



Research Support

Research at CHR is alive and well and we are all looking forward to another successful year in 2007.

Indeed, early next year, we anticipate moving The Foundation for Reproductive Medicine from Chicago to New York City in an attempt to further expand CHR's research efforts. This not-for-profit Foundation traditionally underwrote much of the expenses for CHR's research.

With Dr. Gleicher's full-time engagement in New York City, it has, however, outlived its usefulness in Chicago. We anticipate a festive re-launch of the Foundation, under a brand new Board, in New York City in the first quarter of the coming year.

If you are interested in contributing to our Foundation, either financially or through organizational efforts, please call Valerie at 212-994 4400. We greatly appreciate all help!



Premature Ovarian Aging

New FSH Cut-Off Levels Redefine Definition of Normal

Our strong research interest in POA is continuing. We have been able to establish age-specific baseline FSH levels and have started using those in the diagnosis of POA. Historically, a young woman was recognized with diminished ovarian reserve (what we now call POA) only if her baseline FSH level exceeded 10mIU/ml. Based on our

AGE SPECIFIC b-FSH LEVELS	
<33 Years	<7.0 mIU/ml
<33-37 Years	<7.9 mIU/ml
<38-40 Years	<8.4 mIU/ml
≥41 years	<8.5mIU.ml

research, we have now come to recognize that the cut-off levels between normal and abnormal ovarian function, at younger ages, lie at much lower FSH levels.

In other words, under the old cut-off of 10mIU/ml, many women with POA have been overlooked. Moreover, such women can be expected to be disproportionately represented amongst infertility patients, especially amongst those with the non-diagnosis of unexplained infertility. Indeed, in a recently submitted paper on POA we calculated rather surprising prevalence levels for POA in our, granted, obviously pre-selected, and therefore biased, patient pool. The table summarizes age-

(*) At, or above, age 41 we consider all patients to suffer from diminished ovarian reserve, and the diagnosis of POA, therefore, no longer appears appropriate.

specific baseline FSH levels for various age groups.

As these data quite well demonstrate, even if our practice, because of CHR's special expertise in this area, attracts a disproportionate number of POA patients, the prevalence of POA in all fertility practices has to be very high. And many amongst those are currently not properly diagnosed because age-specific FSH levels are not utilized.

To facilitate accurate, diagnosis women, we have, as colleagues, distributed with above listed baseline FSH levels

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Ob/Gyn community, with the recommendation that women with abnormally high baseline FSH levels, even if they still are below 10mIU/ml, be considered suspicious for POA and be referred to a fertility specialist for further evaluation.

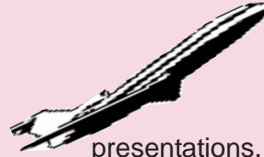
Time is of essence in such patients. Therefore, the recommendation for a quick referral to a specialist is necessary. We presented the baseline FSH data at the Annual ASRM Meeting, last November, in New Orleans. A manuscript has been submitted for publication. *If you would like one of our reference cards, describing age specific baseline FSH levels, call us at 212-994 4400 and we will gladly mail you one.*

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abnormally high

CHR News

Where in the world is...?



The year 2007 is shaping up as a record year for invited CHR presentations. Apart from submitted presentations at scientific meetings, like the Annual ESHRE and ASRM meetings, the following invitations have been extended:

Norbert Gleicher MD already spoke in early January in Tel-Aviv, Israel on premature ovarian aging and in March will give Grandrounds in the Department of Obstetrics and Gynecology at the NYU University Hospital in New York City on the diagnosis and treatment of ovarian aging.

Also in March he will also speak at the World Congress for Controversies in Obstetrics and Gynecology in Barcelona, Spain, on indications for preimplantation genetic diagnosis (PGD). In April, he is invited to a conference in Amman, Jordan, where he will present on the aging ovary. On May 3 he will be at Yale University in New Haven, Connecticut, where he will give a lecture to students and residents on autoimmunity in reproduction, which is then followed by a Grandrounds lecture to the whole department on ovarian aging.

Straight from the Yale lectures, he will be rushing to the airport to catch a flight to Athens, Greece, where he is invited to lecture on the CHR's DHEA experience. In June he is invited to present Grandrounds in Los Angeles on the topic Gyneco-Radiology. After a summer break he is invited to speak in November at the Annual Ovarian Physiology Conference in Japan on the aging ovary.

Event Schedule for 2007

CHR presents the 2007 Grandrounds event series in New York City. Join us for cocktails, dinner and a lecture:

March 13, 2007

Speaker:

Suzanne Steinbaum, MD

Topic:

"Analyzing Cardiac Risk in Women"

April 17, 2007

Speaker:

Mark Surrey, MD

Topic:

"Controversies in PGD"

May 8, 2007

Speaker:

Terry Davies, MD

Topic:

"Autoimmune Thyroid Disease in Pregnancy"

June 2, 2007

Speakers:

Norbert Gleicher, MD

and

David Barad, MD

Topic:

"Annual Research Update"

If you are interested in attending one of these free events, please call (312) 876-1506 or e-mail ascarpinato@thechr.com to register.

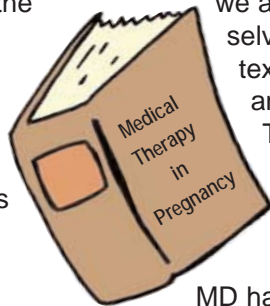


Medical Therapy in Pregnancy Online Fourth Edition Online with Updated Chapters

We would like to introduce you to the online edition of "Principles and Practice of Medical Therapy in Pregnancy" which, over three editions, has become the most highly regarded hard copy textbook on the management of medical diseases during pregnancy.

After three highly successful printed editions, there was consensus that the future of this unique text had to be adjusted to the electronic revolution that had swiped the academic world of publishing. Instead of a 4th printed edition, we have decided to present this comprehensive

textbook in a constantly updated electronic format.



By going to an electronic format, we are also pleased to introduce ourselves as the 3rd publisher of this textbook. After Plenum Medical and Appleton & Lange, it is now TM-Publishing, a fully owned subsidiary of Trebron Management, that has become the official publisher of this classic text. Norbert Gleicher MD has been the principle editor of this textbook through its three editions. You can view updated chapters at MedicalTherapyinPregnancy.com.

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CHR Publications

Abstracts, Letters, Manuscripts of 2006

A number of important CHR publications have appeared in print since we published our last UPDATE. We want to take this opportunity to summarize them:

Gleicher N, Weiner R, Vietzke M. The impact of abnormal autoimmune function on reproduction: Maternal and fetal consequences. J Autoimmunity 2006; 27:161-5

In this study Gleicher et al report that offspring from mothers with autoimmune diseases demonstrate a significantly increased risk of developing autoimmune diseases, though not necessarily the same autoimmune conditions as their mothers. The authors also



speculate that the risk for autoimmune diseases in offspring may be affected by the mode of their delivery, with vaginal delivery increasing, and cesarean section delivery decreasing the risk. The study also confirms that women with autoimmune diseases show lower fecundity (i.e., conception rates) than normal controls.

Gleicher N, Barad D. "Ovarian age-based" stimulation of young women with diminished ovarian reserve results in excellent pregnancy rates with in vitro fertilization. Fertil Steril 2006; 86:

1621-5

In this study Gleicher and Barad report on 62 women, all under age 35, with evidence of premature ovarian aging. When these women

were stimulated with the kind of protocol, usually reserved for older women, their ongoing pregnancy rate with IVF was surprisingly high at 32%, and not significantly different from that of a control group of women with normal ovarian function. Their cumulative pregnancy rate was lower, since they produced fewer extra embryos than control patients, and therefore, had fewer frozen-thawed cycles. Overall, this report contradicts the widely held

belief that women with evidence of POA have very poor IVF outcomes, and demonstrates that, if treated with an ovarian stimulation geared at their "ovarian age" pregnancy chances are still surprisingly excellent.

Barad D, Gleicher N. Effect of dehydroepiandrosterone on oocyte and embryo yields, embryo grade and cell number in IVF. Hum Reprod 2006; 21:2845-9

For regular readers of our UPDATES this material will sound familiar. The time to publication is for most medical journals, unfortunately, quite long. In this second formally published paper on CHR's DHEA experience, we report that DHEA not only improves egg and embryo numbers, but also egg and embryo quality. UPDATE readers will recall that we since have also been able to demonstrate that DHEA increases pregnancy chances and shortens time to conception. DHEA also makes more euploid embryos available

for embryo transfer, though we do not know yet whether this is due to larger embryo numbers, a decrease in aneuploidy rate, or a combination of both.

In addition to the above mentioned three full-length papers, CHR authors also published two letters-to-the editor in Human Reproduction and five

abstracts in Fertility and Sterility, which appeared in print within the last few weeks. Another five CHR papers are currently in press, which means that they are destined for publication in the near future. An additional 13 manuscripts have been submitted and are in various stages of the peer review process.



Randomized DHEA Studies in Europe

The most exciting news regarding DHEA supplementation is its increasing utilization around the world. We have received positive feedbacks from many countries, including Japan, Israel, Australia and Taiwan. As a consequence, we expect published studies on DHEA from a number of sources.

Maybe even more importantly, we are very pleased to announce that we have concluded a research agreement with the largest IVF center in Austria (Professor Zech), under which we will cooperate with our Austrian colleagues in a blinded, prospectively randomized study of DHEA in Europe.

As we have repeatedly noted on previous occasions, the double blinded, prospectively randomized study is, of course, the best available study format and we are, therefore, very pleased to have gained access to a study population that will allow such a trial, which we hope to start in early 2007.

In the meantime,

we are continuing the active utilization of DHEA in women with physiologically aged ovaries (i.e., women above age 42), premature ovarian aging (POA) and anticipate to publish at least three more follow-up studies during 2007.

Based on an anecdotal report from an Israeli colleague, who allegedly has seen ovarian responses after DHEA supplementation in women with established premature ovarian failure (POF), we have also started looking into the utilization of DHEA in POF patients.

Even though we are skeptical about the success of such an approach, we, nevertheless, feel that it may be worthwhile trying.

If you, or someone you know, are under age 37, have been diagnosed with POF, and are interested in trying a 4-5 months course of DHEA in attempts to reestablish ovarian function, please contact us at 212-994 4400 and ask for an appointment with either Dr. Norbert Gleicher or Dr. David Barad.

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25 YEARS LEADING IN INFERTILITY CARE

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