Inflammation has many definitions but the shortest and probably, therefore, best is the response of tissue or the body to injury and infection. Injury does not have to be traumatic but can occur as part of natural physiological processes. For example, ovulation, the release of an egg from the ovary at mid-cycle, is an inflammatory process; and so is implantation, as the embryo invades the mother’s endometrium. Indeed, the onset of labor is also considered an inflammatory process.

Yet, at the same time, inflammation is a typical characteristic of many pathological processes. So, for example infections lead to inflammation, as do so-called inflammatory diseases, autoimmune diseases and as does trauma.

Inflammation, therefore, at the same time can be an essential physiological process and a pathological process, as now increasingly recognized, associated with poorer implantation rates for embryos and increased miscarriage risk for established pregnancies.

Every inflammatory process is associated with local invasion by certain families of white blood cells, which have distinct functions, including secretion of lymphokines/cytokines which, in turn, have distinct physiological functions. CHR investigators under

The Importance of Inflammation in Human Reproduction

Treatting the older female patient

It does not happen too often that prominent medical journals express gratitude to authors for submitting manuscripts; but this is exactly what happened to CHR investigators when the Publisher of the Journal of Endocrinology wrote a letter of appreciation to CHR’s Medical Director and Chief Scientist, Norbert Gleicher, MD, who was the senior author on the paper Gleicher et al., Improvements in IVF in women of advanced age. J Endocrinol 2016;230(1):F1-6, acknowledging that this manuscript “was one of the most read articles in the journal during 2016, with not less than 1152 downloads.”

The article had been written at the invitation of the editors of the journal, with the primary goal of reviewing recent progress in the IVF treatment of older women. CHR’s investigators were likely selected for this task because, except for CHR, hardly any other IVF centers in the world have been addressing this subject in the literature.

This, indeed, was pointed out by the authors of the manuscript as a significant flaw of current IVF treatments all over the world, which, in their opinion, often push older infertile women too quickly toward egg donations. A second very important point made by the authors was the observation that embryo selection methods, which seek to define “best” embryos, in older women are mostly counterproductive, actually reducing pregnancy and live birth chances. This particularly refers to extended embryo culture to blastocysts stage.

International Developments in the IVF Field

The Importance of Inflammation in Human Reproduction

In this issue, we cover:

In Focus

1. Effects of menopause: Page 4
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the leadership of David H. Barad, MD, MS, CHR’s Director of Clinical IVF and Senior Scientist, recently completed a study, which demonstrated that two typical inflammatory blood markers had statistically highly significant predictability if elevated; C-reactive protein (CRP) was highly associated with diminished IVF outcomes (pregnancy and live birth rates), while Interleukin 6 (IL-6) was highly associated with increased miscarriage risk.

A so far only still electronically published study, demonstrated that preconception low-dose aspirin restores diminished pregnancy and live birth rates in women with low grade inflammation (based on elevated CRP) (Sjaarda et al., J Clin Endocrinol Metab 2017; doi.org/10.1210/jc2016-2917). This study is of great interest not only because it confirms our above noted finding that elevate CRP negatively affects IVF outcomes but because, combined, both studies suggest that there, likely, is a quantitative correlation between CRP levels and adverse IVF outcomes.

CHR has been treating patients with evidence of inflammation with low-dose aspirin for decades. Yet, probably reflective of the fact that over 90% of CHR’s patients present after multiple earlier IVF failures elsewhere, our patients, still, demonstrated the association between high CRP and significantly reduced pregnancy and live birth rates, suggesting that in more severe cases of inflammation, low-dose aspirin may not be sufficient. CHR, therefore, increased in patients with elevated inflammatory markers aspirin dosages to a full adult aspirin.

In coming months, we will return in these pages repeatedly to the subject of inflammation since we strongly believe that the female immune system in women with infertility deserves more attention than it received over the last few decades, with inflammation playing very important enhancing as well as inhibiting roles in successful reproduction.

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**IN FOCUS**

This feature presents microscopic images from CHR’s laboratories, edited by our Director of the Division of Laboratories and Senior Scientist, David F. Albertini, PhD.

Pictured here are 3 embryos in various stages of dividing from 3 to 4 cells. Here at CHR we are using a variety of very powerful new imaging techniques so we can learn about the forces that will take the one-celled zygote all the way to a blastocyst, which in humans will contain about 100 cells. The vast majority of those 100 cells will become the placenta while the remaining ones, perhaps 10-20 will give rise to the fetus. Research at the CHR continues to probe the ways that our genes, here shown as chromosomes (black) interact with miniature muscles (known as the cytoskeleton, red) to ensure that the correct number of chromosomes will end up in each cells comprising the embryo.

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Young Woman with "Unexplained Infertility" Revealed to Have Hypoandrogenic PCOS

Case: A 29-year-old woman, never pregnant, presented with a history of primary infertility of ca. 24 months duration. She reported a first menses at age 14, and remained regular in a 26-28-day cycle even once she came off oral contraceptives, ca. 2 years earlier. Her medical history was negative except for a diagnosis of Hashimoto’s thyroiditis at age 22. She received thyroxin supplementation of 0.075µg. She had been receiving fertility treatment at another center over the preceding 8-9 months with a diagnosis of unexplained infertility. Treatment consisted of 3 clomiphene citrate/ insemination cycles, followed by 2 IVF cycles. Both IVF cycles were characterized by very large follicle numbers but, in comparison, also by relatively few oocytes.

Review of her medical records revealed a BMI of 23, normal FSH and estradiol levels, and AMH of 5.8ng/mL. Her TSH was normal and she still demonstrated mild positivity in thyroid peroxidase and thyroglobulin antibodies.

Analysis: Upon presentation, this patient was by the treating physician immediately suspected of being a hypoandrogenic polycystic ovary syndrome (H-PCOS). This newly described PCOS phenotype is, likely the equivalent or a subgroup of the Phenotype D PCOS under Rotterdam Criteria. It was recently described (Gleicher et al., J Steroid Biochem and Molec Biol 2017; doi.org/10.1016/j.jsbmb.2016.12.004), and is characterized by exclusively appearing in lean women with mostly regular menses, at youngest ages (20s) by hyper-androgenemia (and sometimes mild hyper-cortisolemia), which after going through a period of normal androgen levels in the early mid-30s usually converts to hypo-androgenemia (and mild hyper-cortisolemia).

Hypo-androgenism gets worse with advancing age. Hypo-androgenemia is characterized by low testosterone levels, particularly low dehydroepiandrosterone-sulfate (DHEAS) (of adrenal origin) and relatively high sex hormone binding globulin (SHBG). The phenotype is also characterized by a high degree of associated autoimmunity, especially thyroid autoimmunity (ca. 40% positive TPO-antibodies).

Resolution: After laboratory work-up, this patient, indeed, was confirmed in the diagnosis of H-PCOS. She was advised that her presentation, including the relatively small number of retrieved eggs in comparison to on ultrasound seen follicles, was typical. She was also advised that this condition is believed to reflect an autoimmune-induced insufficiency of her adrenal glands, primarily affecting the zona reticularis, which produces androgens. Low androgens, in turn, inhibited her normal follicular maturation in the ovaries and, therefore, produced fewer oocytes and poor quality oocytes. The recommended treatment was androgen supplementation for at least 6-8 weeks, which was given to her via oral DHEA supplementation.

She did not conceive in her 1st fresh IVF cycle at CHR (day-3 transfer) but conceived in her first frozen-thawed cycle and has a normally progressing singleton pregnancy. The number of retrieved oocytes almost doubled in comparison to her earlier two IVF cycles.

Have you seen CHR’s video gallery?

From the basics of infertility conditions to the latest treatment strategies coming out of our center's own research, CHR's physicians and scientists explain everything about infertility and treatments in high-quality videos. Visit the video gallery on your computer or from your mobile devices, and let us know what you think!
and preimplantation genetic screening (PGS), which both, nevertheless, are widely advocated (and clinically utilized) indiscriminately of female age.

We addressed this issue repeatedly in the pages of the VOICE and, therefore, do not wish to be repetitive; but blastocyst culture as well as PGS, in CHR’s opinion, should be avoided in older women (and younger women with low functional ovarian reserve) if pregnancy and live birth chances are to be maximal.

Only so much: A small number of clinical trials have, indeed, claimed that PGS improves clinical pregnancy rates and/or reduces miscarriage rates in association with IVF. These studies, however, uniformly utilized inappropriate statistical formats and, therefore, cannot be considered validations of the procedure. One study, initially designed to prove outcome benefits from PGS, after failing to show them, was redirected to support the argument that PGS facilitates elective single embryo transfer (eSET).

Appropriately designed studies are even sparser and, uniformly, demonstrated no outcome benefits from PGS. Because of very large cycle numbers, though subject to obvious potential selection biases, currently most telling studies on the efficacy of PGS rely on outcome data from national IVF registries. As shown in the figure below, these analyses suggest that PGS, not only does not improve clinical pregnancy and live birth rates in IVF and/or reduces miscarriage rates, as suggested by the PGS hypothesis, but actually reduces pregnancy and birth rates while not affecting miscarriages in standard autologous IVF cycles in the general population and even in best prognosis IVF cycle, utilizing young donor eggs.

Patients most severely adversely affected by PGS are older women or patients with low functional ovarian reserve because their embryos, even in the best embryology laboratories, often do not survive extended culture to blastocyst stage, therefore do not even reach PGS and prevent patients from even reaching embryo transfer. Even more damaging to all poorer prognosis patients is, however, the very high false positive rate of trophectoderm biopsies, wrongly designating perfectly normal embryos as aneuploid and, therefore, to disposal. Since poor prognosis patients usually produce relatively small embryo numbers, every “lost” embryo greatly contributes to poor outcome statistics.

The extraordinary attention this CHR paper received from colleagues after publication, however, suggests that CHR’s message is finally resonating and receiving the attention it deserves in the IVF community.

The effects of menopause

Staying with aging concerns, a rather well designed recent study in Proceedings of the National Academy of Sciences U.S.A. (Levine et al., 2016;113:9327-9332) offers surprisingly strong evidence that menopause accelerates a woman’s biological aging clock. Using a highly accurate epigenetic biomarker of age (“epigenetic clock”) based on DNA methylation levels, the authors report that early menopause was associated with significant epigenetic age acceleration in blood but also with bilateral oophorectomy and a prolonged period from menopause start. Interestingly, only blood but not buccal epithelium and saliva demonstrated these associations, except that saliva demonstrated early epigenetic aging after bilateral oophorectomy, while hormonal replacement therapy “rejuvenated” epigenetic aging. In addition, using Mendelian randomization analysis, the authors reported two single nucleotide polymorphisms (SNPs), known to be highly associated with menopause age, to demonstrate significant associations with epigenetic age acceleration.

Menopause, thus, appears to accelerate epigenetic aging in blood.

And to continue with menopause concerns, a recent review article in Fertility & Sterility (Achilli et al 2016;107:475-482) addressed the efficacy and safety of transdermal testosterone in postmenopausal

Continue reading on page 5
women who suffer from hypoactive sexual desire disorder (HSDD). This disorder is characterized by distress caused by decreased desire or complete loss in sexual desire.

The authors concluded that transdermal testosterone in the short term was clinically effective and safe in treating HSDD, whether caused by physiologic or surgical menopause. Side effects were rather minimal, mostly restricted to development of acne.

**Influenza immunizations for IVF patients: A clinical trial at CHR**
CHR is currently conducting a clinical trial that involves the administration of *Influenza vaccination*. All patients undergoing IVF at CHR are offered participation if they have not yet received the annually available Influenza vaccination. This is a relatively easy trial to conduct because all pregnant women and all women planning on pregnancy are now advised to have an Influenza vaccination (even in pregnancy), and all women in the trial are getting immunized. The randomization of the trial just involves short time differences between administration of the immunization.

Interestingly, only very recently on February 17, 2017 did the *American College of Obstetricians and Gynecologists (ACOG)* issue a new “*Influenza Season Assessment and Treatment Algorithm Announcement*,” which pointed out *highly elevated Influenza activity across the country*, which is expected to continue for a few more weeks.

Influenza immunization is now strongly recommended because, for reasons that have remained unclear, *pregnant women are at increased risks from Influenza*. Moreover, large safety studies of Influenza vaccine, administered during different periods of pregnancy, have found the immunization during pregnancy to be safe. Indeed, as we reviewed in these pages before, large-scale studies in different parts of the world registered significant benefits from Influenza immunization during pregnancy, in that such immunizations by up to half reduced late pregnancy complications like *premature labor* and *preeclampsia/eclampsia*.

It was the latter observation that led CHR investigators toward the currently running Influenza trial because the observation of so radically diminished late pregnancy complications led to the hypothesis that Influenza vaccination may be inducing tolerance pathways, required for normal tolerance of the fetal semi-allograft (the fetus is in 50% foreign to the mother’s immune system) by the maternal immune system. If that could be proven, Influenza vaccination may also beneficially affect IVF outcomes by improving *chances of embryos to implant* and, at the same time, by *reducing miscarriage risks*.

We, therefore, want to take this opportunity to remind all CHR’s patients that we will gladly administer Influenza (“flu”) vaccinations free of charge to anybody who so far has not been immunized. Just ask your coordinator!

**Finally, some good news on human gene editing**
It was all over the news on February 14, 2017 that the science advisory group formed by the *National Academy of Sciences* and the *National Academy of Medicine* finally published its long-awaited report on *human germline editing*. A subject frequently discussed in these pages, it so far remains unaffected by issuance of this report, with human germline editing, currently, practically prohibited by the *Food and Drug Administration (FDA)*, which has declared its regulatory power over the subject in the U.S. but has refused to address it (under Congressional mandate), when challenged to do so by scientists. One excuse frequently heard was that the *FDA* was waiting for the opinion of this influential advisory group.

It is difficult to assess how much priority the Trump administration will assign this issue. Optimists, who are expecting significant changes at the *FDA* in attempts to speed up the agency’s approval processes, are hoping that Congress will no longer block review and potential approvals of research in this arena by qualified investigators. Pessimists, on the other hand, see this subject at the very end of a long to-do list the administration faces, and wonder whether the right-to-life faction among Republicans will not completely block all approval activities the *FDA* might consider.

Only time will tell; in the meantime, we can only hope that the federal government will carefully consider the recommendations reached by this influential advisory group. Including a multitude of caveats and cautionary notes, the group, basically, endorsed *careful experimentation with genetic alteration of human eggs (“crossing the germ line”), sperm and
embryos, though only in prevention of births with genes causing serious diseases/disabilities, in absence of reasonable alternative treatments and if plans exist to follow potential effects through multiple generations.

As we noted repeatedly in these pages, in collaboration with colleagues at Rockefeller University in New York City and The Salk Institute for Biological Studies in La Jolla, California, CHR is ready to start several projects involving genetic germline manipulations, once the FDA allows such projects after Institutional Review Board approval, with or without FDA review. We, therefore, want to be counted among optimist when it comes to expectations we have of the Trump administration. We hope we are correct!

How accurate are commercially offered genetic screening tests?

Genetic testing in medicine is becoming more prevalent in many medical specialties but nowhere with greater intensity than in reproductive medicine. From carrier screening of parents to preimplantation genetic testing of embryos for chromosomal abnormalities (PGS) or single gene diseases and other genetic abnormalities (PGD), over early prenatal blood testing for cell free DNA, chorionic villus biopsies (CVS) or amniocenteses for chromosomal abnormalities or carrier status for recessively or dominantly inherited diseases, genetically related testing has become ubiquitous. A whole laboratory industry has grown up around reproductive testing, with more and more and more testing recommended by professional organizations, often just fronts for commercial interests.

It, therefore, was refreshing to read Opinion No. 690, where American Congress of Obstetricians and Gynecologists (ACOG) just issued an updated recommendation on “Carrier Screening in the Age of Genomic Medicine,” offering a satisfactorily restrained set of recommendations, here summarized:

- Ethnic-specific, pan-ethnic, and expanded carrier screening are acceptable strategies for pre-pregnancy and prenatal carrier screening. Each obstetrician–gynecologist or other health care provider or practice should establish a standard approach that is consistently offered to and discussed with each patient, ideally before pregnancy. After counseling, a patient may decline any or all carrier screening.
- If a patient requests a screening strategy other than the one used by the obstetrician–gynecologist or other health care provider, the requested test should be made available to her after counseling on its limitations, benefits, and alternatives.
- All patients who are considering pregnancy or are already pregnant, regardless of screening strategy and ethnicity, should be offered carrier screening for cystic fibrosis and spinal muscular atrophy, as well as a complete blood count and screening for thalassemias and hemoglobinopathies. Fragile X premutation carrier screening is recommended for women with a family history of fragile X-related disorders or intellectual disability suggestive of fragile X syndrome, or women with a personal history of ovarian insufficiency. Additional screening also may be indicated based on family history or specific ethnicity.
- Couples with consanguinity should be offered genetic counseling to discuss the increased risk of recessive conditions being expressed in their offspring and the limitations and benefits of carrier screening.
- Carrier screening will not identify all individuals who are at risk of the screened conditions. Patients should be counseled regarding residual risk with any test result.
- Prenatal carrier screening does not replace newborn screening, nor does newborn screening diminish the potential benefit of prenatal carrier screening.
- If a woman is found to be a carrier for a specific condition, her reproductive partner should be offered screening to provide accurate genetic counseling for the couple regarding the risk of having an affected child. Additional genetic counseling should be provided to discuss the specific condition, residual risk, and options for

DO YOU CARRY A MITOCHONDRIAL DISEASE OR KNOW SOMEBODY WHO DOES?

If you do, please call us at 212-994-4400 for a free consultation in person, by phone or via Skype. CHR is searching for a way to prevent inheritance of these awful diseases in collaboration with colleagues at the famous Salk Institute for Biological Studies in La Jolla, CA. You may be able to help us find a way to prevent mitochondrial diseases in children!
If a carrier couple (ie, carriers for the same condition) is identified before pregnancy, genetic counseling is encouraged so that reproductive options (eg, donor gametes, preimplantation genetic diagnosis, prenatal diagnosis) can be discussed.

Individuals with a family history of a genetic disorder may benefit from the identification of the specific familial mutation or mutations rather than carrier screening. Knowledge of the specific familial mutation may allow for more specific and rapid prenatal diagnosis.

Given the multitude of conditions that can be included in expanded carrier screening panels, the disorders selected for inclusion should meet several of the following consensus-determined criteria: have a carrier frequency of 1 in 100 or greater, have a well-defined phenotype, have a detrimental effect on quality of life, cause cognitive or physical impairment, require surgical or medical intervention, or have an onset early in life. Additionally, screened conditions should be able to be diagnosed prenatally and may afford opportunities for antenatal intervention to improve perinatal outcomes, changes to delivery management to optimize newborn and infant outcomes, and education of the parents about special care needs after birth.

Carrier screening panels should not include conditions primarily associated with a disease of adult onset.

The restraint of these recommendations comes particularly vividly into focus when compared to the irresponsible set of recommendations recently published by the Preimplantation Genetic Diagnosis International Society (PGDIS), last year reviewed in the VOICE, which, very obviously were not evidence based and, very obviously, were guided by commercial interests.

Now comes a paper in the February 16, 2017 issue of Science, in which researchers reported use of an algorithm they developed, which allowed for the detection of DNA mutations in publically available human sequences which were the product of sample processing of specimens rather than true somatic variants (Chen et al., Science 2017;355: 752-756). As it now turns out, practically any DNA sample may be at risk for such artefacts and, especially when clinical judgments (for example in cancer studies) are made based on minute amounts of such DNA samples. When the author’s algorithm (called “Global Imbalance Value” or GIV) was used to investigate two national databases, 41% of a first dataset demonstrated an imbalance score suggestive of artificial damage and 71% of the second set suggested extensive damage.

This paper is of importance because it demonstrates how the genetics laboratory community, whether academic or commercial, constantly overestimates its technical capabilities before applying their genetic assay systems to clinical medicine. Reproductive medicine is, therefore, not alone in decrying the damage caused to patients in their IVF cycles when PGS is applied. Overenthusiasm for unproven hypotheses as well as conscious and subconscious financial interests should not be allowed to control rapidly evolving clinical applications in human genetics.

For increasing numbers of IVF centers, PGS now represents approximately 30% of IVF cycle revenue. In other words, PGS is more profitable than the rest of the IVF cycle. And this does not even consider the profits made by national laboratories that process the trophectoderm biopsies obtained at individual IVF centers. Considering the rather extensive financial interests involved in IVF and genetics communities (see also on page 8, on the continuing commoditization of IVF), one should not be surprised that PGS continues to prosper in the market place, even though objective assessments not only have failed to confirm outcome benefits but increasingly demonstrate considerable harm, especially to poorer prognosis patients.

Clinical effectiveness of egg freezing still undetermined

Also in February, ACOG’s Today’s Headlines commented on a so far only online paper in Human Reproduction in which the authors provide guidance to women and physicians on the number of eggs they should freeze to maximize their chances of at least one conception at a later point. We are mentioning this paper because of its conclusions that: (i) lack of data to support the effectiveness of egg freezing in healthy women is still a problem since most women who have banked their eggs have not yet tried to use them; and (ii) the likelihood of them having a healthy baby with an egg they have frozen (therefore) is not known.

Continue reading on page 8
**International developments: Continued from Page 7**

These are correct and important conclusions! Unfortunately, these conclusions are, however, only rarely communicated to women who are enquiring about egg freezing. As we have previously discussed in these pages, this is also an area in reproductive medicine, which has undergone, for us here at CHR, worrisome commercialization, from establishment of IVF centers that only offer egg freezing and no other IVF services to egg freezing parties for young women, organized by professional corporations with interest in egg freezing.

What is also rarely communicated to women who are interested in fertility preservation via egg freezing is that, unless egg freezing is performed as an emergency procedure in young women who need medical therapies that are toxic to their ovaries, exactly because outcomes from egg freezing are still unknown, the procedure is still considered experimental. Current ASRM guidelines on egg freezing spell this out quite clearly and are correct in restricting removal of the experimental status only for the above-outlined exceptions, where the alternative of having no ovarian function left is clearly inferior to even minimal later success with frozen eggs.

Social egg freezing is, however, widely touted by IVF centers (and the egg freezing industry) as "no longer experimental." It is important to point out that this is not a correct representation and that CHR, therefore, in its consent process very clearly spells out that social freezing should still be considered an experimental procedure. Any medical ethicist will agree that a procedure with unknown outcome must be considered "experimental."

### Commodityization of IVF continues

The practice of IVF all over the world is being taken over by mega-corporations. The most recent announcement came in mid-February from one of the largest IVF centers in the U.S. with headquarters in New Jersey, Reproductive Medicine Associates of New Jersey (RMANJ), which also owns centers in neighboring states (though is no longer affiliated with Reproductive Medicine Associates of New York, RMA New York). The management division of RMANJ and The Valencia Infertility Institute (IVI), which with multiple locations is the leading IVF center in Spain, and has also IVF facilities in various European and Latin American countries, the Middle East as well as in India, announced a combination of their businesses to create a new company, called IVI-RMA Global, with a large majority of shares controlled by IVI. It, thus, appears that, through this deal, IVI is the first non-US mega-IVF company to obtain a major foothold in the U.S. market.

IVI so far has had no IVF facilities in the U.S. but has operated two PGS laboratories in the country. The corporate leadership had let it be known for some time that it was interested in entering the U.S. market. Similarly, rumors in the IVF community had it that RMANJ for quite some time has been looking for a financial partner after The Colorado Center for Reproductive Medicine (CCRM) initiated a country-wide expansion following financing in August of 2015 from TA Associates, a global growth private equity firm.

Interestingly, RMANJ Management as well as its affiliated practices, RMANJ and IVI, will all in their respective countries continue to operate independently under their current names. IVI and RMANJ will oversee several different international business units, including a newly created IVI America, which, apparently, is planned to expand throughout the country. It has been suggested that creation of IVI America, separate from RMANJ, may permit establishment of IVF centers where RMANJ, currently, is prohibited from operating because of non-compete agreements.

IVI described itself in a press release as the largest fertility network in the world, a position further consolidated by the merger with RMANJ.

First attempts to establish national fertility networks in the U.S. started in the 1990 during a period when so-called physician practice management companies became vogue in all medical specialties. These efforts, however, floundered, and this business concept disappeared, with few exceptions, very quickly from the U.S. market. It was reinvigorated over the last decade, initially mostly in Australia and Europe.

In Australia, based on information gleaned from local IVF center websites, most IVF centers today are owned by investor-driven public corporations, which also have expanded into various Asian countries. This commoditization of IVF has been accompanied by increased competition between centers and increased scrutiny, of what the Australian media call the “Australian fertility industry,” over reported IVF success rates. Some of the country’s leading and most prestigious IVF centers have recently been accused of reporting exaggerated pregnancy and live birth rates.

Continue reading on page 9
The effects of these developments in the U.S. remain to be seen. The increasing commoditization of IVF can, however, be expected to accelerate, as the financial industry has identified infertility services as a growth industry, and is offering significant investments.

This is best demonstrated by the serial entrepreneur, Martin Varsavsky who, as Forbes reported on November 8, 2016, is planning on spending $200 million to “end the biological clock.” His business concept to achieve this goal is complex: He believes that all young women should freeze their eggs, so that their future fertility becomes less age-dependent. He further believes that, once they are ready to conceive, they all should undergo IVF with their frozen eggs, every embryo should before transfer undergo PGS “to confirm that it is chromosomally normal.” To be able to offer these services, he has already bought one of the early frozen donor egg banks established in Atlanta and has also made a significant investment into the Reproductive Biology Associates (RBA), a well-respected IVF center that established the egg bank. Purchases and/or investments into other IVF centers around the nation are planned.

At the same time, this endeavor also demonstrates what we here at CHR consider to represent the principal dangers of the industrialization of IVF: it converts the treatment of infertility from a clinical practice to the sale of individual, often unproven, commodities, like social egg freezing (as above discussed still undetermined in its effectiveness), donor egg banking (which we demonstrated to have slightly lower pregnancy chances than the utilization of fresh donor eggs) and, of course, PGS which, as readers of these pages know, we here at CHR consider a worthless, even harmful procedure for most infertility patients.

In an industrialized IVF setting, sales of individual commodities, however, assume centrality. Considering that PGS adds approximately 30% to the revenue an IVF center collects from an IVF cycle, one should not be surprise that leaders in IVF industrialization, like here mentioned CCRM, RMANJ, IVI and RBA, are all strong proponents of utilization of PGS and other commodities of questionable utility.

One also usually observes that in these settings IVF outcomes are not easily transferable. Even if the “mothership” has excellent IVF results, the “daughter ships” usually do poorer and, on even longer follow up, results of the “mothership” also start declining.

Finally, the experience in Australia should be a cautionary tale, and not only because of above noted allegations that some of the most prominent IVF centers cheated in their outcome reporting. CHR investigators under the leadership of Vitaly Kushnir, MD, CHR’s Director of Fertility Preservation and CME and Assistant Scientist, recently investigated the last 10 years of reported IVF outcomes all over the world. Australia and New Zealand (combined) demonstrated a rather disturbing decline in live birth rates over the second half of that period, which coincided with the rapidly enhancing industrialization of IVF in that region. But in the end, patients should determine which provider frame work they prefer. —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. Follow us, and never miss important news!