Our lead article this month is dedicated to the annual Foundation for Reproductive Medicine Conference (FRMC), which CHR for the third year in a row proudly co-sponsors here in New York City. Likely because in comparison to most other U.S. cities the organization of conferences in NYC is much costlier, FRMC is now the only international annual event in the city in the areas of reproductive medicine and biology, this year again presenting over 30 speakers from all over the world. For the first time this year, however, the conference also offers on Sunday afternoon, November 18, a half day of lectures and comments from some of the leading experts in infertility, specifically directed at patients. This “Clinical Fertility Day for the Public” includes an interactive Q&A session with the experts on panel. If successful, the plan is to make this Clinical Fertility Day for the Public a steady feature of the conference because, as we will discuss in our lead article, the ultimate goal of this annual conference is the betterment of clinical care in reproductive medicine.

Continuing Education

Gearing up for the annual Foundation for Reproductive Medicine Conference (FRMC)

- The third FRMC opens on November 15 with workshops and concludes with Clinical Fertility Day for the Public.

If there is a “craziest” month in the year for CHR, then for the last three years November clearly qualified. It is now the third year in a row that CHR co-sponsors with the Foundation for Reproductive Medicine (and this year for the first time also with the New Hope Fertility Center in NYC) an international conference on Reproductive Biology and Clinical Reproductive Medicine and Infertility in that month (this year November 15-18), which in only a few short years among an ever-increasing number of conferences, still, succeeded in developing a remarkable following because of its unique concentration on innovative translational ideas.

The first two weeks of November, therefore, are hectic because of last minute organizational preparation for welcoming over 30 speakers from all over the world and making sure that the hotel venue is well prepared for all contingencies. Most of the third and fourth weeks of the month are taken up by the conference and hosting a large number of visitors from all over the world who attend the conference and want to take the opportunity to visit CHR.

The basic concept of the FRMC from the very beginning was that by bringing together in one room leading basic scientists and clinicians, who in the preceding year produced interesting and innovative new research, the audience will not only be informed about where the cutting edge of knowledge in the field currently lies but, often, significantly before these materials appear in peer reviewed medical journals.
The first-ever event for fertility patients and advocates to interact directly with leading experts, gain insights into the most cutting-edge treatment innovations and make lasting connections, in conjunction with the 3rd Translational Reproductive Biology and Clinical Reproductive Endocrinology conference of the Foundation for Reproductive Medicine.

<table>
<thead>
<tr>
<th>Time</th>
<th>Session Topics &amp; Speakers</th>
</tr>
</thead>
<tbody>
<tr>
<td>2:00 pm</td>
<td>Fertility preservation: When should a woman worry about her future fertility, and what are her options? Vitaly A. Kushnir, MD</td>
</tr>
<tr>
<td>2:20 pm</td>
<td>Is IVF the best first treatment for all infertility? Pasquale Patrizio, MD, MS</td>
</tr>
<tr>
<td>2:40 pm</td>
<td>Is there evidence-based treatment for implantation failure? Neeta Singh, MD</td>
</tr>
<tr>
<td>3:00 pm</td>
<td>Is there clinical value in testing embryos for chromosomal abnormalities before transfer? Norbert Gleicher, MD</td>
</tr>
<tr>
<td>3:20 pm</td>
<td>Highly Individualized Egg Retrieval in older women and younger women with Premature Ovarian Aging David H. Barad, MD</td>
</tr>
<tr>
<td>3:40 pm</td>
<td>Coffee Break Light refreshments will be served.</td>
</tr>
<tr>
<td>4:00 pm</td>
<td>Endometriosis: An anatomical, endocrinological and immunological condition Norbert Gleicher, MD</td>
</tr>
<tr>
<td>4:20 pm</td>
<td>Precision ovarian preparation for customized IVF John Zhang, MD, MSc, PhD</td>
</tr>
<tr>
<td>4:40 pm</td>
<td>Is there male fertility treatment beyond ICSI? Sherman J. Silber, MD</td>
</tr>
<tr>
<td>5:00 pm</td>
<td>An expert panel answers questions David H. Barad, MD, MS</td>
</tr>
</tbody>
</table>
Commercialization of IVF

Prominent IVF center announces PGS/PGT-A 4.0

Yet another innovation cannot overcome fundamental fallacy

It is hard to believe but, as Ellie Kincaid, an Assistant Editor at Forbes in the last issue of the magazine reported, what we here at CHR have only been joking about, has in fact happened: The 4th consecutive version of PGS/PGT-A (PGS/PGT-A 4.0) has been introduced to the market place.

Following a by now well-rehearsed pattern of bringing to market a new version of PGS/PGT-A whenever the pressure against further utilization of the procedure mounts, the Colorado Center for Reproductive Medicine (CCRM), which in recent years has branched out all over the country with satellite centers, including in New York City, announced that the center now offers “non-invasive” PGS/PGT-A (4.0) for clinical use that does not require embryo biopsy because, whether an embryo is chromosomally normal or not, will now be determined from testing spent media in which embryos have been cultured.

This idea has been around for a few years and the VOICE, really jokingly, predicted that this new “hypothesis” would likely become the next version of PGS/PGT-A. As a number of laboratories, however, started reporting very disappointing correlations between chromosomal assessments of media and embryo biopsies, we started believing that our suspicion would not be realized after all. But here we go again, because the PGS/PGT-A industry, simply, never disappoints:

Obviously increasingly desperate as the opposition to embryo biopsy required for PGS/PGT-A, to significant degrees, damages an embryo’s implantation potential. PGS proponent, of course, have been claiming that embryo biopsy does not damage embryos (as they did claim with PGS 1.0 until they started pushing for PGS 2.0 and PGS 3.0 and, suddenly, discovered that embryo biopsy in PGS 1.0 had, indeed, caused damage).

Paulson is, of course, correct because it has been known for decades that how many times an incubator door is opened relates to an embryo’s chances of implantation (the more openings the lower the implantation chances). How anybody with any understanding of embryo culture can then claim that biopsying an embryo’s trophectoderm and removing a whole bunch of cells (5-7 on average) while letting the embryo breath room air, does not affect implantation, is quite mind-blowing. But, then again, who can be surprised by yet another completely baseless and unsupported claim from the PGS/PGT-A industry? The whole evolution of this test/procedure has been built on illusive claims, never validated promises and, of course, in clinical practice in over 20 years never proven efficacy, as ASRM and SART recently again restated.

So, now, according to Forbes, CCRM announces through their spokesperson Mandy Katz-Jaffe, PhD, that their center “developed a protocol in-house that is ready for prime-time release clinically.” She is also quoted as saying that “the largest risk factor for an aneuploid embryo is the mother being older than 35,” and claiming that “other randomized trials and meta-analyses have absolutely shown higher pregnancy and live birth rates with preimplantation genetic testing of embryos.” The latter two statements are obviously absolutely incorrect because the studies Katz-Jaffe is referring to were performed in highly selected women with very good prognosis and excluded poorer prognosis patients from consideration, a reporting technique CCRM is well known for, and which artificially inflates to significant degrees a center’s outcome reporting, as CHR investigators last year reported in detail [Kushnir et al., Reprod Biomed Online 2017;35(2):161-164].

Which leaves Katz-Jaffe’s new claim of having a new non-invasive clinically PGS/PGT-A system ready for clinical use and “ready for prime-time.” Her words were not accidentally chosen because the first major paper CHR investigators in 2008 published, speaking up against utilization of PGS 1.0 in
Introducing CONFLAM Forte™, new from Fertility Nutraceuticals, LLC

The only comprehensive inflammation-modulating nutritional supplement, designed specifically to improve female fertility*

- **CONFLAM Forte™** is the only comprehensive female fertility supplement designed to calm down immune systems that have become hyperactive due to inflammation*.
- **CONFLAM Forte™** was designed in consultation with the Center for Human Reproduction (CHR), a fertility center in New York City with special expertise in immunology of reproduction. CHR also endorses the product.
- Every batch undergoes a rigorous triple-step quality assurance process.

### Causes of excessive inflammation

- Obesity
- Infections
- Autoimmune diseases
- Allergies
- Others

### Effects of excessive inflammation on female fertility

Excessive inflammation can make the immune systems hyperactive, negatively affecting women's fertility. Infertile women also demonstrate a higher prevalence of excessive inflammation, which can reduce pregnancy rates and increase miscarriage risks. Physicians and patients are often unaware of immune system hyperactivity, because it can be completely asymptomatic.

### Also from Fertility Nutraceuticals

<table>
<thead>
<tr>
<th>Also from Fertility Nutraceuticals</th>
<th>FERTINATAL® DHEA for Women</th>
<th>OVOENERGEN™ CoQ10 for Women</th>
<th>ANDROENERGEN™ CoQ10 for Men</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trusted by leading specialists</td>
<td>Endorsed by Center for Human Reproduction (CHR)*</td>
<td>Endorsed by Robert F. Casper, MD*</td>
<td>Widely recommended by leading urologists</td>
</tr>
<tr>
<td>Fertility-specific designs*</td>
<td>75 mg/day of micronized DHEA supports egg development via an androgen-rich ovarian environment*</td>
<td>999 mg/day of CoQ10 in oil-suspended softgels provides antioxidant protection and supports robust mitochondrial energy metabolism in healthy gametes*</td>
<td></td>
</tr>
</tbody>
</table>

**Available directly & exclusively from Fertility Nutraceuticals**

www.FertilitySupplementStore.com

Nutraceuticals for the next generation

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease. *Fertility Nutraceuticals, LLC, pays licensing fees to CHR and Dr. Casper.

“Rx” pad orders & wholesale inquiries:
(212) 628-0851 - info@FertilityNutraceuticals.com
21 E 69th Street, New York, NY 10021 USA
We previously reported in the pages of the VOICE that the infertility industry all over the world is in a race toward consolidation. The concept of establishing nationwide medical practice networks actually first arose in the 1990s when, literally overnight, multi-billion dollar practice networks were bought up by investors, with the idea of serving a quickly consolidating medical insurance industry, which in only a few short years had radically reformed itself from being run by regional medical insurance companies to national players, as bigger insurance companies swallowed up smaller ones or merged to create a size more appealing to investors.

What later on Wall Street was called the “physician practice management bubble,” ended as quickly as it had started after two of the leading practice management companies reported disappointing earnings. Within less than a year, billion-dollar companies had disappeared, and many investors were left with egg on their faces.

Consolidation of medical practices became in the U.S. again popular when Obamacare introduced the concept of comprehensive provider networks, including hospitals and physicians, as contract combined partners for insurances and government. Hospitals, especially in big cities, therefore, started buying up private practices all over the country, resulting in some cities in the almost complete disappearance of private practice.

Because this model was expected to result in cost savings, hospitals were expected to unify practice patterns following agreed-to standards of care, also alleged to improve quality of care. As so often is the case, things did not always work out as expected: Cost savings were not really possible when many services, previously performed in private offices, were moved into hospitals, where hospitals’ additional overhead charges (which the government allows) actually increased costs. It, therefore, remains to be seen how this experiment with the U.S. healthcare system will work out. Our prediction is that within a few short years we will experience a substantial physician deficit in private practice, and physicians will, once again, leave low paying hospital employments and reopen private practices.

But this is not meant to be the subject of this communication. Here, we, specifically, want to concentrate on what is happening in the infertility arena because almost no week passes without yet
another U.S. IVF center having sold out to outside non-physician investors. This trend in infertility practice first started and peaked in Australia and New Zealand, where now only three companies control almost 100% of the IVF market. Since this consolidation has taken place, IVF live birth rates in Australia and New Zealand have plummeted, currently standing at approximately 15% of IVF cycle starts (less than half of U.S. rates).

Concomitantly, costs of IVF services have increased for a variety of reasons, not the least because of introduction of “add-ons” to routine IVF, which do not, as promised, improve IVF outcome, and in some patients actually decrease pregnancy and live birth chances. If one follows Australian media reports, the public also appears increasingly dissatisfied with IVF services.

Entry of investor money into IVF practice in Australia/New Zealand apparently negatively affected outcomes and, at the same time, also raised costs. This, of course, should not surprise. After all, after outside investments, IVF centers not only, as before, must earn the upkeep of staff and other expenses but, must service the debt of the investment and demonstrate profit. As purchasers of IVF practices in the 1990s quickly noticed, that can be extremely difficult because financial incentives for physicians rarely work if they are guaranteed a reasonable base salary. As a consequence, at least in the 1990s, revenues usually decreased in first years after purchases by as much as a third.

Considering what happened in the 1990s, one would expect investors to be aware of this risk and cautious in their practice purchases. Interestingly, some we spoke to were not! Who fails to study history is, of course, destined to repeat the same mistakes and this is, as we believe, currently happening.

Investors cannot afford declines in revenue because such a development immediately debases their investment. As a consequence, medical practices are under tremendous pressure to develop new revenue sources, and this is where above-noted “add-ons” come into play. Once that happens, IVF cycles, which are already prohibitively expensive, significantly increase further in costs without benefit for patients and, in many cases, actually resulting in reduced pregnancy chances.

The IVF field is not alone in demonstrating these negative effects from investor-driven consolidations. Another area in medicine that is perceived by Wall Street as a similarly favorable target for consolidation, is dermatology. Lo and behold, a huge scandal just broke in the New York Times a few days ago. (David E. Sanger, New York Times October 27, 2018, page B1): Like in the IVF field, large sums have been spent by investors in buying up private dermatology practices. Early in October the Journal of the American Academy of Dermatology (AAD) published on its website a study that had investigated the consequences of this development. Once an article is peer reviewed and appropriately revised, it may be accepted for publication. When this
happens, the paper is considered “in press” and usually appears in print within a few weeks to months.

In this case, however, the already accepted “in press” paper, suddenly, disappeared from the website and, when authors and others started to inquire why and how that could have happened, no reason was given.

As it turned out, the editor of this prestigious journal found himself under tremendous pressure from private equity firms that had invested in the field and from prominent dermatologists, some in the highest ranks of the Academy after the paper appeared on the journal’s website because, as observed in association with IVF, dermatology practices also demonstrated immediate negative outcome effects once they were under control of outside financial investors. One of the findings was that investors primarily acquired practices that were billing outliers, i.e., billed more than other practices. Moreover, once acquired, many practices opened their own pathology labs, creating an opportunity for further expanded billing.

This undue influence of financial interests on practice, of course, does not only exist in dermatology. The IVF field has been experiencing it for years, and we on a number of prior occasions pointed out obvious conflicts of editors of medical journals in our field, which affected which papers were or were not accepted for publication. Similarly, economic influence of investors must be anticipated. After all, their obligation toward their stake holders is profit and improving valuations for their investments. It remains the physicians’ responsibility to protect patients when all of the changes are happening.

And this is where, in our opinion, the field has failed, not only in Australia and New Zealand but also in Europe, Asia and here in the U.S. We are writing this article because in this country we are still at the relative beginning of these changes, though they are speeding up quickly. The table summarized New York-area practices that now are under investor management or strong investor influence. Remarkably, even the New York University Langone Fertility Center has recently joined one of the biggest investors in the field, Prelude Fertility.

Another reason why we here at CHR are skeptical about this investment boom in IVF is, paradoxically, that insurance coverage for IVF is expanding. Insurance reimbursement rates, however, have not increased in over a decade and, indeed considering inflation, have significantly declined. It, therefore, is very difficult to even cover costs of IVF cycles, when reimbursements only come from insurance companies.

And this is yet another reason why above twice noted “add ons” come into play. They usually are not covered by insurance and, therefore, clinics are free to charge even insured patients for their use. An IVF cycle reimbursement of, let’s say $4,500, then can easily grow to $8,500, if PGS/PGT-A, for example, is added to the cycle together with additional “add-ons.” Many IVF centers, especially those who serve many patients with IVF insurance coverage, therefore, have become financially dependent on “add-ons” to remain economically viable, even if they do not improve IVF outcomes and, sometimes, even may lower pregnancy and live birth chances.

Since we believe that most useless “add-ons” are under increasing pressure (PGS/PGT-A...)

Table 1: New York region IVF centers with outside investment ownership

<table>
<thead>
<tr>
<th>Center</th>
<th>Buyer</th>
<th>Year</th>
<th>Financing</th>
</tr>
</thead>
<tbody>
<tr>
<td>NYU Langone Fertility Center</td>
<td>Prelude Fertility</td>
<td>2018</td>
<td>Lee Equity Partners</td>
</tr>
<tr>
<td>RMA-NJ</td>
<td>IVI-Spain</td>
<td>2017</td>
<td>IVI/RMA-NJ Global*</td>
</tr>
<tr>
<td>Sher Fertility Institute</td>
<td>IntegraMed</td>
<td>2015</td>
<td>Segard Holdings</td>
</tr>
<tr>
<td>The Colorado Center for Reproductive Medicine</td>
<td></td>
<td>2015</td>
<td>TA Associates</td>
</tr>
<tr>
<td>Extend Fertility</td>
<td></td>
<td>2016</td>
<td>North Peak Capital</td>
</tr>
<tr>
<td>New England Fertility</td>
<td>Prelude Fertility</td>
<td>2017</td>
<td>Lee Equity Partners</td>
</tr>
</tbody>
</table>

*IVI/RMA-NJ Global claims to be the biggest IVF network in the world with 2400 employees, including 200 MDs and 300 research scientists, in 70 clinics in 13 countries.
Because of the unique patient population CHR serves, our center, fortunately, is not under these economic pressures and can afford to offer our patients the treatments they need, and not treatments that run up cycle revenues. With only less than 15% of CHR’s patient revenue coming from insurance company payments, we are in a position to charge for CHR’s services commensurate with the costs of our services. Since over 90% of our new patients come to CHR after they have had, usually multiple, failed IVF cycles elsewhere, they quickly recognize the differences between CHR’s treatment approaches and what they had experienced before, and between CHR’s and others’ service levels.

Our healthy margins also permit us to offer generous income-based discounts for patients without insurance coverage for IVF and for active duty military personnel.

CHR’s long-term strategy is, therefore, no secret: The more other IVF centers are absorbed into these rapidly expanding commercial clinic chains, the more CHR’s services will be needed and appreciated because CHR’s individualized approaches to fertility treatments, simply, cannot be replicated in a chain-clinic organization.

---

**Letter from a Patient**

“There is nothing more that I can do for you. The only way you have a chance of getting pregnant is with using donor eggs.” Thinking about the day these words were said to my husband and I still brings tears to my eyes. But that is all they are: words.

I’ve never been one to give up easily and those words led me to begin my own research, which resulted in finding Dr. Gleicher and his team at CHR. From the first phone consultation, Dr. Gleicher’s confidence and knowledge were clear. He did not agree with my diagnosis and ordered testing to confirm. And so our journey began.

It wasn’t always easy, consulting with doctors in New York, while living in Michigan, but the team at CHR did everything they could to help us through the process. The team had one goal and that was to safely get us a healthy baby.

And they did! It didn’t happen overnight, and at times it felt as if it might not happen at all, but through it all, we knew that if we had a chance, it would be with this team of doctors. In April of 2018, my husband and I welcomed our healthy, beautiful, perfect daughter, Kaisa, into the world.

I am so grateful that we found Dr. Gleicher and CHR. CHR truly changed our lives. It saddens me to think that there are others out there who have received an incorrect diagnosis, and I hope that by sharing my story, maybe I can help just one person.

Carrie Cohoon
Questions from the Public

1. Is it worthwhile trying to reduce FSH levels?

This is one of the most frequently asked questions at CHR since almost all of our center’s patients present with elevated FSH levels. And the answer in an overwhelming majority of cases is, no, it is not worthwhile to attempt to reduce FSH levels.

Some colleagues believe that IVF cycles with lower FSH values have better outcome chances than cycles with low values. We don’t believe this to be the case, and the principal reason is obvious: FSH is not the disease; high FSH levels are only the symptom of poor ovarian function. Lowering the FSH (which can be done easily in a few short days by raising estrogen levels) will treat the symptom and not the disease. It’s like treating the fever in an infection with aspirin, instead of treating the causative bacteria with an antibiotic.

The belief that high FSH must be lowered before an IVF cycle can be initiated, causes an additional problem: Many physicians use this argument to delay cycle starts in women in whom they don’t really want to initiate cycles (i.e., poorer prognosis patients). Since time is a significant enemy in women with low functional ovarian reserve (LFOR), any unnecessary delays in starting treatment must be avoided, including this one.

On a side note, FSH levels are also much less predictive of dehydroepiandrosterone (DHEA) positive effects than AMH levels. While AMH quite frequently improves with DHEA supplementation, FSH levels drop much more rarely. The reason is that FSH levels are also strongly influenced by estradiol levels and AMH is not.

2. Can IVF outcomes be predicted based on FSH and AMH levels?

To a certain degree, yes, IVF outcomes can be predicted based on FSH and AMH levels. However, unfortunately, this is true only in limited ways. Lower FSH and higher AMH are always predictors of better IVF outcomes than values at the opposite range, but by far the most important predictor of IVF outcome is female age (or the age of an egg donor). The “younger” the eggs, of course, the better!

Here is a good example: If a 22-year-old female presents with FSH of 20.0 mIU/mL (at this age, a normal level should be below 7.0), the patient’s LFOR is, of course, of concern, but with appropriate treatments this patient still has an extremely favorable prognosis with use of her own eggs at CHR. If, however, a 46-year-old woman presents with the exact same FSH of 20.0 mIU/mL, her prognosis will be much poorer. Again, the reason is simple: As women age, the chance declines per egg and/or embryo to achieve a pregnancy. We, therefore, compensate by transferring more embryos into the uterus. However, a 46-year-old woman with FSH 20.0 mIU/mL will produce only very few eggs, often not enough to give her a reasonable pregnancy chance.

To a degree, similar considerations also apply to AMH values, but even extremely low AMH values do not have the same negative connotation as high FSH values do. Again, especially in younger patients, we have established hundreds of healthy pregnancies even in women with no detectable AMH.

3. Why does CHR not use the antral follicle count (AFC)?

Many colleagues, especially in Europe, frequently use the so-called antral follicle count (AFC) to assess functional ovarian reserve (FOR). As AFC denotes in its name, it represents an assessment of the so-called antral follicles in both ovaries. Although antral follicles are the smallest follicles visible on ultrasound, they represent quite an advanced stage of follicle maturation. Indeed, they are already beyond what is called the small growing follicle stage, where DHEA and human growth hormone (HGH) are effective in affecting the number and quality of the eggs.

The AFC has been demonstrated to correlate reasonably well with FSH as well as AMH levels in determining FOR. At CHR, our studies have, however, suggested that the sonographic assessments of AFCs differ too much between...
physicians. This does not mean that CHR does not look at AFCs and often even records them but CHR does NOT use AFCs to determine stimulation protocols for each patient. Instead, the reliance is on FSH, AMH, estradiol levels and very accurate follicle size assessments. The latter has in recent years gained additional importance because of Highly Individualized Egg Retrieval (HIER), which, considering CHR’s patient population, now a majority of the center’s patients are treated with.

Should we freeze all embryos and transfer them later?

Over the last few years some colleagues have started to propagate the so-called all-freeze protocol for most, if not all, IVF cycles. What they mean by that is embryos should practically never be transferred in a fresh cycle because, based on their hypothesis, the endometrium in stimulated cycles is much less favorable to implantation than in natural cycles.

We have addressed this hypothesis before in the VOICE, concluding that the studies on which this hypothesis was based on where statistically highly inappropriately manipulated. Certainly in poorer prognosis patients, including older women, we feel that all-freeze cycles can to significant degrees negatively affect IVF outcomes because eggs from older women (and embryos made from these eggs) do not freeze and thaw as well as those from younger women. CHR, therefore, views unnecessary embryo freezing as “giving pregnancy chances away for no good reason.”

Poorer prognosis patients, of course, can afford this much less than better prognosis patients, who often produce excess embryos and where loss of some embryos really does not as much matter.

CHR considers all-freeze cycles yet another “fashion-of-the-moment,” which more harms than benefits. It is also an additional example for what, unfortunately, is just too common practice in our specialty, which is investigating treatments in highly selected (and usual good-prognosis patients) and then applying the results of those studies to all patients. In most IVF centers good prognosis patients represent only approximately 20% of all patients. In other words, in the other 80%, such “fashions-of-the-moment” either offer no benefits or even cause harm to IVF outcomes, as in this case.

There is also another reason why all-freeze cycles have become popular in some IVF centers and that reason is that all-freeze cycles allow for relatively easy manipulation of a center’s IVF cycle outcome reports. As CHR investigators not too long ago demonstrated, some of the most prominent IVF centers in the nation are among the most profound abusers of the embryo-banking (another term for all-freeze cycles) loophole [Kushnir et al.; Reprod Biomed Online 2017;35(2):161-164]. When their real outcomes were analyzed excluding embryo banking cycles, those centers actually demonstrated lower live birth rates than the median rates of all other IVF centers.

There is also another reason why all-freeze cycles have become popular in some IVF centers and that reason is that all-freeze cycles allow for relatively easy manipulation of a center’s IVF cycle outcome reports. As CHR investigators not too long ago demonstrated, some of the most prominent IVF centers in the nation are among the most profound abusers of the embryo-banking (another term for all-freeze cycles) loophole [Kushnir et al.; Reprod Biomed Online 2017;35(2):161-164]. When their real outcomes were analyzed excluding embryo banking cycles, those centers actually demonstrated lower live birth rates than the median rates of all other IVF centers.

OPEN POSITIONS

Both require professional and pleasant demeanor, good interpersonal and communication skills and ability to multitask.

Please submit resume to Ms. Jolanta Tapper at jtapper@thechr.com for consideration.

Clinical Coordinator/Nurse: RN/NPL or equivalent to join our excellent team of IVF coordinators. Prior IVF experience and knowledge of a foreign language preferred, but we will train the right individual. This position involves a large amount of close and independent interaction with patients. We offer a highly collaborative work environment between physicians, clinical coordinators and embryology staff, competitive salaries and benefits as well as opportunity to participate in research.

Medical Assistant: Must have at least one year of clinical experience and be able to draw bloods, assist physicians during ultrasound and pelvic exams. This is a full-time position. Must be available to work on a rotating basis late afternoons and weekends.

CHR is seeking a qualified physician with proven research interest to join the center’s team of clinicians and biologists. Commensurate with qualifications, appointment are available at junior, assistant, associate and senior scientist levels.

CHR offers competitive salaries and benefits, coupled with strong incentives linked to research efforts and publication success. In combination with the freedom of a private practice set-up, this position offers a unique opportunity for individuals interested in exploration of the unknown and in pursuit of discoveries suitable to quick translation into clinical practice.

The position is available immediately.

Please submit CV to Ms. Jolanta Tapper at jtapper@thechr.com for consideration.
Based on most recent publications, the conference presents in a single room the year’s Who’s Who in reproductive biology and clinical reproductive medicine for an authoritative annual update on newly evolving paradigms in basic sciences and clinical medicine. A conference like the FRMC, simply, does not exist anywhere else in the world, which is why we have been welcoming hundreds of attendees from over 40 countries to NYC every year. FRMC offers both clinicians and scientists a unique and intimate framework for interactions and exchanges of ideas.

The 3rd annual meeting of the FRM to stimulate paradigm changes and translational collaborations among basic scientists and clinicians in reproductive medicine

4 Pre-Conference Workshops
- Egg donation is only a second-best choice: What can be done to offer patients best outcomes with their first choice, their own eggs?
- Avoiding unproven add-ons, and getting back to the basics in IVF
- Is it “fresh” or is it “frozen,” and is it “slow-freezing” or “vitrification?”
- From the Brivanlou Laboratory at Rockefeller University, seeing human embryos like never before

Main Conference Sessions
- **Breaking News Lecture:** Understanding the fragile X mental retardation 1 (FMR1) gene better further enhances its importance | Ethan J. Greenblatt
- Where our journey is leading to: Parts I-V
- Paradigm Change I: Clarifying the significance of chromosomal abnormalities in human embryos
- Paradigm Change II: Changing the thinking about PCOS
- Debate: When is the right time to refer a patient into egg donation?
- Paradigm Change III: Individualizing IVF practice for best outcome by age and functional ovarian reserve
- Hidden treasures discovered
- Most interesting ESHRE and ASRM Presentations
- Yet Unpublished Data
- **FRMC Closing Lecture:** Will human embryos fly? | Ali H. Brivanlou

This activity has been planned and implemented in accordance with the accreditation requirements and policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint providership of Primary Care Network (PCN) and the Foundation for Reproductive Medicine. Primary Care Network is accredited by the ACCME to provide continuing medical education for physicians. Primary Care Network designates this live activity for a maximum of 22.75 AMA PRA Category 1 Credits™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

For program information, visit the conference website: [http://kaywa.me/1ApI1](http://kaywa.me/1ApI1)
Such early knowledge then opens a number of rather unique opportunities: For clinicians it offers a chance to be among the first to benefit from new treatment ideas for their patients (and there will be a good number of those at this year’s conference), while for basic scientists any new knowledge leads to more questions that must be answered as quickly as possible. But probably most importantly, the Foundation for Reproductive Medicine Conference (FRMC) offers a truly unique opportunity for clinicians and basic scientists to ponder over three intensive days of interactions how to advance reproductive medicine in all aspects by translating new knowledge obtained by basic scientists as quickly as possible into clinical products that serve the betterment of patient care.

FRMC is, however, by no means an “industry conference.” Very much to the contrary: Not only does the conference mandate detailed disclosures of potential economic conflicts from speakers but does, in contrast to many other medical conferences, not accept program sponsorships and/or sponsored speakers by industry. The conference, indeed, in its first two years obtained a strong reputation of intellectual independence and for “speaking the truth.”

From the beginning, the FRMC attempted to differentiate itself from other conferences by following two distinct mottoes: The first, “think differently,” not only encourages critical thinking but often strongly challenges commercial interests, which in many areas of medical practice (unfortunately including reproductive medicine) in recent years have gained undue influence on clinical practice, and even on what is presented in medical conferences and in medical journals after alleged peer review. The New York Times just recently reported on a quickly developing scandal, involving seemingly nefarious influence of “industry” (in this case, of companies that buy up private dermatology practices and then gouge prices) on specialty societies as well medical journals in Dermatology (New York Times October 27, 2018, page B1).

In fertility practice, as we discussed in these pages repeatedly, similar nefarious influences, unfortunately, also to significant degrees influence practice in many different ways and, at times, control publication processes mostly through selection of conflicted peer reviewers. The FRMC sees it as one of the core functions of this conference to refuse such biases. Practically this means that this conference does not strive to be “politically correct” and does not try to be “popular.” What it does attempt as a core value is to present best current knowledge without the usual commercial influences.

To pursue such a policy is tough at a time when traditional commercial sponsors of scientific conferences have greatly cut back on support, whether for budgetary reasons or because federal laws have greatly restricted such support. When companies do spend money on support, one, therefore, cannot blame them for wanting the greatest possible influence on what transpires in their fields of commercial interests at a conference. FRMC will, however, not compromise on this point, and the conference is, therefore, mostly dependent on registration fees to cover its substantial (New York City) costs. Since the financially responsible party is the Foundation for Reproductive Medicine, CHR, therefore, is grateful for any financial support given to this not-for-profit research foundation. Donations are, of course, tax-deductible according to the law, and can be sent to the FRM online or by mail to:

Foundation for Reproductive Medicine
21 E 69th Street, New York, NY, 10021, USA

The FRMC’s second motto is to learn about "paradigm changes you may not hear about elsewhere." This second motto is a clear consequence of trying to present the newest of the new in the field, often even before publication. This, of course, requires the necessary connections with leading research centers to become aware of important development at such early stages. A good example is Prof. Evelyn Telfer’s talk on in vitro oocyte maturation from primordial follicle stages at this year’s conference. We were aware of this work since CHR’s David Albertini, PhD, has been collaborating with Prof. Telfer on this
In order to present the most important developments in the field at the conference, the final speaker schedule is filled progressively over a full year. As important subjects are published or as the Program Chairs of the conference become aware of such work even if unpublished, invitations go out to the investigators for next year’s conference. In practical terms this means that the Program Chairs in advance never know what the main topics of next year’s conference will be. But main topics universally evolve, usually representing the areas where most progress has been made over the preceding year.

This year is no exception: Though a bigger than ever diversity of subjects is addressed, two subjects are repeatedly represented in multiple sessions. They are the fragile X mental retardation 1 (FMR1) gene and preimplantation genetic testing for aneuploidy (PGT-A), until recently called PGS (preimplantation genetic screening). Research on both of these subjects over the last year has greatly advanced the current understanding of the importance of the FMR1 gene in ovarian recruitment and follicle maturation and our understanding of what PGT-A/PGS can and cannot do in helping in the process of best embryo selection. Both of these subjects have also in previous years received attention at the FRMC but never as much as this year. Interestingly, CHR investigators have been on the forefront of research in both of these areas but will this year defer to colleagues from all over the world to provide most updates on these two “hot” subjects.

The FRMC was always open to laypeople but, understandably, was only rarely attended by patients or other interested lay-parties. The conference organizers, therefore, this year for the first time added a full half day of lectures to the program, specifically geared at lay people, and addressing many of what the Program Chairs felt were the most important clinical subjects for the public. Upon completion of the scientific meeting on Sunday, November 18, starting at 2:00 pm, leading experts will, therefore, in short sessions address these clinical subjects before giving the public the chance to ask questions and/or present factual cases to a panel of experts. If successful, this “Clinical Fertility Day for the Public” will become a constant feature in coming years. For registration, please visit the conference website.
Elsewhere in this issue of the VOICE, we discuss that a prominent IVF center through an article in Forbes magazine recently announced a new method of testing for chromosomal abnormalities in blastocyst-stage embryos (PGS/PGT-A 4.0). The new PGS/PGT-A relies on testing of embryonic DNA in spent media, in which embryos were incubated. The claim behind this announcement is that embryos no longer have to be biopsied, which makes PGS/PGT-A a non-invasive test.

Following a lengthy interview with the Forbes writer, Ellie Kincaid, Norbert Gleicher, MD, CHR’s Medical Director and Chief Scientist, was extensively quoted in the article published online on November 9, 2018. Dr. Gleicher was among a group of skeptic scientists interviewed by the writer, including Richard Paulson, MD, past president of ASRM, who said he was "very much opposed to selling the public another unproven technology." In his interview Dr. Gleicher stressed that a non-invasive test is always superior to an invasive test, but only as long as its results were also equally reliable.

In the case of PGS/PGT-A at blastocyst-stage, proponents of any testing methodology, whether invasive or non-invasive, however, have to deal with one additional problem, namely that many embryos that at blastocyst-stage truly demonstrate aneuploid cell clusters, self-correct downstream in following days by killing off abnormal cells and absorbing those via apoptosis, while normal cells continue to divide, resulting in entirely chromosomally normal pregnancies. As a recent worldwide survey of IVF centers suggests (to be presented for the first time at the upcoming FRM Conference in New York City between November 15 and 18, hundreds of healthy offspring have been born worldwide from transfer of, by PGS/PGT-A declared aneuploid and/or mosaic, embryos.

CHR is currently recruiting patients for a clinical trial of ovarian rejuvenation for patients with premature ovarian failure (POF), utilizing platelet rich plasma (PRP). The PRP procedure itself will be free of charge to study participants.

Normal costs associated with ovarian stimulation and subsequent IVF cycles if follicles develop, including cancellation fees, will be the participants’ responsibility.

Please call us at 212-994-4400 if you are interested in participating in the study.

Ovarian Rejuvenation Study

CHR in the Media

Help your eggs’s maturation process with OVOENERGEN CoQ10 for women*.

- 333 mg of oil-suspended, pharmaceutical-grade CoQ10
- Protects eggs from oxidative stress and supplies them with energy for normal development*
- Used successfully at Center for Human Reproduction (CHR) in IVF patients with low functional ovarian reserve and poor egg quality*

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.
association with IVF had the title, “Preimplantation genetic screening: ‘established’ and ready for prime time?” [Gleicher et al., Fertil Steril 2008;89(4):780-788]. Here at CHR, we consider this word-play as a compliment toward our decades-long efforts to educate colleagues and the public about the harm PGS/PGT-A brings to IVF.

And what is CCRM’s “ready for prime time” new test based on? Fourteen (14) patients, presented in an abstract that claimed that 88% of embryos had enough DNA in their spent media to do the testing and, among those, only in 80% did results in media correlate with embryo biopsy results. In practical terms this means that among 100 women undergoing this test, 88 will demonstrate enough DNA and that ~30/100 (30%) will have paid for the test without getting a result. To claim a “ready for prime-time” test based on such a small number of investigations, on such a small number of patients and with a 30% embryo loss rate before even knowing how well those results correlate - not with a trophectoderm biopsy but the true ploidy of the embryo - is simply outrageous.

As we have stated before in these pages, and as also at least one critic of the CCRM announcement noted in the Forbes article, it appears high time for the Food and Drug Administration (FDA) to intervene by prohibiting the routine clinical use of PGS/PGT-A (on a side note, Norbert Gleicher, MD, CHR’s Medical Director and Chief Scientist, was also quoted in the Forbes article, reflecting CHR’s negative opinion about utilization of PGS/PGT-A).

CCRM in the Forbes piece also announces an apparently upcoming clinical trial of their new test but, interestingly, patients will, still, have to pay for it. This is, however, exactly one of the principal issues CHR has decried for so many years: Not only has PGS/PGT-A in 20 years of practice never demonstrated clinical benefits (and at least in some women with small embryo numbers actually shown negative effects on pregnancy and live birth rates) but patients have, in addition, spent significant additional money on a useless and potentially detrimental procedure, when IVF is already too costly for many.

And now the saga continues with PGS/PGT-A 4.0 all over again, even though it is now almost universally accepted (some additional evidence will be presented at this month’s FRM Conference, discussed elsewhere in this issue of the VOICE) that trophectoderm aneuploidy at blastocyst stage is an almost universal phenomenon in human embryos and that many, if not most of these aneuploidies, being mitotic rather than meiotic, self-correct after implantation. Hundreds of healthy newborns following transfers of allegedly chromosomally “abnormal” embryos bear witness to this fact better than any prospectively conducted study of PGS/PGT-A at blastocyst stage can ever demonstrate.

If embryos self-correct in a high percentage of cases downstream from blastocyst stage, what then is the purpose of testing embryos at blastocyst stage, even if such testing were accurate and non-invasive? It is high time to recognize that the PGS/PGT-A failures of 20 years have never really been the consequence of inadequate laboratory techniques and technologies but are the consequence of most basic biological realities of the human embryo. CHR investigators have been making this argument since their above cited paper in 2008. Even the most perfect techniques and technologies, therefore will never be able to predict at blastocyst stage which embryo will be euploid or aneuploid further downstream after self-correction mechanisms have done their job.

The PGS hypothesis, therefore, simply does not work! After all, we do not select our future employees in grammar school, even though the best students will statistically, likely, make somewhat better employees than the worst. Some really bad ones may, however, become the next super-star, while some early starts often fade. By testing embryos at blastocyst-stage, selecting best employees in grammar school is, however, exactly, what PGS/PGT-A does. Time to stop!

-The CHR
Fighting for every egg and embryo!

Staying Connected
New informational material on treatments or news coverage on fertility breakthroughs, the best way to stay up to date on CHR’s activities is via our social media channels. Never miss important news!