



THE CHR VOICE

CLINICAL CARE • RESEARCH • EDUCATION

23 Years Leading In Infertility Care

Center For Human Reproduction

Fall 2004, Volume 24

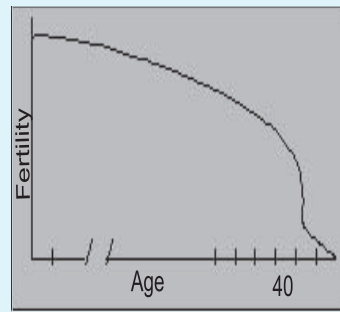
Can we rejuvenate ovarian function? Online Egg Donation

Current dogma holds that the ovarian function of women declines with age. This means that a woman's chance to conceive declines as she ages and that, even years before she enters full menopause, she experiences so-called *functional menopause*, - a period when conception is no longer possible. The accompanying figure to the right summarizes in cartoon format what this means for the average woman: fertility declines slowly until approximately age 37 to 38, when this decline starts to accelerate. After age 40, spontaneous conception, as well as pregnancy after infertility treatment, becomes *difficult*. After age 42, pregnancy becomes *almost impossible* and after age 43 a *miracle*. Using a woman's own eggs, we and others have been unable to ever establish a pregnancy after age 45 that led to delivery.

This decline in female fertility with age has been attributed to the fact that women are born with their eggs and that, from birth, the number of remaining eggs within the ovary constantly declines. In addition, the genetic material within these eggs ages, and as this aging process proceeds, more errors in genetic translation processes take place, resulting in an increase in chromosomal abnormalities in embryos. Since nature is smart, a large majority of these abnormal embryos are not allowed to implant and, consequently,

implantation rates per embryo and, of course, pregnancy rates, decline.

Two medical and physiological dogmas have been at the basis of the professional belief that there was nothing to be done about this aging process



of the female ovary. The first such dogma involved the above listed fact that women are born with all the eggs they ever will have. This dogma was recently called into question when colleagues from Harvard Medical School in Boston, Massachusetts, quite convincingly demonstrated that, at least in the mouse, egg production in the ovary appeared to continue even after birth. (*Nature* 2004; 428:145-150) A second, widely held dogma holds that, as a woman ages, she will, under ovarian stimulation, produce less and less eggs (and embryos) and that this process is one hundred percent irreversible.

We now have developed preliminary evidence at CHR-New York that this dogma may also have been revised. And here is the exciting story that led us towards this discovery:

Imagine that an older woman, who, in accordance with the expectations of her age, produces only very few eggs and embryos, even if her ovaries are stimulated with a maximal dosage of medication, could start taking a medication which, over the span of a few months, would revert her ovaries to the functionality of 20-year old ovaries.

A fantasy? Preposterous?

This would have been our response only a few months ago!

A possibility, probably even likely, is what we have come to believe after a rather unusual journey, greatly helped, and actually initiated, by one of our patients.

This patient came to us when she was almost 43 years old with a request to take her into in vitro fertilization (IVF). She, however, at that point had no intention of conceiving and wanted us to freeze all of her embryos for potential future use. We strongly advised her *against* such an approach because, at age 43, we expected to get only few eggs per IVF cycle. Moreover, at that age, the risk of chromosomal abnormalities in embryos was exceedingly high (at least 60% and, possibly, as high as 90%) which meant that a very large quantity of embryos would have to be frozen. She, therefore, would have to undergo a large number

If no other treatment works any longer, for many women, *egg donation* becomes a wonderful option. The principle question often becomes *where* and *how* to secure a good egg donor. Because the ongoing recruitment of good egg donors requires large human and financial investments (it has to be an *ongoing* process, independent of demand, because donor demand is never predictable and even carefully prescreened donors do not remain available forever), only a very small percentage of IVF programs care to establish their own egg donor pools. Many other programs refer their patients to egg donor agencies which often charge exorbitant fees for their services but, even if they can, they do so at increased costs to the patient. Because of these complexities, even many competent IVF programs simply choose to forego egg donation and either do not offer the service or offer it half-hazardly. To the public, such programs often do not want to acknowledge that they do not have a functioning egg donation program and that they frequently hide behind fictitious waiting lists which in reality are only reflective of an empty donor pool.

At CHR, egg donation has played a central role since it has become apparent that through egg donation, we can offer older women and women with premature ovarian failure the option of becoming biological mothers after all. Egg donation has, therefore, occupied our scientific and clinical interests for almost two decades and we search constantly for ways to improve the experience.

At our website, www.centerforhumanreprod.com, you will find

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Rejuvenate ovarian function(cont. from page 1)...

of cycles to accumulate enough embryos for a reasonable future pregnancy chance. Despite our advice to the contrary, the patient insisted on proceeding and, indeed, in her first cycle, as expected, produced only *one* egg and embryo, respectively.

We once again recommended against proceeding into a second cycle and strongly urged the patient to consider either egg or embryo donation as an alternative. She, however, was insistent on continuing in her approach.

And then something miraculous happened: *As this patient proceeded from cycle to cycle (and as of this point, the patient has undergone nine consecutive, monthly IVF retrievals), in every cycle she produced more and more eggs and more and more excellent looking embryos for cryopreservation. Indeed, in her so far last cycle (the 9th overall), we had to step down the medication dosage from maximal stimulation because, like a much younger woman, in her 8th cycle she had shown signs and symptoms of mild ovarian hyperstimulation. The patient, as of this point, has 66 embryos cryopreserved and has in her last two cycles given us an average of 18 eggs per cycle and allowed us to freeze an average of 13.5 embryos.*

These are numbers which would make a 20 year old proud. For a 43 year old, they are unprecedented!

We were, of course, quite surprised by what we were witnessing until, after her 6th IVF cycle, the patient confided in us that, after her disappointing 1st cycle, she had gone to the internet and had investigated what she could do to improve her ovarian function. In doing her

research, she found two papers. One suggested that acupuncture may have mild benefits for pregnancy chances with IVF (though not really for ovarian function), while the other suggested a mild improvement in ovarian function with the oral administration of an over-the-counter available food additive, called *Dehydroepiandrosterone(DHEA)*. She initiated treatment with both modalities early in her 2nd cycle but, of course, did not tell us out of fear that we might disapprove.

Once she told us, however, we saw a possible explanation for a previous unexplainable observation and immediately researched the literature to see whether we could find any support for the assumption that either one of her two interventions might be contributing to the obvious *rejuvenation* of her ovaries. We found *no* evidence that acupuncture might exert such a radically beneficial influence on ovarian function. However, to our great surprise, we found considerable support for the assumption that DHEA (and possibly other male hormones) might have such an effect.

One swallow, of course, does not make spring and one case in medicine *never* proves a discovery (or, as in this case, also potentially disproves a dogma). Yet, this case is in many ways absolutely unique because this patient conducted a study which, in accordance with good study technique, was "blinded" to the treating physicians since through six IVF cycles, we were unaware of the patient's treatments. In addition, in over 20 years of IVF prac-

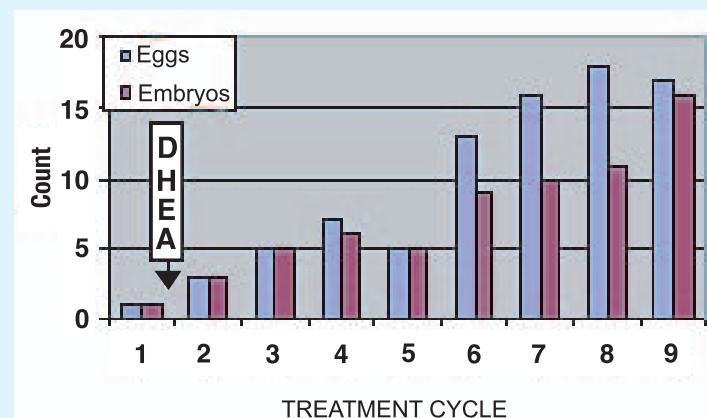
tice, we have never seen *one* patient undergo *nine consecutive* monthly IVF cycles. She, thus, served as her own control patient over a prolonged time period which, in many ways, represents an ideal study protocol. Even though our experience is, therefore, currently still very limited and even though we, therefore, are advising our patients about the use of DHEA with great caution, we are, at the same time, extremely excited and have instigated a number of prospective studies which, hopefully, will confirm the revolutionary effect of DHEA on the ovarian function in older women.

The figure below shows the cycle-to-cycle (horizontal axis) increase in oocyte and embryo numbers (vertical axis) that were obtained from this patient. As the figure also demonstrates, it appears that the maximal effect of DHEA therapy becomes only apparent after at least three to four months of treatment. This may, indeed, be the reason why the one prior report in the literature that had suggested a beneficial effect of DHEA on ovarian function reported only a minor such

effect, not comparable at all to the radical rejuvenation of ovarian function observed in our patient.

If future studies can, indeed, confirm the rejuvenating effect of DHEA on the ovarian function in older women, such a development would be nothing but revolutionary. The aging ovary currently represents the only still unresolved fertility problem. For practically every other problem, in either female or male, reproductive research over the last two decades has found solutions. The only solution for older women or women with prematurely aging ovaries has been egg or embryo donation which, of course, deprives the female of genetic maternity. While a wonderful solution if genetic maternity is no longer possible, every woman would, of course, rather conceive a genetically related offspring. And, in at least some cases, it now appears that we may be in a position to help after all!

If you wish to participate in one of our clinical trials of DHEA, please call our New York Center at (212) 994-4400.



To respond to any specific fertility questions or issues, please e-mail us at tweidner@thechr.com or visit our website at centerforhumanreprod.com and click on contact us.

Certified Medical Education

Medical knowledge changes at an increasingly rapid pace and with such change comes the need for *continuous medical education* (CME). Physicians are now by many state Boards required to obtain a minimum amount of CME hours (or credits) per year in order to maintain their licenses. However, most physicians do not need such prodding by licensing bodies because, by choosing medicine as a career, every physician has essentially committed themselves to a process of life-long learning.

As the pace of change has increased, so has the need for CME and the technology that allows us to offer new knowledge. What once was offered by traditional textbooks and, to a lesser extent, the written journal article, is now increasingly provided by the internet, oral communication via lecture or CD, or the electronic journal. The slide projector has become a relic of the past and the personal computer has become our pen, paper and slide projector, all in one.

Here at CHR, we have taken CME very seriously from the beginning. "Education" is, after all, part of our organizational motto: *Clinical Care-Research--Education*. We, therefore, always have made sure that *all* of our health care providers, whether physicians, clinical or laboratory staffs, receive CME on an ongoing basis allowing them to stay at the cutting edge of knowledge in their respective fields. This is, of course, not only important in maintaining clinical excellence but also in remaining at the cutting edge of clinical research. Therefore, the three parts of our motto are really fully interdependent!

Our strong commitment towards education led us, almost 10 years ago, towards the arduous process of apply to *The Accreditation Council for Continuous Medical Education (ACCME)* in an attempt to become licensed to award CME credits to physicians.

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CHR in the Media

ABC News, May 2004

ABC News' Sylvia Perez recently interviewed CHR's Dr. Norbert Gleicher for a piece on available opportunities in Gender Selection. The article "Boy or Girl, You Choose," available at

www.abc7chicago.com, aired May 25, 2004. This piece covers new technologies, Microsort and Preimplantation Genetic Screening (PGD), created specifically for Gender Selection. These procedures are generally available to couples who are dealing with issues such as the elimination of

genetic diseases or "family balancing. While such procedures are considered to be in their beginning stages, in the interview, Dr. Gleicher is quoted as saying, "We are doing things very responsibly and I think in the end...we are making beneficial steps to society."

CHR News

CHR founder and sole proprietor, Norbert Gleicher MD announced in mid-June the sale of Medical and non-medical assets of the CHR-Illinois operations to The Reproductive Genetics Institute (RGI) and affiliated entities. RGI has been known as one of the leading providers of preimplantation genetic diagnosis (PGD) and its founder, Yuri Verlinksi Ph.D, is considered by many to be the preeminent preim-

plantation geneticist worldwide.

Dr Gleicher will remain affiliated with CHR-IL and RGI for the foreseeable future and will remain, therefore, available to his Chicago patients, though at a reduced schedule. The sale will give him more time to spend on the further development of New York City's CHR and will greatly expand his availability in New York.

Drs Gleicher and

Verlinksi have been professional collaborators and friends for many years and see this asset sale as a unique opportunity to combine their respective strengths to benefit CHR's large patient population. The clinical operations in Chicago will be headed up, as Medical Director, by Ilan Tur Kaspas, MD, who previously worked as a fertility specialist CHR-IL.

Message from a Patient

Starting a family was always something that we assumed would be easy. Unfortunately, that turned out to be untrue. Both of us faced fertility issues and we knew we would have to seek help in our quest to have children.

Luckily, we found CHR. Dr. Barad told us about our options and gave us newfound hope. He took the time to explain the steps and made us feel very comfortable. All throughout the process, the entire staff at CHR was warm and professional, helping us through the tests and

the procedures. We would look forward to coming there and seeing everyone at CHR. They always answered all our questions and put us at ease during this emotional time. They truly helped give us confidence that we were taking the right step and that we could, indeed, have the children we had planned to have.

We knew that many people have to go through IVF many times before a successful pregnancy. We were very fortunate as we were successful our very first time. We are overjoyed that

through the skilled efforts of CHR, we are expecting twins this fall.

We know that there is no way we could have accomplished this without the help of Dr. Barad, Dr. Gleicher and the CHR staff.

Thank you so much for making the dreams of parenthood a reality and making the process easier by being so kind and encouraging during our time at CHR.

*Barbara Clain & Andrew Yaeger
Forest Hills, New York*

Would you like your CHR experience featured in a future edition of *The CHR Voice*? If you are interested in submitting your experience or pictures, please contact the CHR Editorial Office through Contact information on Pg.4

Center For Human Reproduction

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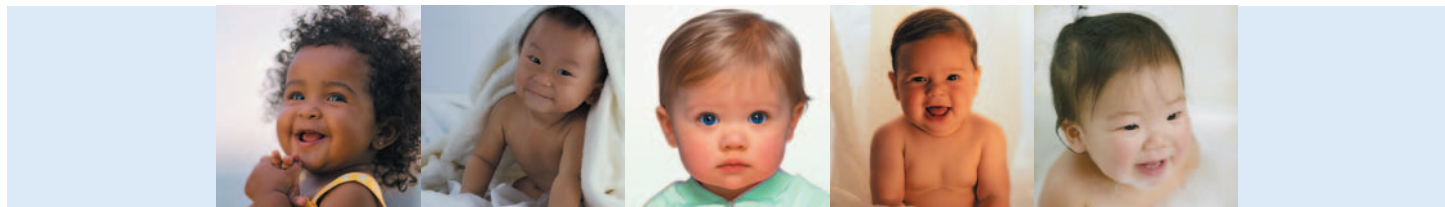
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Certified medical education (cont. from page 3)

Traditionally, only medical schools, hospitals, or educational organizations are granted such accreditation. Yet, as probably the only private (infertility) practice in the country, we succeeded in receiving such accreditation a number of years ago and were reaccredited for a second time last year. We are extremely proud of this accomplishment and have used our status to offer colleagues a CME-program which over the years has become New York's most popular OB/GYN program, with practically every one of our monthly events being oversubscribed.

These monthly events are announced at our website and registration can be done through the internet or by Fax. In an

attempt to improve our communication and education abilities with physicians, we are currently in the process of establishing a reliable e-mail address list. *We, of course, guarantee the absolute confidentiality of e-mail addresses and would never allow their use to any third party.* Physicians in the medical specialties of OB/GYN, Urology, and Family Practice, located in the larger New York metropolitan area who would like to participate in our expanding CME programs are, therefore, invited to contact us by e-mail at kmehta@thechr.com. Once registered with their e-mails, they will automatically receive our future, expanded CME offerings free of charge.

Online egg donation (cont. from page 1)

an automated donor/recipient matching site which allows potential egg recipients from all over the world to enter their egg donor "wish list" (i.e characteristics they are looking for in an egg donor) and the program will immediately show a summary of donors who best match those characteristics. In other words, an Asian-Indian woman, seeking an egg donor of identical ethnicity in San Francisco will immediately know how many such donors are available in CHR's donor pool, instantly being provided with what her options are.

Because we have over 250 prescreened donors in our pool representing almost all ethnici-

ties, religions and other characteristics couples are usually looking for, a majority of couples in need of an egg donor can instantly be matched and will be in an egg donation cycle within four to six weeks from first contacting us.

This huge selection of carefully prescreened donors is probably unmatched anywhere in the world. More importantly, however, by applying the newest web-based techniques to the matching process, we have been able to give patients the optimum in egg donor selection. That is exactly what every recipient couple is looking for once they have made the decision to go to an egg donation.



THE CENTER FOR HUMAN REPRODUCTION
CLINICAL CARE · RESEARCH · EDUCATION

FALL 2004 GRANDROUNDS - NEW YORK
Tuesday, October 12, 2004 @ 6:00 P.M.

Welcome to CHR's second Grandrounds-NY event for the Fall 2004 Season,
A CHR Seminar: Can ovarian aging be affected after all?

We are very pleased to announce the speakers as:

Norbert Gleicher, M.D., Founder and Medical Director, CHR
Adj. Professor, NYU School of Medicine
Visiting Professor, Yale University School of Medicine

Topic: "Evidence that we can positively affect the prematurely aging ovary"

David Barad, M.D., Clinical Director of IVF, CHR-NY
Clin. Assoc. Professor, Albert Einstein College of Medicine

Topic: "Evidence that we may be able to rejuvenate ovaries above age 40"

Objectives: Upon completion of the presentation, the audience will:

1. Understand the process of ovarian aging;
2. Be aware of recent research developments which call into question some longer standing dogmas on ovarian aging;
3. Understand treatment options for aging ovaries.

Etoile

109 East 56th Street
New York, NY 10022
212.750.5656

Cocktails: 6:00 P.M.

Lecture: 7:00 P.M.

Gourmet Dinner: 8:00 P.M.

RSVP by accessing www.centerforhumanreprod.com/newyork_events.php
E-mailing kmehta@thechr.com or Faxing 312.876.1498

Physician's Name _____

Address/City/State/Zip _____

Phone/Fax/E-Mail _____

How did you hear about CHR's Grandrounds-NY? _____

Participants will earn one (1) hour of Category 1 CME credit

*If you are not a physician and wish to attend at your own expense, please contact us.

The Center for Human Reproduction (CHR) is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians. The Center for Human Reproduction takes responsibility for the content, quality and scientific integrity of this CME activity.

This event is sponsored in part by The Foundation for Reproductive Medicine, a not-for-profit organization.