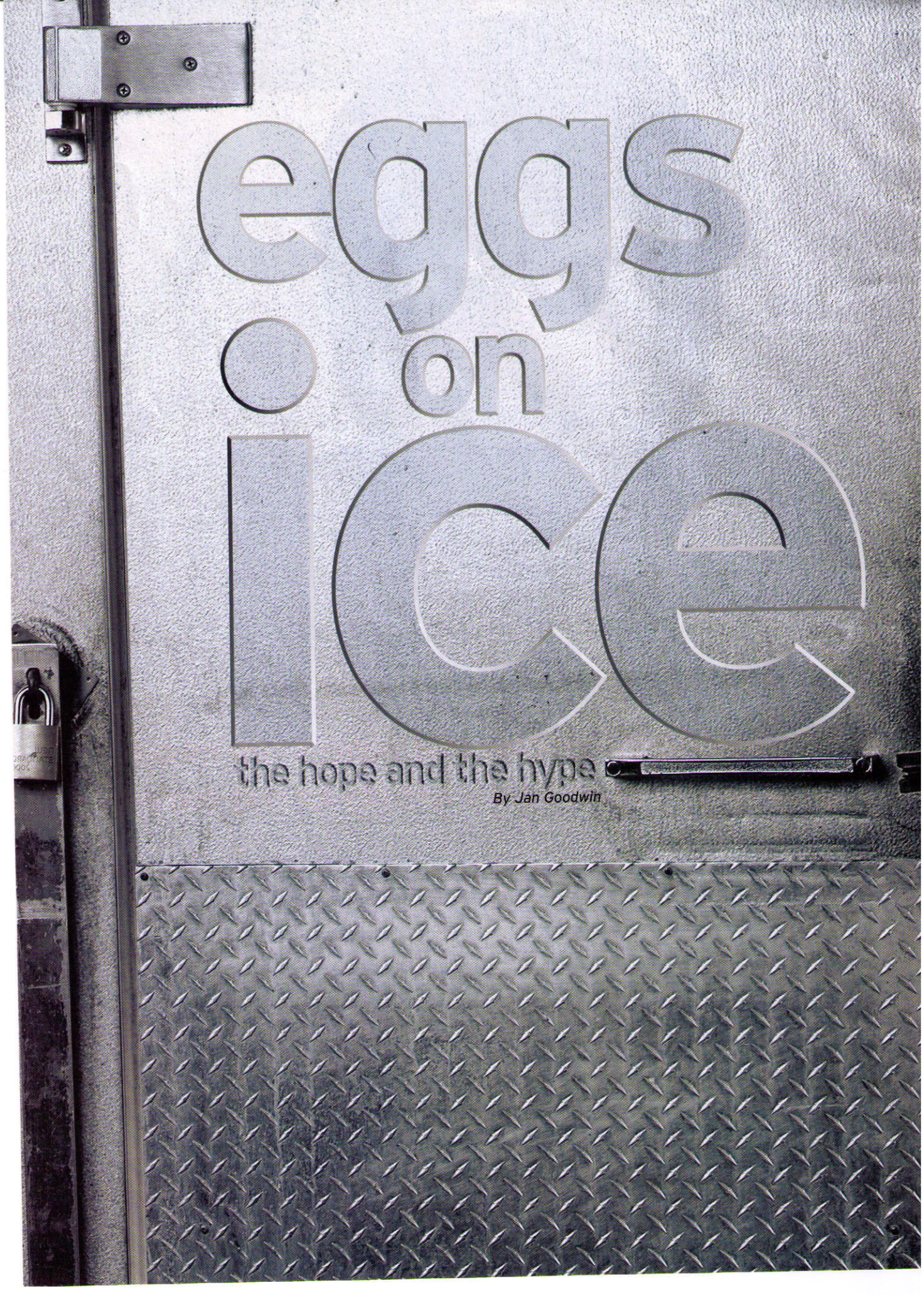

eggs on ice

the hope and the hype

By Jan Goodwin

New technology for freezing human eggs is offering women the hope of preserving fertility threatened by illness or age. Can the technology actually deliver?

As a minister's wife, Mitzi Hamby, of Chattanooga, Tennessee, found that she was often throwing baby showers at her home. "It seemed everyone I knew was having babies, except me," she says. "When the guests left after every baby shower, I would crumple into tears." And Mother's Day events at her church were so painful, she couldn't even bring herself to attend.

The Hambys knew there was a reason they were having problems. "My mother-in-law had taken DES [diethylstilbestrol, a drug prescribed to some pregnant women between 1938 and 1971, because it was mistakenly believed to prevent miscarriages]," explains Mitzi. "Marty and I knew that DES offspring often had difficulties with reproduction. During our six years of trying to have a baby, we learned that Marty had a low sperm count and low motility. I'd see families enjoying outings with their children, and it got to where I couldn't stand it; I'd have to go home. It took such a big toll on me. I was sure we would never have a child. It was so painful to Marty, he couldn't even talk about it."

Now, as Mitzi watches her six-year-old, tow-headed, twin daughters dive to the bottom of the local pool, she calls them her little miracles. "I'll never forget that first ultrasound. I could see two jelly beans pulsating. It was Mary-Beth and McKenzie's tiny hearts beating. I cried then, and I cry every time I watch the video, but these days, it's tears of joy."

CHRIS MCENTRY

Mitzi, now 42, was the first patient at the Florida Institute for Reproductive Medicine in Jacksonville, Florida (where the couple used to live), to use eggs that were fertilized after having been frozen. "I was the first to request the procedure and the second to deliver," says Mitzi, "because I miscarried initially."

Freezing eggs is not the same as freezing fertilized eggs, which become embryos and are considerably easier to preserve. While freezing sperm has been done for decades, freezing eggs is a much newer, and more difficult, procedure. So far cryopreserving (a scientific term for "freezing") eggs is still considered experimental, but the Florida Institute has reportedly achieved more pregnancies using frozen eggs than any other facility in the nation. While thousands of babies have been born worldwide using frozen embryos, only slightly more than a hundred so far have been born using cryopreserved eggs.

"To-date, we've seen 33 babies born through our program, and have seven more pregnancies in the pipeline," says Kevin Winslow, M.D., a reproductive endocrinologist and director of the Florida Institute, where the use of frozen eggs has been the main focus of the center's clinical research for the last six years. "Since what we are doing is very new technology, our work is monitored by a medical board at the Baptist Medical Center in Jacksonville, part of the University of Jacksonville," he says.

Worldwide, thus far, there have been some 130 babies born from frozen, or cryopreserved eggs, according to Dr. Winslow. "As far as I'm aware, the only other center to have a significant number of births from cryopreserved eggs is the University of Bologna in Italy," he says. There, Dr. Rafaella Fabbri, an Italian biologist and embryologist, pioneered egg freezing for her in vitro fertilization (IVF) patients, because under Italian law it is illegal to freeze embryos.

It was their own religious beliefs and feelings about freezing embryos that led Mitzi Hamby and her husband to request this procedure. "We believe that life begins at conception," she explains. "So once those eggs were fertilized and became embryos, each was a living being [to us]. I couldn't imagine having live embryos going unused."

how it works, how well it works

The egg freezing process is much like the first half of an IVF cycle (for more information, see the box, opposite). Dr. Winslow was able to retrieve 20 of Mitzi's eggs, a higher number than normally achieved with hormonal stimulation. More typically, 10 to 12 eggs might be harvested. In Mitzi's case, however, only 15 of the eggs turned out to be viable enough to freeze. Of those, six survived the thawing process and were fertilized. But just four started cell division and were implanted. "And only two of those survived, and went on to become Mary-Beth and McKenzie," says Mitzi.

Such poor odds are, in part, why egg freezing is still considered experimental technology. Human eggs contain considerably more moisture than sperm, making them more difficult to freeze. If ice crystals form during the freezing process, for instance, they can act like razors within the eggs and cause chromosomal damage, explains Eric Surrey, M.D., president of the Society for Assisted Reproductive Technology (SART), an organization that promotes and advances the standards for assisted reproductive technology in the United States. "When the cell is being frozen, it expands and can also explode, just like a frozen pipe in winter," says Dr. Surrey. "So the cell has to be shrunk to make it survive." And there is little published data regarding long-term storage of cryopreserved eggs.

Until recently, freezing eggs was an option offered mainly to women facing loss of their ovaries or loss of ovarian function due to surgery or illness (such as cancer). For these women, the low odds of success were still better than the alternative, which was no chance of biological motherhood in the future.

a new clientele

But now, despite the still-low success rates and the high costs not usually covered by insurance—between $10,000 and $15,000 depending on the center—a growing number of clinics around the country are offering this procedure to affluent single women, usually in their thirties, who want to bank still-young eggs for when they are older. Lawyers, physicians, professors, executives—these women may not have met Mr. Right yet, or are so immersed in their careers they don't yet have time to step off the fast-track long enough to become mothers. But no matter what the heavy professional demands on their lives, some of these women are aware of their biological clocks ticking away and are willing to take steps to try and "stop time" until they are ready for motherhood.

"It's amazing how many very educated and accomplished women just don't know that their chances of becoming pregnant diminish as they get older," says Christy Jones, the founder of Extend Fertility in Boston, which has a network of five fertility centers across the country—in California, New

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> There is no question that egg cryopreservation is exciting technology, and the wave of the future. But we are not there yet.

York, New Jersey and Texas—offering egg freezing to women wishing to preserve their fertility as they become older.

"There are women who believe they will be easily able to conceive up to age fifty, and that is just not the case. Biology intended for us to have children in our twenties," says Jones. "There is a steep drop in fertility in the 30s, and by the time a woman is 40, she only has a 5 to 10 percent chance of conceiving naturally."

One advantage to banking young eggs, according to Susan Treiser, M.D., Ph.D., co-medical director of IVF-New Jersey, which has one of the largest egg donation programs in the country, is that the increased risk of babies born with Down Syndrome to mothers 35 and older would drop. "If the eggs were frozen at, say, age 25," she says, "then the incidence of Down Syndrome would remain that age, even if the eggs were transferred to a 40-year-old woman's uterus."

Jones started her company in 2003, and last year she secured the distribution rights to the formulation of egg freezing and thawing solutions (patent pending) that came out of Dr. Fabbri's work in Italy. The solutions enable the eggs to be slowly frozen so that they are more likely to be fertile when thawed.

None of Extend Fertility's centers have achieved a live birth yet... because they have not attempted one. Says Jones, "We began operating in June 2004, and since the initial stage before egg retrieval takes three months, we only started freezing eggs last December." And so far none of the clients who have had their eggs frozen so recently

how egg freezing works:

The process for cryopreserving eggs is similar to that of the first half of an IVF cycle. Hormones are injected daily for 10 to 14 days to force the ovary to ripen multiple eggs. Vaginal ultrasounds are performed every 2-3 days, along with the monitoring of the blood estrogen level. If there is concern that an individual is developing ovarian hyperstimulation syndrome, the cycle can be cancelled and restarted using lower hormone doses.

retrieval

When the majority of follicles are fully mature, egg retrieval, done under sedation, is performed. Typically, the retrieval procedure takes from 15 to 30 minutes, depending on the number of eggs produced.

storage

Eggs are then stored in special holding tanks filled with liquid nitrogen. "Based on data from cryopreserved fertilized eggs, we do not believe there is a shelf life limit for cryopreserved eggs," says Dr. Winslow, "but until we have established pregnancies with eggs frozen for very long periods, we cannot absolutely assert this. The longest we have frozen eggs which then resulted in successful pregnancies, is two years."

There is no charge for the first five years of egg storage at Dr. Winslow's center; after five years, the fee is $200 annually. The storage fee at Extend Fertility centers is $500 a year.

questions you should ask before you have eggs cryopreserved

1) How many live births has this center achieved?
2) What is the average number of eggs that must be cryopreserved to produce a live birth?
3) How much does this procedure cost, including medications and annual ongoing cryopreservation storage fees?
In general, health insurance will not cover the cost of egg freezing, but it's always worth checking.

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B C MOLLER/GETTY IMAGES

Austin, Texas, froze her eggs last August. She says that undergoing the procedure was expensive, especially since there are no guarantees, but that women should choose how they spend their money based on their own priorities. "Mine are having children one day," she says, adding that she keeps photographs of her ten frozen eggs in her baby book. "It's very exciting. I call them my girls, since that is what they are for now, as it's the sperm that determines sex of the baby." She stresses, "If I wanted to have veneers on my teeth or cosmetic surgery or go on a fabulous trip, I would have saved the money to do it. Freezing my eggs gave me an option I wouldn't have had otherwise. And since I want to be a mother one day, to me, the expense was worth it."

As with every other medical procedure, women have to weigh the odds for themselves and then decide whether the gamble is worth their money. More and more women, like Grace Drake, are deciding that it is. ✽

ovarian tissue transplants

–the future of female fertility?

Last September, a healthy baby girl was born to a 32-year-old cancer survivor in Belgium, who had had her ovarian tissue cryopreserved before undergoing chemotherapy and radiation therapy that could have left her sterile. This was the first ever successful live birth to a woman whose ovarian tissue had been removed, frozen, and re-implanted. But the claim of success is still being debated in medical circles, as doctors admit it's impossible to determine whether the re-implanted ovarian tissue released the hormones and egg necessary for the pregnancy, or whether the ovary that had remained in the woman's body was functioning when she conceived.

Six months previously, in March 2004, Cornell University's Kutluk Oktay, M.D., chair of the American Society for Reproductive Medicine, successfully transplanted ovarian tissue to a cancer survivor's arm and abdomen, producing eggs that were then fertilized into embryos. Thus far no baby has been born from this procedure.

Even more recently, researchers in the Netherlands and South America have successfully transplanted a woman's entire ovary to her upper arm. The procedure was done at the same time as the women's cancer treatment (which was localized to the pelvic area, and would not affect the arm), and made freezing the ovary first unnecessary. In spite of these promising steps, ovarian tissue transplants remain a very experimental procedure with unknown promise. "The data is very, very poor on reimplanting frozen ovarian tissue," says Dr. Winslow. "Researchers have been trying to do this for 15 years, and the one questionable case in Belgium is the only pregnancy to-date. Because the data has been very discouraging, a lot of experts have lost interest in continuing with it."

That certainly doesn't stop women from hoping. Last December, Julie Love, a 24-year-old Florida student, opted to have her ovarian tissue frozen. "Julie was going to lose the ovary from which we took the tissue," explains Fort Myers, Florida, fertility specialist Craig Sweet, M.D. "And because of medical problems, the chances are very high she will eventually lose the other one." Dr. Sweet says that obtaining the tissue–which contains thousands of potential eggs–was a straightforward procedure, as was freezing it. "But what is entirely experimental is the thawing and successful later use of that tissue. Both Julie and I took a leap of faith in the hope that technology will catch up with us."