

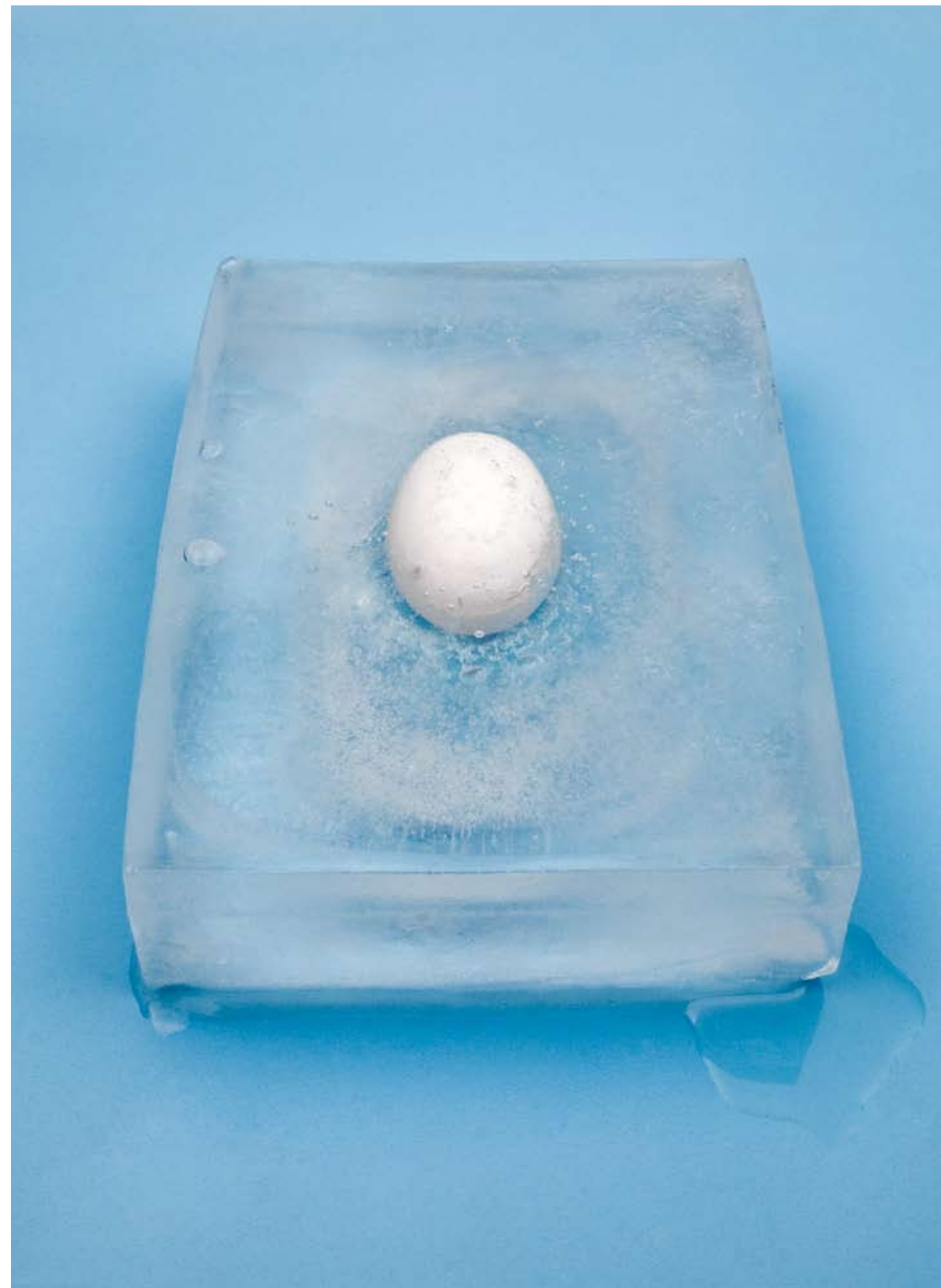
DEEP

Does a new
technique for
freezing eggs allow
women to stop the
biological clock?

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PHOTOGRAPH BY
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FREEZE



ALLISON FRANK

keeps coloring books in her office, a tiny onesie in her dresser drawer, and a syringe in her kitchen because she wants to be a mother. All she's missing is a baby.

¶ This is why, for twelve mornings in a row in January, she sat on her black leather couch and hunched over the coffee table to mix her injection: saline solution plus Bravelle, a highly purified form of a hormone that stimulates egg growth. Then she loaded the syringe, flicked the tip, pushed the plunger gently to release any air bubbles, lifted her shirt, and injected herself in the abdomen. Then she left for work.

chief reason fewer than 600 frozen-egg births have been reported worldwide and that the procedure is still classified as experimental.

Frank's eggs are different. When they were frozen in January, RBA used a new method called vitrification—a technology, pioneered at this clinic, that its architects say will revolutionize the world of assisted reproduction, making the process of in vitro fertilization (IVF) less costly and more efficient than ever before.

Frank's eggs are different for another reason. Unlike the vast majority of the eggs in the bank at RBA, they're not waiting to be picked out of a line-up for use by a couple who cannot conceive on their own. She's part of a small but growing number of women who are taking advantage of egg freezing as a means to preserve their own fertility. RBA is one of the few clinics to offer this service to women thirty-eight and younger as part of a new "egg bank" program, launched in 2008.

At thirty-seven, Frank has met plenty of Mr. Rights, but never at the right time. In recent years she has come to realize that fertility is precious and fades steadily. So she paid about \$10,000 for medication, the retrieval procedure, and the storage of her eggs in RBA's bank. "I'm still optimistic I'll be able to start a family the old-fashioned way," Frank says. "But just in case it doesn't happen soon or happen at all, I have a little insurance policy."

In her job as a salesperson at Mercedes-Benz of Buckhead, Frank kept up her more typical routines—extolling the virtues of luxury cars to Atlanta's elite, sweeping in when a colleague was overwhelmed by a buyer with pesky toddlers in tow, remembering to get cakes for her coworkers' birthdays—but all the while she was preoccupied with what was going on inside her body. Her eggs were growing. She had the ultrasound pictures on her phone to prove it.

On days thirteen through sixteen Frank shifted to once-daily shots of Ganirelix to control her hormones. And on day seventeen she was injected with Ovidrel to trigger the release of the mature eggs from her ovaries. Thirty-six hours later, her mother drove her to Reproductive Biology Associates in Sandy Springs. There Frank changed into a hospital gown and warm socks with rubber pads on the bottom and was sedated. Ten minutes later she woke up, went into the recovery room, and then went home.

The fourteen eggs that the doctors extracted from her body are now frozen in a drum that looks like a propane tank. More than 700 eggs exist in similarly suspended animation here in the lab at Reproductive Biology Associates. Many were preserved over the last decade using a slow-freeze technique that can create ice crystals on the cell and damage the egg, making survival after thaw more difficult. That's the



Fertility treatment is big business, spawned by the sometimes all-consuming human desire to have children and the biological reality that some bodies just can't do it or need help in the endeavor. RBA has been pushing the limits of this branch of medical treatment since 1983. The private company was cofounded that year by Dr. Hilton I. Kort, who studied with Sir Patrick Steptoe, the doctor who in 1978 carried out the world's first successful human IVF birth. In that case, the mother's egg was removed, put in a petri dish, fertilized with the father's sperm, then implanted back in the mother's uterus. The resulting baby, Louise Brown, made big headlines and kicked off significant controversy over whether doctors were playing God by introducing science into reproduction.

The controversy has grown and shifted with every advance in assisted-reproductive technology. In 1984, when Georgia's first baby from a frozen embryo was born, concerns arose that these fertilized eggs—which many people believe are living beings—might end up “abandoned” if a couple no longer needed them. In fact, there are now more than 400,000 such embryos in clinics around the country. (RBA says it has “very few” but did not give an exact tally.)

Researchers and doctors realized that a solution to these ethical and moral conundrums was to focus on the eggs alone, since most people don't view eggs on their own as “life” (they “die” every month when a woman has her menstrual period, the way skin cells die when they slough off). Clinics already stored anonymous sperm for later use; why not do the same with eggs? RBA created an anonymous egg donation program in 1992, the first such program in Georgia; within five years the clinic reported the first births in the Western Hemisphere from frozen donor eggs.

Egg donation has its share of critics, who say young and naive women are treated like fertility factories, pumped full of damaging chemicals without being informed of the risks. And while using eggs instead of embryos does erase some moral issues, there are still some subtler concerns. “The issue is not the egg-freezing itself,” says Paul Root Wolpe, the Asa Griggs Candler Professor of Bioethics and director of the Center for Ethics at Emory University. “It's that the freezing is one of the steps on the way to IVF and the creation of an embryo. Eventually you'll still be faced with the same ethical concerns.”

Dr. Andrew A. Toledo is a religious man, so the way he grapples with these dilemmas in his work as RBA's medical director is to remind himself that this is the patient's choice—he doesn't push IVF, but he provides it. And he uses it, too; his second wife recently gave birth to a child conceived through IVF at RBA, using her own “fresh,” or unfrozen, eggs. There's a photo of the happy family in his office, along with a framed four-leaf clover and a stone engraved with the message “Miracles Do Happen.”

Toledo would probably put a P.S. on the back of that rock: Mira-

cles do happen, but for women with advancing maternal age, those miracles often require a lot of scientific and medical help. Women are waiting longer and longer to have children, and for that they pay a price with their fertility. Though a female fetus is born with 2 million potential egg cells, the number drops to 300,000 by puberty, and a total of only 500 will be ovulated at a rate of once a month. To illustrate the result of this continual egg loss, Toledo pulls out a chart and points to the bars that go from tall to short across the page. “By age thirty-five a woman's chances of conceiving per month is decreased by half,” Toledo says. “The downward slope continues until, by age forty-five, the natural fertility rate per month is approximately 1 percent. That's what a lot of women don't realize. They think they look very healthy and don't look their age, but the eggs act their real age.”

Like so many patients who get that speech in Toledo's office, Allison Frank hadn't really known her fertility could run out so quickly. The where-did-I-come-from filmstrips she watched in grade school health class didn't discuss this, and the after-school specials about teen pregnancy sent one message loud and clear: If you have unprotected sex you will get pregnant, no matter what, no matter when. As an adult, she saw the magazine covers featuring stars in their forties and fifties who were pregnant or gave birth to healthy babies—Cheryl Tiegs, at fifty-two, insisted her surrogate-born twins came from her own eggs—and continued to buy into the fertility myth.

It was only after Frank saw an episode of *The Oprah Winfrey Show* that she realized time might be running out. Featured on the program was

Martha Stewart's daughter, Alexis, who at forty-two was spending an average of \$28,000 a month on fertility treatments and high-tech procedures and getting nowhere.

Frank went to her gynecologist, Dr. Michael D. Randell in Atlanta, and explained her situation: I'm single, I want to have a family the conventional way, but at almost thirty-seven I'm afraid that by the time all the stars align my eggs will be no good. So he suggested she visit RBA. There, in January, she met with Dr. Daniel B. Shapiro, RBA's former medical director and now the head of its new egg bank. He told her about a way she could stop her biological clock cold.

Picture a flock of penguins toddling to a hole in the ice and flopping one at a time into the frigid water. Now picture one brave penguin dive-bombing off an ice cliff into the freezing pool below. This, Shapiro says, helps illustrate the difference between the slow-freezing method that's been in practice since 1986—with limited success—and the new technology called vitrification.

With the old, slower method, the freezing process takes place

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Deep Freeze

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in stepwise fashion over a period of about ninety-eight minutes. If there's any water left in the egg at all, the slow process makes it possible for ice crystals to form. "Ice crystals act like little knives on the inside of the cell, stabbing the cell from the inside out, possibly cracking the egg, making it nonviable," Shapiro says.

The vitrification method takes about sixty minutes from start to finish, though the actual "freezing" of the eggs takes less than a second. "It's actually not true freezing," Toledo explains. "It's supercooling and does not promote ice crystal formation." The survival rate for slow-frozen eggs is 84.1 percent. For vitrified eggs, it's 93.1 percent. The rate of pregnancy with slow-frozen eggs is between 24 and 42 percent, according to some reports. With vitrified eggs at RBA the pregnancy rate is about 70 percent—similar to the rate with "fresh" eggs.

Another difference between fresh, slow-frozen, and vitrified egg IVF is cost. With

fresh eggs—those harvested from a donor, fertilized, then implanted in the mother without any freezing involved—there's a monetary cost of about \$25,000 (lower if a donor is not used). There's also another, softer cost: Mother and donor must synch their schedules, creating logistical hassles and delaying the process. That softer cost is erased with IVF with slow-frozen eggs, but the financial cost is about the same. With fast-frozen eggs at RBA, a round of IVF is priced much lower: about \$16,500. The main reason for the price difference is that vitrified eggs have higher survival and success rates than slow-frozen eggs, and unlike fresh eggs can be stored and used whenever.

That price tag already is catching the eyes of infertile couples not just from Atlanta but from across the country and abroad. "The majority of patients who are coming in to do this are couples using donor eggs," Toledo says. Another market for this service is among women who are preparing to undergo medical treatments like chemotherapy that may leave them infertile. Finally, there are women like Frank, freezing their eggs as a means to stop the biological clock.

"We're now just starting to see young women come in from all over, specifically to freeze their eggs before it's too late. That typically costs around \$7,000 for the freezing and for storage in the bank for two years. After that there's a nominal fee for keeping them here," Toledo says.

In some ways, it may seem like this procedure should be a no-brainer for financially secure women in their twenties and early thirties who want children but aren't ready to have them yet. But psychologists caution against taking such a casual approach. "Doing this doesn't mean you can set your own biological clock. You can put a snooze on it and you'll know that when you come back in your forties you'll have eggs to use, but you still may not be able to get pregnant exactly when you want to be," says Marjorie Blum, an Atlanta-based psychologist who has been working with issues of fertility for twenty-five years. "This does give a greater amount of independence—you don't have to rush into a relationship or be a parent before you're ready, just to have a child—but there's still no guarantee."

It's true; RBA makes no guarantees. But

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the clinic is proud of its success rate so far. RBA's first successful slow-freeze IVF birth took place in 1997. As of February 2009, there have been ninety-four transfers and thirty-two deliveries, and there were thirty-three ongoing pregnancies.

So far there hasn't been a significant increase in abnormality reported among babies born from this form of IVF. Certainly with all kinds of IVF there often is a higher incidence of multiple births, as with the controversial California woman known as "Octo-mom," who gave birth to octuplets after six frozen embryos were implanted. (In response, some Georgia legislators have introduced a bill that would limit the number of embryos created in a cycle and allow a maximum of two implanted in patients under forty and three in those forty and older.) But some studies, including one published in November by the Centers for Disease Control and Prevention, are beginning to suggest that IVF babies of all kinds—fresh embryo, frozen embryo, fresh egg or frozen—could have a higher likelihood of defects such as a hole in the heart, a cleft lip, or an improperly formed esophagus. IVF also has been associated with rare imprinting disorders such as Beckwith-Wiedemann syndrome, which can increase the risk of childhood cancer. And some researchers believe that IVF babies are more likely to develop autism, though some experts point to a different link: Autism often occurs in the offspring of highly intelligent parents, and it's those kinds of parents—older, wealthier, well-educated—that often seek IVF for infertility. These findings are considered preliminary, and researchers say they believe IVF does not carry excessive risks.

At RBA, one set of triplets from vitrified IVF was born early, but all three children are now healthy. In another instance there was a major complication during delivery

that was unrelated to RBA. Really, it's too soon to say whether babies born from vitrified eggs will have more problems; the technology is too new. "Three percent of all deliveries have a major abnormality. That hasn't changed in more than 100 years," Shapiro says. "Will there be a problem with [vitrified-egg IVF]? I don't think so. But there might be. I have to concede that."

Other clinics aren't waiting to see what happens. They're trying to jump on this trend before a company like RBA can go nationwide (something the clinic is considering now). But at this point, very few clinics use vitrification technology. It takes a very delicate hand and precise timing not only to freeze the eggs but to warm them and inseminate them properly. Very few practitioners in the world have mastered the processes. "Although we are not the only practice freezing eggs, we have become the only one in the world to make egg-freezing routine," Shapiro says.

After hearing all of this from Shapiro, Frank was sold. She decided she would dig into her savings and ask her mother for a loan to cover the cost of getting her eggs vitrified and stored in RBA's egg bank, where they'd reside until she was ready to use them.

“Look at that little thing. It's my ladybug.” Frank was lounging on the couch in her cozy Inman Park condo, gently stroking her ultrasound photo with one finger, almost cooing over the cluster of cells that did indeed look like the insect. In just a few days she would be heading into the lab at RBA to get these eggs removed for freezing.

She once thought life started much later than this—maybe when the baby's heart began to beat? But looking at the fuzzy black-and-white picture, she saw the eggs as something tangible, emotional, important

and alive. “They’re delicate little things,” she says. They contain her genetic material and will be meshed with the genetic material of a beloved partner to create a beautiful baby. That’s always been her hope, anyway. She’s wanted to be a mother ever since she was diapering and babysitting her four younger siblings while growing up in Rochester, New York.

The night before her egg-retrieval procedure, Frank woke up again and again. She wasn’t scared of going into the operating room. She was thinking about the fact that having the eggs frozen would create so many questions she couldn’t yet answer: If I date a guy and tell him I’ve frozen my eggs, will he think I’m weird and desperate? What if I fall in love with a man and we’re able to conceive children on our own—what will happen to the eggs? Will I be okay with donating them to infertile couples, and knowing there could be a child out there who is, biologically, partly mine? Would I donate them to close friends, like the one who was recently diagnosed with cancer and now can’t conceive? If I don’t find the right partner for myself, when will be the right time to go ahead and do this on my own?

If Frank doesn’t get married, she assumes she’ll have some of her eggs artificially inseminated with specially selected donor sperm and implanted into her uterus. If she gets a successful pregnancy, she’ll move to Florida to be with her mother and her mother’s partner and create a new, improvised kind of family. If somehow Frank’s frozen eggs don’t survive to become viable embryos that she’s able to carry to term, her plan B will most likely involve donated embryos. She hasn’t ruled out adoption, but deep down she wants most to carry a child. The gestational connection is more important than the genetic.

At 7:30 on a January morning, Frank got in the car with her mother and headed to RBA. In the operating room, she changed into her hospital gown and was sedated. A doctor inserted a wand-like ultrasound probe into her vagina to locate her eggs, then passed a needle through the vaginal wall and into her ovary to remove fourteen. Ten minutes later the procedure was over, and Frank was in recovery, her abdomen just a little bit sore, as though she’d done too many crunches or been punched. Soon after, she was sent home to rest.

That’s when the embryologists went to

work in the lab. In this white-walled room, a silent scientist in scrubs and a paper bonnet placed one of Frank’s eggs in a petri dish and carefully carried it to a metal table with a plastic hood, then set a simple kitchen timer to thirty minutes. Under the watchful eye of Dr. Zzolt Peter Nagy, the lab’s director and the scientist who helped pioneer the vitrification technique, she waited. When the timer beeped, she turned her attention back to the dish and, using an enzyme found in the head of sperm, gently rubbed off the cells that surrounded the egg. The egg was left for two hours, and then vitrification began.

The scientist withdrew all of the water in the cell and replaced the fluid with a series of solutions designed to protect the egg during the fast freeze, each round of solution stronger than the last. She removed the egg from the petri dish and placed it inside a skinny tube that looks like a plastic cocktail stirrer, then put that tube inside a larger tube and placed it on a hook. Then she opened a metal drum. White fog poured out like the smoke from a witch’s cauldron. The scientist lowered the hooked tube through the clouds of liquid nitrogen and into the drum. She shut its lid and wheeled the drum toward the wall.

When the day comes that Frank is ready to use her eggs, the tube will be removed from the drum and the eggs thawed. Then they’ll be placed in a dish next to Nagy’s \$40,000 microscope. Through the lenses he’ll watch as sperm—maybe from Frank’s husband, maybe from a donor—squiggle in another dish. He’ll isolate one sperm, then turn a dial that controls a pin-thin stick and gently roll the stick over the sperm’s tail to temporarily immobilize it. Using another dial, he’ll suck the sperm into a syringe. Then he’ll bring one of Frank’s thawed eggs into the frame. Using his dials he’ll maneuver a needle to the edge of the egg, ever-so-carefully pierce its skin, and inject the sperm inside. Then he’ll coax the embryo out of the frame and repeat the process with several more eggs.

Frank hasn’t had dreams about this process, or about frozen babies or thefts or power outages at the clinic and unintentional thaws. She sleeps the sleep of the calm and prepared. “I’m glad I did it. I have no regrets. I’m not as pressured, which may help me to find the man I’m supposed to meet,” she says. “My biological clock is ticking, just not so loud.” ■