages. The success of the transfer of cryopreserved-thawed embryos for IVF and Donor Egg patients has now reached a remarkable pregnancy rate of 38%. As a consequence, the results of the transfer of “fresh” and “frozen” embryos from a single stimulated IVF cycle can yield cumulative pregnancy rates as high as 55-65% (representing the so-called “total reproductive potential”) depending upon the individual patient characteristics.

Undoubtedly, ART is the treatment of choice for many infertility conditions, sometimes after failure of first-level treatments, but in others as the initial therapeutic option of choice. We are thrilled to share these results with you and remain hopeful that our proficiency and dedication will allow us to help your patients achieve their dream of creating a family.

## The Clinical Research Center at the Jones Institute for Reproductive Medicine

David Archer, M.D.

Director, Clinical Research Center and Fellowship Program

Jones Institute for Reproductive Medicine, Eastern Virginia Medical School  
Norfolk, VA

The Clinical Research Center at the Jones Institute conducts studies primarily in the area of women's health, although some studies also include male volunteers. Currently, the Clinical Research Center is seeking postmenopausal women to volunteer for several studies including a study on the effects of two osteoporosis medications on bone mineral density, a hot flash study, and a two-year clinical trial comparing the effects of two currently marketed hormone replacement therapies. The CRC is also beginning a safety and efficacy study involving HRT and prevention of endometrial hyperplasia and a comparison study involving bazedoxifene, a selective estrogen receptor modulator/conjugated estrogen combinations in postmenopausal women.

Of special note is the osteoporosis study because there is no placebo involved. All participants will receive active medication that is known to inhibit bone loss.

A number of studies involving various types of contraceptive drugs or devices are also either underway or ready to begin. The BufferGel study is

evaluating the effectiveness of a contraceptive gel used with a diaphragm compared with another currently marketed gel with diaphragm. Particularly important is this contraceptive gel's potential

*Particularly important is this contraceptive gel's potential microbicidal or germ-killing effect, which could, if proven true, mean possible protection against HIV.*

microbicidal or germ-killing effects, which could, if proved true, mean possible protection against HIV. Vaginal microbicides are inexpensive and are available to women without a prescription, increasing their attraction as a means of protection for birth control.

The Clinical Research Center is also currently looking for young women to volunteer for an intravaginal ring study comparing

calendar-based use of the vaginal ring to four-week cycle use. The CRC also expects to begin enrollment in the near future in a number of other contraceptive studies. A second vaginal ring study is planned using the Nuva Ring as the study device for the summer of 2002; and enrollment should begin within the next month for a study comparing the Oves Cervical Cap and the Orthoflex diaphragm, both used with Gynol II spermicide for efficacy as a barrier device.

## Jones Institute for Reproductive Medicine Participating in Male Factor Infertility Clinical Trial

*Kimberly Kinney, MSN, Women's Health Nurse Practitioner  
Jones Institute for Reproductive Medicine  
Eastern Virginia Medical School  
Norfolk, VA*

A contributing male factor is identified in approximately 40% of infertile couples. Despite this high percentage, there are limited options available for treatment of this population. The need is evident for the development of non-invasive, cost-effective forms of treatment. The Jones Institute for Reproductive Medicine is participating in a multi-center prospective randomized study involving PROXEED<sup>®</sup>, a nutritional supplement containing acetyl-L-carnitine and L-carnitine. According to Sigma-Tau Pharmaceuticals, manufacturer of PROXEED<sup>®</sup>, these metabolic cofactors have been shown to play an important role in the development, metabolism, and function of spermatozoa.

This multi-center trial is also being conducted at other university-based centers in the United States. It is a randomized, double blind, placebo controlled trial with a projected total of 240 subjects from the combined sites. The subjects are required to take the supplementation, in powder form, mixed with four ounces of liquid, twice daily for six continuous months. Data is collected, by semen analysis, three times during the course of the study, a baseline before beginning the supplement, after three months of supplementation, and after six months of supplementation. At each point a semen analysis with morphology is done, with a repeat analysis one to two weeks later, for a total of six. A carnitine assay is also performed with one sample from each

time frame. With the screening semen analysis, testing for antisperm antibodies using the immunobead method is also required.

Seminal fluid and intra-sperm values for total carnitine, free carnitine, acetylcarnitine, and acetylcarnitine to free carnitine ratio will be evaluated and compared throughout the course of the trial. The primary objective, or endpoint, is the number of motile sperm. Secondary endpoints include percent of motile sperm, concentration of motile sperm, Kruger strict morphology, grade of forward progression, and pregnancy.

The target population is healthy males between the ages of 20 and 49 who have experienced difficulty conceiving for a minimum of 12 months, and have two semen analysis that demonstrate either sperm concentration greater than 1 million/ml, but less than 20 million/ml, and/or motility less than 50%. Exclusion criteria include, but are not limited to sperm motility less than 5%, sperm concentration less than 1 million/ml, history of undescended testes, presence of palpable varicocele, or a history of vasectomy, orchiectomy, or obstructive pathology of the urogenital system.

The screening period for interested subjects includes a history and physical, two semen analyses,

*Continued on Page 7*

## Male Factor Infertility Clinical Trial

*Continued from Page 6*

serum FSH and testosterone, and the signing of an informed consent, approved by the Institutional Review Board at Eastern Virginia Medical School. Once the subject is determined eligible, a three-month supply of the medication is randomly dispensed.

The medication is packaged in individual doses containing L-carnitine 2g and acetyl-L-carnitine 1g, or a placebo. The subject is contacted every four weeks to monitor compliance as well as any adverse effects. After three months of supplementation, at the time of the second set of semen analysis, the remaining medication is dispensed. Any unused

medication is returned at the conclusion of the study. Compensation is available for qualifying subjects that complete the study protocol.

This clinical trial is currently ongoing with available enrollment. The randomization groups will not be disclosed until the completion of the study. A deadline for final data submissions has not yet been established. If you would like additional information regarding this study, please contact the study coordinator, Kimberly Kinney, at The Jones Institute for Reproductive Medicine, (757) 446-7100, extension 8454, or by e-mail at [kinneykj@EVMS.edu](mailto:kinneykj@EVMS.edu).

## The Clinical Research Center at the Jones Institute for Reproductive Medicine

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Two other contraceptive studies should begin by early Spring 2002: one study using a transdermal patch for contraception, the other study comparing the contraceptive efficacy of a different transdermal patch with an oral contraceptive.

Studies in other areas of health for which volunteers are needed include a study of individuals—both male and female—with Diabetes Type II currently being treated with sulfonylureas alone, and a clinical trial for young women who

suffer from dysmenorrhea or painful periods. Although the term “dysmenorrhea” may sound quite intimidating, young women who have only one day of cramping may qualify to be in the study.

Anyone wishing to find out if they or a friend might qualify for one of the studies being conducted at the Clinical Research Center may either call the 24-hour hotline number at 757-446-5808 or they can visit the Clinical Research Center’s website at [www.crc-evms.org](http://www.crc-evms.org).

*Address Service Requested*

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