

# ELLE

APRIL 2004

## ICE, ICE BABY

*Want to hit the snooze button on your biological clock? Entrepreneur Christy Jones is bringing the latest technology in freezing human eggs to a clinic near you.*

In the lounge of Spangler Center, at the heart of Harvard Business School, hives of strikingly confident and ambitious women in their twenties and thirties buzz about—assessing job offers, critiquing financial models, turning over plans for entrepreneurial ventures. Heading into their final term, these women, groomed to achieve early and high, seem to have their pick of opportunities.

That evening, however, tucked in the corner of a lively Cambridge bistro, five HBS classmates are talking about babies—specifically, their fear about not having any before time runs out. Around school, they're quick to clarify, the issue is never discussed. "Sex isn't taboo, but this is," says Laetitia Pichot de Cayeux, who at 25 is the youngest at the table—"this" being the inevitability that their professional dreams will collide head-on with their prime babymaking years. One woman, a brunet in a black cashmere sweater and pointy-toe mules, has been mostly silent while she listens and takes notes. She is Christy Jones, a 34-year-old entrepreneur turned student who has invited her classmates to talk about the business she is about to launch—one she believes may avert, or at least postpone, this crash.

Jones' idea is to roll out a national chain of egg-freezing centers over the next few months. Few if any of the attendees had even heard of egg freezing before Jones' venture became the buzz of the business school. "I'm just jealous I didn't think of it first," quips Lesley Solomon, 32, who is looking to open a yoga studio franchise. Solomon says she would love to be Jones' second customer—right after Jones herself, who's first in line.

Egg freezing is a new frontier in fertility technology that promises to prolong a woman's childbearing years by pushing the pause button on the aging of her eggs. A woman can bank some of them, putting them on ice when they are young and typically healthy—on her thirtieth birthday, for instance. Since freezing stops all biological activity, five or 10 years later, when a baby fits more neatly into her timetable, she can retrieve her reproductive assets: the healthy eggs of her 30-year-old self.

The technology has been the focus of intense research around the world since the early 1980s. While some hundred-plus babies have been born from frozen eggs—the first in 1986 and several dozen since then in the U.S. and Italy—thousands of other attempts have failed. (Success rates converge in the low to mid 20 percent range.) Still, egg freezing has finally reached the point where in vitro fertilization (IVF), which uses implanted embryos, was when it became widely available in the mid '80s: experimental but feasible. If improvements continue, egg freezing has the potential to free women from the inexorable biological clock.

This, it didn't take Jones long to figure out, could be a big idea.

## BEATING THE ODDS

It wouldn't be her first. Fifteen years ago, as a 19-year-old Stanford undergraduate, Jones cofounded Trilogy, an innovative software company that sells operating tools to Fortune 500 companies, which last year raked in an estimated \$150 million in sales. Like many of her HBS classmates, Jones spent her twenties grinding away in a fluorescent-lit office, taking only two vacations in a decade. "I didn't really date until I was 29," reveals Jones, who has been seeing the same boyfriend for four years. "Work was too intoxicating." But unlike even the fast-trackers among her peers, she soon hit pay dirt. She traded in her Trilogy shares to launch an e-commerce software company, PcOrder, which she took public, drove to a \$1.5 billion market capitalization, and then sold back to Trilogy in December 2000 for \$100 million. She was 31, had been on the cover of Forbes magazine three times, and was ready to take a step back.

"I always thought I'd work away my twenties and then have a family in my thirties. It didn't exactly happen that way," Jones muses. Despite having excelled in jobs typically held by seasoned male executives, she chose to attend HBS for two years—a legitimate way to bide her time while figuring out the next legitimate thing to do. It didn't take long for lightning to strike again. While living with her parents in their Santa Barbara home before starting her first semester, a dinner-table conversation about a friend's fertility woes prompted her mother to quip about Jones and her three younger sisters, "Maybe you girls should just freeze your eggs." Before the dishes were dry, Jones had Googled enough information on the nascent technology to know that her mother's offhand remark was chillingly prescient.

Jones' own story is paradigmatic of her generation's catch-22, laboriously detailed in Sylvia Ann Hewlett's controversial 2002 book *Creating a Life: Professional Women and the Quest for Children*, which pumped out statistics about infertility and unintended childlessness among high-achieving women like some sports-fanatic boyfriend. Around then, *Time* and *Newsweek* both ran alarmist headlines trumpeting the dwindling reproductive odds for professional women who postpone pregnancy, setting off enough panicky cocktail conversation to give every woman over 25 hot flashes. To Jones, it seemed as if all of her friends were either fretting over their reluctance to get pregnant or, if they were trying, their inability to conceive. Even Oprah dissolved into tears on her show over the fact that she'd never had kids.

Powering the new fertility obsession was a mix of unmistakable demographic trends: The number of unmarried women between 30 and 34 more than tripled between 1970 and 1998; and those between 35 and 39 who were still single increased almost as dramatically. No surprise then that women were not getting to diapers and sleepless nights anywhere near when their mothers did: By 2001, the birthrate for women in their mid to late thirties had more than doubled since the late '70s.

Pregnancy procrastination, and the rapidly improving success rates of reproductive technologies, have fueled a fertility business explosion. In 2001, the number of clinics in the U.S. ballooned to 421, from 281 six years earlier. In 2001 more than 100,000 assisted reproductive technology procedures were performed, a 66 percent jump in five years. With treatments averaging \$10,000, and many women submitting to multiple rounds, more than \$1 billion is spent annually on such procedures. (This doesn't include the cost of other methods such as drug-induced ovulation and intrauterine injection, not to mention New Agey approaches from acupuncture to herbal brews.) Still, three quarters of attempts using any of the primary CDC-tracked procedures result in nothing but disappointment.

The culprit is clear: old eggs. "Age is the number-one factor," says Marcelle Cedars, MD, the director of Reproductive Endocrinology and Infertility at the University of California San Francisco. "It's like the old real estate adage: location, location, location. In fertility, it's age of the female, age of the female, age of the female." (Though this is true for conception, new research has leveled the biological blame in another area: As men age, mutations in their sperm may contribute to certain genetic disorders in their offspring.) Still, few women know just how critical egg age really is, believing that if they are fit and healthy, getting pregnant shouldn't be an issue. (Only 22 percent of women who answered a 2002 Match.com survey thought 40 was too late to have a baby.) This attitude is being borne out all over the country, including at the largest fertility clinic in San Francisco. "Most of the women who come in here are healthy. They're here because they're 40," says Pacific Fertility Center lab director Joe Conaghan. "It's a 40-year-old egg you're trying to get pregnant with. Those eggs just don't perform as well. You can see it—young eggs look brilliant and beautiful. Old eggs are dark and grainier," says Conaghan.

Women are born with a lifetime supply of eggs—some 2 million of them. Over time, the supply of healthy eggs diminishes, at first steadily—about 25 to 30 a day, beginning at puberty—and then, through a woman's late thirties, at a faster clip. Amazingly, the body ovulates the best eggs first. So by 34, the age Jones will be at her Harvard graduation this spring, the egg supply contains a significant percentage of defective eggs. "At 40," says Conaghan, "at least half your eggs are genetically abnormal." (The data on the exact age at which viability dwindles is somewhat circumspect as most studies have been done exclusively on infertile women.)

Egg health and shrinking inventory explain why IVF success rates drop as women age: At 35, around one third of IVF attempts result in a live birth; by 40, half that number of attempts produce a baby, according to current CDC data. Two years later, the odds nearly halve again. Inversely, the chance of an IVF pregnancy ending in miscarriage almost doubles from 35 to 40. The risks of many genetic disorders also increase exponentially: At 30, the likelihood of having a Down's syndrome baby is one in 952; by 40, it's one in 106.

By suspending time, egg freezing could significantly alter the fertility landscape. First, though, women must go through a procedure that's arduous and costly—as much as \$15,000—buying themselves, at best, a chance.

#### **FROZEN IN TIME**

For Amanda (who asked to have her last name omitted), a 39-year-old single San Francisco finance executive whom Jones contacted for the inside scoop on her egg-freezing experience, some chance was better than none. "I want to be able to say I took advantage of every opportunity," she says. "Doing this gave me the courage to wait for true love." In October, Amanda froze eggs at Stanford University's Reproductive Endocrinology and Infertility Center (REI), one of only a handful of clinics in the U.S. currently offering the procedure. The program began in 1999 for cancer patients who wished to preserve their eggs before chemotherapy destroyed them. A little over a year ago, following a steady stream of calls from pleading women, REI began to offer egg freezing to healthy patients.

The entire process, from consultation through freezing, took six weeks. First a reproductive endocrinologist assessed Amanda's candidacy for egg freezing, the first criterion being age; most programs have a cutoff of 38 to 40. Then her ovarian function was evaluated to determine her likelihood of maturing the necessary number of eggs—ideally a dozen or more, though many women proceed with fewer. Two factors are used to predict the condition of the ovaries: level of FSH, a hormone that increases during menopause, and antral follicle count. Women who have more antral follicles (women in their late thirties average eight) tend to mature more eggs. Amanda had 12 antral follicles and low FSH. She produced 11 eggs for freezing.

For three weeks, occasionally while sitting in traffic on the way to work, Amanda shot a cocktail of hormones (Perganol, Gonal-f, and Lupron) into her hip, stimulating her ovaries to mature multiple eggs (the same process used in IVF). Then the eggs were extracted from her ovarian follicles with a long needle during a 15-minute procedure requiring twilight sleep, and prepared for freezing.

Maintaining the viability of an egg while freezing it is an intricate process. The largest cells in the body, eggs are very watery. Because water expands as it freezes, eggs tend to behave like pipes in winter. Ice crystals can form, “which can act like little razor blades and puncture the [shell] like a balloon,” explains Barry Behr, PhD, the head of Stanford’s In Vitro Fertilization and Assisted Reproductive Technologies Laboratory. Plus, the DNA in a maturing, unfertilized egg waiting to split and bind to sperm DNA is in a particularly delicate state, making egg freezing much more challenging than freezing an embryo. The two prevalent techniques, slow-freezing and vitrification (fast-freezing), differ in the way in which the eggs are prepared and the speed at which they’re frozen, but reported success rates are comparable. Amanda’s eggs were preserved using slow-freezing and dipped in baths of increasingly concentrated solutions of sucrose and propanediol, which acts like antifreeze. Finally, eggs are loaded into tiny cocktail-like straws, placed in a steaming tank of liquid nitrogen, and slowly brought to minus 196 degrees centigrade. “At minus 196, time stops,” says Behr. “It doesn’t matter if you freeze for an hour or 10 years.”

When a woman is ready to get pregnant, eggs are thawed (in a reverse staging of sucrose and propanediol baths) and fertilized in the lab. Several embryos are implanted in the uterus and, if all goes well, carried to term. About 60 to 80 percent of frozen eggs survive the thaw, so a woman who begins with 10 has an average of seven to fertilize. Fertilization rates for frozen eggs are around 70 percent, leaving four or five viable ones. Commonly in implantation, some of the embryos will not take. This roulette game explains the procedure’s low success rate and why some women, including Amanda, opt to do more than one round of freezing to boost their odds.

### **EGGS IN ONE BASKET**

Late this spring, Jones expects to open the first of two Extend Fertility clinics on the West Coast. She will freeze her own eggs sometime before opening. “When it’s good enough for me, it’s good enough to open our doors,” Jones declares, every bit the savvy marketer. She’s been thinking of hiring a documentary film crew to follow her through the process. “I realize I may end up being the egg-freezing poster girl,” she says, blushing, as she tends to do whenever attention is focused on her. “But,” she quickly adds, “this isn’t about me. It’s about what this can do for women.” (Jones, who is tight-lipped about her long-distance relationship with her boyfriend, says only that he is “very supportive” of her decision to freeze.)

Rather than build her own clinics, Jones is partnering with existing fertility centers. Women who call Extend will likely be sent to one of two places: Huntington Reproductive Center Medical Group near Los Angeles, the largest fertility operation on the West Coast, or Stanford REI. By piggybacking with top-tier clinics, Extend Fertility gains instant credibility and infrastructure. In return, it provides these clinics with an infusion of new clients. Jones plans to open New York and Boston locations by fall and 20 or so more over the next five years.

Securing the imprimatur of Stanford REI was an important step for Jones. Previously, Linda Giudice, the chief of the Division of Reproductive Endocrinology and Infertility at Stanford Medical Center, opposed the university’s foray into egg freezing for healthy women. Her view, like that of many of her peers, was that the technology wasn’t fully cooked, and she worried that many women would put themselves through an onerous process only to walk away empty-handed. Others would count on the viability of their frozen eggs, putting off babies they were now in a position to have. But improvements in the technology changed her mind. “What Extend is proposing is a service to women,” Giudice says now. “Women have choices about when to go to school, have a job, and get a partner, but not everybody has the same options at the same time. Now women can freeze eggs if they foresee that ovarian aging may be at odds with their personal circumstances.”

Giudice’s 180-degree turnaround is something of a bellwether for what is occurring throughout the fertility field. “There is a growing interest, absolutely,” says UCSF’s Cedars. At the last American Society for Reproductive Medicine (ASRM) annual meeting, in October 2003, egg freezing was the topic of one of the plenary sessions. “This in itself is significant,” says Lynn Westphal, MD, an ob-gyn and the director of Stanford Medical Center’s egg donor program. “There’s no longer the sense that this is on the fringe.”

At that meeting, researchers from the University of Bologna, Italy, where about 20 percent of the world’s frozen egg babies have been born, made a promising announcement: Success rates using frozen eggs, now above 20 percent, were nearly on par with those of frozen embryos. What’s more, Thomas Kim, MD, the medical director of CHA Fertility Center, a fertility clinic in Los Angeles that began offering egg freezing in 2002, reported on a recent study of six IVF patients whose eggs he had frozen, three of whom had babies. (Previously, the Florida Institute for Reproductive Medicine claimed that 45 percent of its patients went home with a baby—but most of the women were 35 or younger.)

“Even two or three years ago, success rates were just a few percentage points—to get involved seemed like a bad idea. Now people are very hopeful,” says Fred Licciardi, MD, the associate director of NYU School of Medicine’s division of Reproductive Endocrinology, which plans to offer egg freezing later this year. “The sense is we just need to do a little better.”

We don't need to make major leaps." The ASRM, however, is cautious "We have not yet found a technology that works reliably with a very high success rate," says Sean Tipton, ASRM's spokesman. "There are a number of technologies that are getting close; it is very promising. But we are not there yet."

Some prominent fertility physicians need a lot more data to be convinced. "I feel very strongly that this technology is absolutely not ready for prime time," says Zev Rosenwaks, MD, the director of the Center for Reproductive Medicine and Infertility at Weill Medical College of Cornell University and New York-Presbyterian Hospital in New York City. "Women should not feel that [egg freezing] is preserving their reproductive function. My biggest concern is the issue of false security." Michael Soules, MD, the director of the division of Reproductive Endocrinology at the University of Washington School of Medicine, asserts that "most of the clinics don't have much experience freezing eggs." Even at CHA Fertility Center, more than 50 women have frozen eggs but only seven have used them.

Jones, nonetheless, is having an "If we build it, they will come" moment. A keen entrepreneur, she sees a rapidly improving technology and hears murmurs about competition. Also, she knows that her early patients will become "ambassadors" spreading the word. With the support of Behr, who recently signed on as Extend's scientific adviser, Jones points confidently to IVF's marketplace entry in the 1980s. The technique, which has produced more than a million babies worldwide, launched with a 10 percent success rate. "IVF was even less accepted than egg freezing," says Behr. "Look at newspaper headlines from those days—they're full of words like *charlatans* and *aliens*."

Initially, Jones will fund the business with her own fortune. "If I'm not willing to put my money behind this, why should anyone else?" she asks. She's already had serious interest from dozens of potential customers, many of them HBS classmates. "I'm hard-pressed to find someone who *doesn't* want to do this," says Jones. A professor who has been advising her is as convinced as her students. "Christy has a problem, but an empty waiting room is not it," says Frances Frei, an associate professor of business administration. "It's explosive demand."

Jones' calculations show that there are some 300,000 women out there just like her hard-driving, career-oriented classmates. (She arrives at this by counting the top 10 percent of wage earners among the approximately 3 million single women ages 30 to 34.) At \$15,000 a pop, and with some women doing multiple rounds, profits could reach the billions of dollars. Also, Jones points out, she expects to serve cancer patients, egg donors—even mothers who are on the fence about having another kid. (In an Extend survey of 230 women, 13 percent of the women who said they would "seriously consider egg freezing" already had a child or were pregnant.)

Jones, too, is motivated by the profound social implications the technology may have—on dating, for one. "My guy friends all say, 'Market this to men. It takes the pressure off. Guys will love you,'" Jones says. Clearly men are feeling the effects of fertility panic too. In San Francisco, one 34-year-old consultant and his serial-dating friends have coined a term for women frenetic to find a mate and have a baby: *cougars*. "You can spot them a mile away, like a dog smells fear," he says.

Egg freezing is an antidote to this demeaning dynamic, says Laetitia Pichot de Cayeux, at Jones' bistro focus group. "You're in a much more powerful position vis-à-vis men. By the time women are 32, men view us as desperate. Now they're going to have to keep us around. It takes the power back."

Despite the idea's seductiveness, for egg freezing to take hold, twenty- and thirtysomething women will have to premeditate their fertility concerns in ways they never have before and abandon the universal knee-jerk reaction to learning their reproductive odds: "I don't want to know." Says Amanda, "This decision is wrapped up in a whole lot of things women don't want to face: Am I ever going to meet someone? Am I going to have a baby of my own?" Buying an insurance policy against infertility is unlikely to top the to-do lists of those who hold out hope through their thirties that marriage and family are just around the corner—especially when it costs so much and requires an invasive procedure they may never need.

The women who most assuredly will call are likely to be pushing 40. But "once it feels like an issue, it's often too late," says Stanford's Westphal. "When women would do anything and pay any amount, they may already be out of time."

All that may change, though, as Jones' "ambassadors" spread the word. "At first I didn't want to go public with it," says Amanda. "Now I bring it up socially." Indeed, news of the technology is starting to seep into the common vernacular. Recently, Amanda was on a blind date, firing back responses to the fortysomething banker's fusillade of "interview" questions about her career path, past relationships, and inevitably, desire for kids. Puzzled, perhaps, by her unruffled response to the topic of babies—or maybe trying to sound au courant—he leaned back and asked, "So, did you freeze?"

"As a matter of fact," she said, "I did."