

Judy Stern, Ph.D.: The accidental career

By Amos Esty

Just before midnight on July 25, 1978, Louise Brown was born in a British hospital. The birth marked a biomedical milestone: doctors had harvested four eggs from Louise's mother, Lesley Brown; fertilized them in a lab with sperm from Lesley's husband, John; and implanted one of the resulting embryos in Lesley's uterus. It was the first successful use of *in vitro* fertilization in humans.

At the time, Dr. Judy Stern was a Ph.D. candidate in zoology at the University of Tennessee at Knoxville. She was hard at work on her dissertation on reproduction in rabbits, which involved implanting embryos in the small animals. "I remember saying, sometime in the '70s, something to the effect of, 'They'll never do this in humans,'" Stern recalls. "And that was just right before Louise Brown was born."

Stern, the director of the Human Embryology and Andrology Lab at DHMC's Fertility Center, remains amazed at the success of assisted reproduction. "It's quite unbelievable that it works," she says. She mentions the ability to freeze an embryo as an example. "You stick it in a liquid nitrogen freezer at minus 196 degrees centigrade, and then you come back three years later and you thaw that embryo out," she explains. "You transfer it, and nine months later there's a baby. That's still fascinating to me."

Stern never expected that she would spend much of her career helping to improve such techniques. After completing her Ph.D. in 1979 and spending two years as a postdoctoral fellow at Duke University Medical Center, Stern arrived at Dartmouth in 1981 to take another postdoctoral position. In 1985, as that fellowship was ending, she learned that DHMC was considering starting an infertility clinic. "I was here, and they were looking for someone to run the lab," she says. "It was kind of a 'right place, right time' kind of thing." Stern, now an associate professor of obstetrics and gynecology and of pathology, has been director of the lab ever since.

In recent years, she has also helped lead a national effort to develop effective guidelines for providers of *in vitro* fertilization (IVF). She is the current chair of the research committee of the Society for Assisted Reproductive Technology (SART), an organization of infertility treatment providers, and she has studied questions such as how

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Grew up: South Queens, New York

Education: SUNY-Binghamton '72 (B.A. in biology), University of Tennessee at Knoxville '79 (Ph.D. in zoology)

Postdoctoral training: Duke University Medical Center and Dartmouth Medical School

Books written: *The Ethics of Scientific Research: A Guidebook for Course Development* and *Research Ethics: A Reader* (both with Deni Elliott)

Observation on the places she has lived: "I've been moving to smaller and smaller towns my whole life."

Hobbies: Playing the piano, gardening, folk dancing

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many embryos should be transferred in a given IVF cycle. That issue has been much discussed of late because of the recent California "octo-mom" case, in which a woman gave birth to octuplets after having six embryos implanted at an IVF clinic; two of the embryos divided, leading to the birth of eight infants. The uproar intensified when it was discovered that she had gone through five previous IVF cycles and already had six children. Cases such as this one make Stern shake her head. "It's a disaster," she says.

Stern thinks the media coverage of the octuplet case exaggerated the lack of regulation in the field. In fact, she says, SART's guidelines have improved the way fertility treatment is delivered. The organization gives "a lot of attention to what individual clinics are doing," she says. Stern explains, for example, that SART is on the lookout for clinics that report high numbers of multiple births over a period of three years. In the California case, there was not three years of data indicating a problem at the clinic in question. But, she adds, this example has prompted SART to reconsider its monitoring methods.

There has been talk of legislation, instead of regulation by the profession, as a way to prevent rare problems such as the California octuplets. But this worries Stern, particularly given the link between IVF treatment and other politically sensitive issues. In the weeks after the case in California came to light, state legislators in Georgia discussed a bill that would have limited the number of embryos that could be transferred to a woman's uterus and the number of eggs a provider could fertilize. The bill would also have defined embryos as human beings, leading critics to claim that lawmakers saw regulation of IVF as a backdoor way of limiting access to abortion. For now, the Georgia bill has been put on hold, but Stern remains concerned. The problem, she says, is that "the law is always way behind the complexity of the situation and way behind the technology."

Good fertility treatment, Stern says, should maximize the possibility of a successful pregnancy while minimizing the risk of multiple births, but that's not an easy balance to find. "You're always in a bind between wanting to get a pregnancy at all, a delivery at all, and having high-order multiples," she says. The problem with treatments that result in twins, triplets, or even greater numbers of in-

fants is that both the babies and the mothers face higher risks. Multiple births are associated with low birth weight, premature birth, a higher risk of infant disability or death, and higher rates of caesarean section.

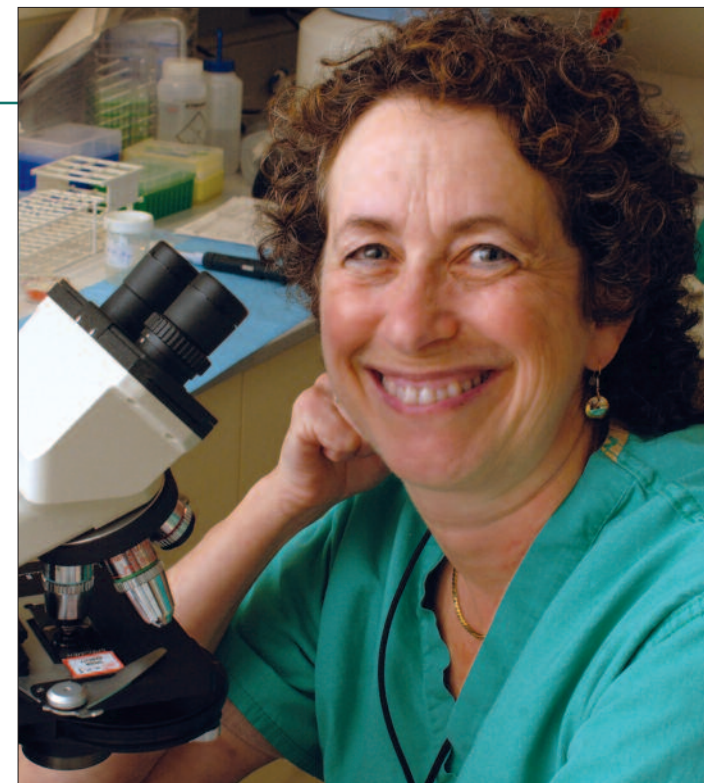
Recently, Stern led an effort to reassess the optimal number of embryos to transfer in women aged 38 and older, for whom IVF is less likely to be successful. As the technology has improved, providers have started to transfer fewer embryos in younger women, but practices hadn't changed for older women.

With colleagues from SART, Stern studied data from thousands of IVF cycles to find out if transferring more embryos actually resulted in a higher success rate. They found that in 38-year-old women, transferring three embryos showed better results than transferring two embryos but that beyond three the success rate did not improve. For 39-year-old women, four embryos marked a similar limit. In women 40 and older, rates did increase with more than four embryos. As a result, the group concluded that three embryos should be the limit for 38-year-old women, four for 39-year-old women, and five for women 40 and older.

Despite the evidence, Stern says it can be hard to convince patients that transferring fewer embryos is the best plan. "Many patients see twins as a success," she says. Stern points out that insurance companies usually do not cover IVF, giving patients a financial incentive to maximize their investment. "For a patient who's paying out of pocket," she says, "twins look really good, because then they can have their two kids and that's it—they don't have to come back."

Professionals like Stern have a different outlook. "Twins is not a success," she says. "A healthy singleton pregnancy is a success." In fact, she adds, if insurance companies covered IVF, it might lead to lower overall costs. When treatment results in a multiple birth, there are often high costs associated with both the birth itself and caring for the infants. As a result, insurers end up paying for expensive procedures in neonatal intensive care units. "It's a backward way of thinking about it," Stern says.

Still, progress has been made in changing treatment practices. According to the Centers for Disease Control, which collects IVF data, success rates have improved dramatically in recent years, while the



A nationally recognized specialist in *in vitro* fertilization and the director of DHMC's embryology lab since 1985, Judy Stern was finishing up her doctoral research on reproduction in rabbits when a British woman gave birth to the world's first IVF baby.

number of embryos transferred has consistently declined. In 1996, about 62% of cycles involved transferring four or more embryos. By 2006, that figure had dropped to 16%. Indeed, by 2006, almost 50% of all treatment cycles involved the transfer of just two embryos, whereas in 1996 only 10% of cycles involved just two embryos. At the same time, results improved. The success rate for two-embryo transfers increased between 1996 and 2006 from 14% to 42%.

Stern believes it will take more research to garner further improvements. Currently, providers examine the size and shape of embryos during the days after fertilization to decide which look the most promising—a method that Stern describes as "a very imperfect way of figuring out

which one to transfer." If providers could be more precise at this step of the process, they would be able to transfer fewer embryos and achieve better success with those that are transferred.

It's not easy, however, to find funding for such research. Since 1996, a congressional amendment attached every year to appropriations bills has barred the use of federal money for research that could result in harm to an embryo. Stern says this policy ends up hindering IVF research. Ronald Green, the director of the Dartmouth Ethics Institute and an expert on bioethics, shares Stern's frustration. The current federal policy, he says, is something of a mixed message. It allows IVF to be used but bars research that could potentially improve it. "You have a formal legal prohibition that makes support for a lot of the laboratory work on IVF impossible," he says.

Despite the challenges posed by such constraints, Stern is glad that her career took the turn it did into the then-nascent field of IVF technology. "It's been a very good thing for me to do," she says. Over the past decade, she has shared the complexities of her work with Dartmouth undergraduates in a course on assisted reproduction that she coteaches with Green and psychologist Catherine Cramer. "Judy Stern brings tremendous authority to the class, with her laboratory background and her clinical experience," Green says.

She also brings a sense of wonder at the very fact that IVF is possible. "When you think about it," she says, "it's mind-boggling." ■