

Hot Stuff on the Horizon

Basic Fertility Treatment

There's nothing simpler than artificial insemination. What could be new about this baseline fertility therapy?

Dr. Samuel Prien has created a remarkably simple device that may usher in a quiet revolution in the art of semen collection.

What's wrong with the good old fashioned way of gathering a sample in a clinic bathroom or at home? Plenty, but there've been no major attempts at bettering the process. Prien, professor of reproductive physiology and assisted reproduction in the Department of Obstetrics and Gynecology at Texas Tech University Sciences Center, and graduate student Dustie Johnson have created a sperm collection container that better mimics the environment where sperm thrive best – the male body.

Patients shouldn't notice much unusual about the container's shape. There's just enough patented difference in the product, licensed by Embryonic Technologies, to protect sperm cells from the usual exposure-related shock that they experience during collection. The result: sperm can function better for longer periods of time. More men with low motility could be given a green light for intrauterine insemination, instead of having to use costly in vitro fertilization. Part of Prien's inspiration came from the spatial logistics of Texas. "We have patients who travel up to three hours for treatment," he explains. "For men who simply cannot produce a sample in this setting, that's a problem. Current guidelines say optimal analysis is performed within an hour of obtaining the sample." The new product's combined design and special media could take the edge off for men who worry about their sample's quality.

Will specialists who seem determined to prescribe IVF be eager to use a device that could mean more IUI's and fewer advanced therapies? Prien, who says his clinic is in an area with uninsured patients of modest means, hopes that physicians will look at this advance toward simpler technology as a way "to move people backwards a bit: people who were marginal IUI/IVF candidates, for whom ICSI seemed inappropriate because they didn't have enough sperm to work with... It may affect the bottom line of a clinic, but I believe most fertility professionals will do what's in their patients' best interest."

Animal studies have proven very positive for the semen collection device. Prien says human trials may begin as early as 2006.

Advanced Reproductive Technology

Oocyte Cryopreservation

The past two years has seen a media avalanche about oocyte cryopreservation or egg freezing. That's partly due to how close the technology is to being translated into use for millions of patients. It's also because of visionary business minds acting in collaboration with a community that's quite different from the typical infertility population.

Several years ago, the non-profit organization Fertile Hope started a media campaign about the plight of cancer survivors who beat the odds only to find themselves made completely sterile from the treatment. The type of infertility suffered by these survivors, many of whom were children or young adults, was virtually untreatable. Not long after Fertile Hope opened eyes with their efforts, spearheaded by world renown cyclist, cancer survivor, and parent via IVF, Lance Armstrong, another group was getting their start as a unique business venture. In early 2004, Extend Fertility started garnering mention in a variety of news outlets. The reason: Extend Fertility boldly took an experimental fertility therapy, oocyte cryopreservation, and began marketing it to folks outside of the infertility realm, namely, young women who want to delay childbearing without risking their fertile potential.

The combined markets – cancer survivors and busy healthy women – are benefiting from growth in the “fertility preservation” field.

Egg freezing has almost gone mainstream. One of its proponents is Dr. Alan Copperman, Director of the Division of Reproductive Endocrinology at Mount Sinai Medical Center in New York and Medical Director at Reproductive Medicine Associates of New York.

“Five years ago, we told patients this was not ready for primetime,” says Copperman, who's on the medical advisory board for Extend Fertility. “Ten years ago, we could barely get one of these frozen eggs to fertilize. Today, if we're careful with the technique, we have good survival after freeing, achieve fertilization with ICSI, and see normally developing embryos.

RMA New York specialists have trained in Italy, where government restrictions halting embryo freezing have pushed Italian researchers to the forefront of egg freezing technique. Over 100 babies have been born as a result, most of them in Italy.

The American Society for Reproductive Medicine (ASRM) applauds continued research in the area of egg freezing – they've had a special interest subgroup focusing on Fertility Preservation since 2001 – but their latest pronouncement still discourages the technique's use for anything but experimental trials and preservation prior to chemo or radiation therapy.

“Years from now, we’ll likely have egg banks just like we have sperm banks,” Dr. Copperman suggests. RMA recently concluded research using frozen donor eggs that proved successful for three of the four fertile women in the study. While that success generates more excitement about possibilities for this technique, even RMA will continue using oocyte cryopreservation only for radiation and chemotherapy patients and for preserving future reproductive potential in healthy, fertile women – for now.

As always, Copperman and others caution that while infertility consumers will see more clinics offering oocyte cryopreservation, interested patients should carefully research the level of expertise demonstrated by prospective specialists.

In Vitro Maturation (IVM)

A more established technique that is not as well-known in the United States is in vitro maturation (IVM) in which immature eggs are retrieved then matured in vitro prior to undergoing ICSI and transfer. No fertility drugs are used in IVM cycles.

Dr. Seang-Lin Tan, Chair of McGill University’s Department of Obstetrics and Gynecology and Director of the McGill Reproductive Center in Montreal, is a world leader in IVM’s successful use. According to Dr. Tan, McGill’s own IVM results are comparable to average IVF results in Canada.

IVM is a way to work around the risks of IVF, most notably, the incidence of multiple pregnancy and ovarian hyper-stimulation syndrome. The treatment is simpler and lower in cost than IVF because the major expense of fertility drugs is moot. Clinicians at McGill have demonstrated up to 40 percent pregnancy rates with IVM.

So why isn’t IVM more prevalent in the States?

One of the reasons for IVM’s growth in Canada is the country’s restrictions on paying egg donors. Since Canadian egg donors can only legally be reimbursed for expenses without any additional compensation, there is a shortage of interested donors. Some altruistic women will only consider donating eggs if they can do so without the discomfort from fertility medications. Making IVM available has helped McGill to grow their donor base. Women who are poor responders to standard IVF medication might want to consider IVM. Also, patients who demonstrate a need for in vitro assistance may want to first try the less expensive IVM, and, if successful, move on to IVF. Finally, patients who need to preserve their fertility prior to chemo or radiation therapy can benefit from IVM, since fertility medications’ hormonal actions can make IVF contraindicated in the treatment of some cancers.

Dr. Tan suggests that as IVM’s success rates continue to approach those of IVF, more U.S. practitioners will offer the technique.

Preimplantation Genetic Diagnosis (PGD)

The forecast for preimplantation genetic diagnosis (PGD) continues to become clearer with research. According to Dr. William G. Kearns, Director of the Shady Grove Center for Preimplantation Genetic Diagnosis, scientists are on the verge of resolving a couple of outstanding issues with the controversial technology.

“Once we know, truly, what the incidence of mosaicism is,” Kearns elaborates, “in addition to finding the best and least damaging embryo biopsy method, then we may arrive at a point where we can say with assurance that anyone using IVF should also make use of PGD.” Kearns is actively involved in advancing PGD technology, and he estimates that astounding objectives will be achieved within the next year.

“This technology will give us the ability to do comprehensive analysis for all types of chromosomal and genetic disorders,” says Kearns confidently. “What we’re going to be doing soon will completely change embryo testing.”

Cytoplasm Transfer

Depending on how long you’ve been research infertility treatments, you may not have heard about a controversial, experimental technique called cytoplasm transfer. The reason: its therapeutic use has been effectively outlawed in the United States since 2001.

Does that mean cytoplasm transfer will never be an option? That depends on the national political atmosphere and resulting funding of research.

The technique works this way: the cytoplasm of one woman’s egg is replaced with that of another woman’s egg. The result may be a more viable egg with which to create an embryo. Cytoplasm is essentially the nourishing jelly that surrounds an egg’s nucleus. While this jelly is not the primary location of genetic material (that would be the nucleus’s job), there can be trace birth of what’s called mitochondria within the transferred cytoplasm, and that’s where things venture into the territory of the unknown.

When mitochondrial DNA makes it to the embryo-to-be, the result can be an embryo with genetic material of two females and one male. Whether or not a problem results from one human having three people’s DNA is still unknown because research was effectively halted almost as soon as a few cytoplasm transfer babies were born. Some parents of these first babies have taken their on going attempts overseas, where it is still sometimes available, to have more children by the procedure.

The idea for cytoplasm transfer was dreamed up by Steen Willadsen, Ph.D., as a way to correct for egg deficiencies. The dream was brought to fruition initially by Jacques Cohen, Ph.D., Scientific Director of The Institute for Reproductive medicine and Science of Saint Barnabas (IRMS) where, since 1996, 16 babies have been created and born as a result.

“Here were women who, as a group, failed hundreds of IVF cycles at top programs all over the world,” says Cohen’s colleague, Dr. Serena Chen, Director of IRMS’ Division

of Reproductive Endocrinology and Egg Donation Program. “And this technique enabled them to have normal, healthy children with eggs that everyone had said would never make babies.” Within a matter of a few years, Cohen’s standing as a miracle worker with these families was questioned by the U.S. Food & Drug Administration.

“It’s really kind of heart-wrenching, in a way,” says Chen. “We’re in an environment now that’s not hospitable to research. There’ve been misunderstandings that put cytoplasm transfer in the same field as gene therapy, and that’s really a stretch.

Besides concerns about genetic material transfer, some of the earlier news stories pitched cytoplasm transfer as an answer to the conundrum of “old eggs,” causing reactionary alarm as the public imagined hundreds of geriatric new mothers. Chen explains that was never the intention of the therapy.

“There are women of all ages who are infertile due to “bad cytoplasm,” Chen details, “which leads to persistently poor embryo development in spite of all conventional therapies like changing drugs, labs, media. This therapy was a last resort for them. It’s not treatment for older eggs, which have nuclear problems. Women over 40 are better off making use of donor eggs.

The future for cytoplasm transfer is up in the air. FDA’s current requirements for its therapeutic use simply make research unaffordable for scientists.

Access Issues

Financial Matters

The most common financial question is regarding infertility insurance coverage. Anyone who’s done even a little research has probably learned that it’s a state-by-state thing: some states require insurers to cover infertility treatment (with variations in which treatment is covered and when), some have what’s called a mandate-to-offer (which means the insurer is required to offer it to purchasing employers, putting the ball in the employer’s court), and most have yet to address the issue. When will everyone be covered?

While advocacy groups work from a patient point of view on positively impacting related legislation, some economic researchers have taken the cause to task from a perspective that, hopefully, will present reasonable data that even billion-dollar insurance companies can appreciate.

Dr. Lucie Schmidt, from the Department of Economics at Williams College in Massachusetts, has been funded by the National Institute of Child Health & Human Development to look at the 15 states which had by 2003 enacted any type of infertility insurance mandate and determine any effects on the states’ fertility rates. Professor Schmidt compared fertility demographics of these states to each other and over time.

What she found is that the mandates significantly increase first child birth rates for women over 35. Effect on the overall population's birth rate? Zero.

Previous studies have already demonstrated that existence of an insurance mandate does, as expected, increase IVF utilization (Hamilton & McManus, 2005.) Another intriguing earlier finding is that while clinics seem to flourish in areas where women are more educated and wealthier; there is no evidence that a state mandate attracts clinics. Because she wanted to explore the effects related to all fertility therapies and not just IVF, Dr. Schmidt analyzed birth rates.

While her research does not specifically address the future of state-mandated infertility insurance, Schmidt offers a positive note that as an observer, she believes more states will attempt to mandate coverage.

On the question of who can or cannot afford infertility treatment and what that means to the big picture, attorney Steven Snyder, Executive Director of the International Assisted Reproduction Center (IARC), expresses concern about the millions of people who not only don't have infertility insurance, but who are of too modest means to pay even average fees for treatment.

“Because of the stifling cost of these procedures and the fact that everyone, even people earning minimum wage, wants to be parents,” says Snyder, “those patients have lower-cost alternatives, like finding surrogates over the Internet without professional screening assistance. When people are drawn away from responsibility administered clinics and agencies that follow recommended guidelines, those are the cases that blow up.” Several courts have heard third-party ART cases in which confusion over parental rights is painfully prevalent. Snyder and others worry that these worst-case scenarios create exactly the kind of “news” that could lead to over-reactive regulations here in America. He believes that part of the answer is making sure that everyone can afford infertility treatment, which could include legislation for insurance coverage, in order to prevent mismanaged family-building services from surviving.

Government Regulations

More fertility patients are starting to keep tabs on how government regulations may impact access to treatment.

Most patients are so determinedly focused on their goal of bringing a baby home that they've rarely become involved in bigger-picture matters of access. Part of this is due to the fact that the U.S. still has the least regulated fertility industry in the world. While the ASRM, the Society for Advanced Reproductive Technology, and other organizations work to develop and recommend practice standards and ethics guidelines, the truth remains that American doctors are relatively free to do what they and their patients may want, within reason. So, while patients may want their clinics to be free of human error and poor judgment, most do not believe that regulations are warranted for such things as

whether or not a woman can freeze her eggs, how many embryos a couple can make or transfer, whether non-married individuals can pursue fertility treatment, and more.