Dr. Gleicher Gives the Prestigious Patrick Steptoe Memorial Lecture

As we reported in the last issue of the VOICE, CHR’s Founder and Medical Director, Norbert Gleicher, MD, was invited to give the 2009 Patrick Steptoe Memorial Lecture to the British Fertility Society on January 7, 2009. We are happy to report here that Dr. Gleicher’s lecture on the assisted reproductive technologies was met with great interest and enthusiasm, but also stirred up some controversy, perhaps because his argument that infertility patients are entitled to maximal IVF pregnancy rates is not as widely embraced in Europe as it deserves. (For a list of media coverage of Dr. Gleicher’s BFS lecture, visit www.CenterForHumanReprod.com/about_events.html.)

While, on first impression, the answer to the question “are patients entitled to maximal pregnancy rates?” may seem like a very obvious one, considering some recent developments, it really isn’t. Take, for example, the widely propagated concept of preimplantation genetic screening (PGS) in attempts to improve IVF outcomes and reduce miscarriage rates. While CHR’s investigators for years have been making the argument that PGS may achieve these goals only in carefully selected cases, and in a majority of situations may actually reduce IVF pregnancy chances1, PGS was widely touted and freely integrated into routine IVF practice by many IVF centers. Indeed, only after a prospective Dutch study demonstrated lower IVF pregnancy rates after PGS2, did regulatory bodies suddenly wake up and start to speak out against the uncontrolled utilization of PGS.

Other examples of new IVF modifications abound; invariably they come with no proven benefits but are characterized by adverse effects on pregnancy chances. They are hoisted upon a largely uninformed, or misinformed, public without proper informed consents, simply because they are considered “worthwhile” by some. One such procedure, to which we have continuously opposed, is the routine single embryo transfer (s-ET). Like PGS, s-ET reduces pregnancy chances per embryo transfer without offering significant benefits in return. CHR investigators recently demonstrated this fact in a number of publications3,4,5. Yet, s-ET is still being widely propagated.

In our opinion, many women nowadays simply do not get maximal IVF treatment, worth their hard-earned dollars. Because most of these pseudo-innovations come from Europe, one cannot be surprised that European pregnancy rates are dramatically lower than those in the U.S., a fact first brought to the public’s attention by Drs. Gleicher, Weghofer and Barad in 2006 and 20076,7.

This questionable trend in contemporary IVF practices, of course, explains why we at CHR continue to fight for maximal pregnancy rates for infertility patients. A question with a seemingly very obvious answer, quite clearly, no longer is that obvious!

4 Gleicher and Barad, Expert Rev Obstet Gynecol 2008; doi:10.1586/17474108.3.4.xx
5 Gleicher and Barad, Gynecol Obstet 2008;13: 77-83
6 Gleicher et al., Hum Reprod 2006;21:1945-50
7 Gleicher et al., Fertil Steril 2007;87:1301-5
Our Continued Work on DHEA Receives World-Wide Response

Aside from the fact that CHR physicians broke all records at last year’s ASRM meeting with twelve presentations, bringing the CHR to the top one percent of all the world institutions in visibility, one of the most satisfying moments was when we received feedback from colleagues from all over the world. These physicians, in previously unprecedented numbers, now have embraced the dehydroepiandrosterone (DHEA) protocol, developed at CHR for women with diminished ovarian reserve, elevated FSH levels and/or simply advanced female age. Both Dr. Barad and Dr. Gleicher were approached by physicians from many different countries, who wanted to share their “DHEA success stories.”

At the ASRM meeting, Dr. Ed Ryan from Toronto, Canada, who had previously collaborated with CHR on a report on decreased miscarriage rates after DHEA supplementation (the abstract was presented at the 2006 ASRM Meeting and a manuscript is in preparation), reported his center’s gender experience after DHEA supplementation. Like we here at CHR, he has observed a considerable shift towards male offspring. This was also the observation made by Dr. Mamas, an investigator from Athens, Greece, who this year reported his center’s DHEA success in Fertility and Sterility. He communicated his center’s gender finding in a conversation with Dr. Gleicher. It appears that CHR’s initial observation that DHEA supplementation shifts the gender balance towards more males may, indeed, be correct.

Breaking New Ground: CHR in Research and Education

First-Ever Grandrounds on Fertility Preservation

As most of our readers know, postgraduate medical education is one of CHR’s major dedications, best demonstrated by regular Grandrounds, which for many years CHR has been sponsoring in collaboration with the Foundation for Reproductive Medicine (FRM) for the Ob/Gyn community of physicians. Fully certified to award continuing medical education (CME) credits by the ACCME, CHR has made these events the best attended Grandrounds in the specialty in New York City.

Our very rapid growth in fertility preservation in 2008, however, mandates an expansion of targeted physician populations for our Grandrounds. Since obstetrician/gynecologists are usually not the ones to diagnose malignancies in young females, our postgraduate educational activities have to expand to those medical specialties that do. This, of course, primarily includes pediatric and adult oncologists, but also oncologic surgeons, hematologists and even rheumatologists. All of these specialties routinely face clinical situations that force them to administer treatments, which affect female and male fertility potential. We now see it as our added responsibility to educate colleagues in all of these specialties about the availability and time-sensitivity of fertility-preserving techniques for their patients.

A first very successful CHR Grandrounds event for non-Ob/Gyns was held on September 23, 2008, with Dr. Kutluk Oktay (pictured here) presenting a general update on fertility preservation. Future events are in the planning stages for the new year 2009 as well; stay tuned!

AMH a Better Tool to Assess Ovarian Reserve than FSH?

In 2008, CHR researchers made great progress in the use of Anti-Müllerian Hormone (AMH) as a tool in assessing ovarian reserve. Here, research led by Drs. David Barad (pictured here) and Kutluk Oktay in two independent areas led to surprisingly similar conclusions: Dr. Barad has been investigating how well AMH could predict ovarian performance in IVF. He and his co-investigators were able to demonstrate that AMH was a much better predictor of oocytes (egg) yield and pregnancy rates than follicles stimulating hormone (FSH), but these predictive abilities were much better in normally functioning ovaries than in ovaries with diminished ovarian reserve (Barad et al. Fertil Steril; in press).

Dr. Oktay in parallel investigated the use of AMH in women who had received chemotherapy for various cancers. Chemotherapy, of course, greatly affects ovarian function and, indeed, can put patients into full menopause. He and his co-investigators also were able to confirm that AMH correlates very well with ovarian function; but, like Dr. Barad in regular infertility patients, Dr. Oktay demonstrated that the ability of AMH to reflect ovarian function decreases as ovarian function becomes abnormal, in this case as a consequence of chemotherapy. (A manuscript has been submitted for publication.)

Both studies suggest that AMH under normal circumstances is probably a better indicator of ovarian function than FSH, but loses this ability as ovarian function becomes abnormal. These findings furthermore suggest that AMH can also be used as a parameter to assess egg quality.
CHR’s Effort in Identifying POA Risk Factors Extends Hope

Investigators at CHR recently identified two high risk groups for premature ovarian aging (POA): women with abnormal triple CGG counts on the FMR1 (fragile X) gene and women with abnormal autoimmune function (Gleicher et al., Fertil Steril doi:10.1016/j.fertnstert.2008.01.098. and Gleicher et al., Fertil Steril doi:10.1016/j.fertnstert.2008.01.099). The FMR1 gene, in particular, has been one of the main targets of research at CHR for about two years, and we have made considerable progress.

In brief, the number of CGG repeats on this gene directly relates to the risk of developing premature ovarian failure (POF). While this has been known for some time, we were the first to demonstrate that not only POF relates to excessively high CGG repeats, but milder forms of ovarian senescence (premature ovarian aging; POA) do so as well. Moreover, we have been able to confirm that the risk for POF and POA increases as the repeat counts deviate further from the apparent norm (29-30 repeats) in either direction (high or low counts). These findings have an obvious clinical significance: in addition to more accurately diagnosing infertility, we may be able to predict the future fertility of young women.

Risk for POA, of course, does not denote that everybody will develop POA. Young women identified to be at risk should, however, be carefully monitored. Annual ovarian function tests with FSH and AMH evaluations, if done age-specific, will allow for the early identification of those who really are developing POA. For such women fertility preservation may then represent a very good idea.

It goes without saying that the younger she is at the time of fertility preservation, the better the result. This is important to recognize because the younger the eggs are at the time of cryopreservation, the higher their pregnancy chances, once they are thawed out, whether as eggs or embryos.

POA can be familial. In other words, daughters of women who experienced early menopause (normal age is ca. 52), are also at an increased risk for early menopause. A history of early menopause usually reflects a history of POA. Since women in past generations had children at much younger ages, POA did not represent as much of a clinical infertility problem as it does today. Women who experienced early menopause are, therefore, well advised to encourage their daughters to have their ovarian functions tested at relatively young ages. With the addition of the Institute for Fertility Preservation, CHR is now in an excellent position to offer future fertility options for young women who are identified as carrying high risk of developing POA later in life.

No Need to Break That Piggy Bank!

In view of recent world-wide economic events, we in 2009 expect to see significant differences from prior years: In difficult economic times, even those lucky enough to maintain their employment often see benefits cut. Often, amongst the first to go are fertility or even general medical benefits. We, therefore, anticipate that many amongst our patients will financially be even more challenged by the significant expenses of fertility treatments this year, and are committed to assist wherever and whenever we can be of help.

This may, therefore, be the right time to remind our patients of our income-based discount program. In consideration of the high costs of infertility treatments, CHR offers significant discounts on regular fees to patients/couples below a generous income ceiling. If you don’t have insurance coverage for fertility services, and if fertility treatments unreasonably stretch your financial resources, then speak to our staff. The front desk staff will advise you of our discount program and the clinical staff may be able to help you with the costs of fertility medications. There is nothing wrong with asking for help; we are here to help!

Oldest Embryo Ever

In the context of elective fertility preservation, we recently cryopreserved an embryo from a 49-year and 11-month old woman, which very likely is the “oldest” human embryo ever cryopreserved. Indeed, we were unable to find evidence in literature that a human embryo was ever produced in a woman of this age. This, therefore, very likely, is not only the “oldest” human embryo ever cryopreserved, but also the “oldest” human embryo ever produced by a clinical fertility center.

This patient came to us, while already in an ovarian stimulation cycle. We were able to retrieve one oocyte, which was normally fertilized. It, by day three after fertilization, progressed to a good quality embryo, fulfilling our center’s criteria for cryopreservation.

Based on her age and the potential negative effects of cryopreservation, she is fully aware of her small chances of conception. She has initiated DHEA treatment and is planning on further cycles, when her life as a mother of older children can accommodate pregnancy.
2008 was truly a remarkable year for the media’s attention to CHR. In July, Dr. Gleicher’s lecture on twin pregnancies at the ESHRE meeting stirred considerable controversy in the British press. Shortly thereafter, national news shows such as Today Show and Early Show prominently featured CHR doctors (Dr. Oktay for fertility preservation; Dr. Gleicher for DHEA). Media coverage of CHR was not limited to broadcast media: Newsweek ran a story on Dr. Oktay’s work on fertility preservation for cancer patients. Links to these media pieces are available at our website, www.CenterForHumanReprod.com/about_events.html.

With the realization that educating not only patients but also the public at large is critical to CHR’s mission, we are working on enhancing our presence in the audiovisual arena. Preliminary videos have already been posted on our website, and more are in the hatching for 2009. These video pieces, primarily on cutting-edge infertility treatments, are designed to educate the public in a manner more approachable, perhaps, than written text.