

# The New York Times

## Lowering Odds of Multiple Births

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The doctors are responding to an unintended consequence of the success of in vitro fertilization — that it is often too successful. Since 1980, when the technique became available in the United States, the rate of [twins](#) in all births has climbed 70 percent, to 3.2 percent of births in 2004.

Much of the increase, experts say, is a result of in vitro treatment. The rate of triplets and higher-order multiples increased even more from 1980 to 1998. It is not that twins or triplets are undesirable, doctors say. But multiple pregnancies often lead to risky preterm births and other complications. With that in mind, fertility centers are trying to lower the odds of such pregnancies, even at a cost of slightly lower success rates.

“Now is the time for all of us to rethink what is the paradigm of a successful I.V.F. [pregnancy](#),” said Dr. Aaron K. Styer, a reproductive endocrinologist at the [Massachusetts General Hospital](#) Fertility Center in Boston. “Is it a pregnancy without regard to the number of gestations or a pregnancy with a singleton live birth?”

In I.V.F., a woman is given ovulation-induction hormones to produce multiple eggs, which are retrieved, fertilized with her partner’s sperm and transferred back to her uterus. The more embryos transferred, the higher the likelihood of multiples.

To achieve the goal of a single healthy baby, clinics are focusing on transferring fewer embryos and on developing more sophisticated ways to identify the healthiest embryos with the greatest chance of success.

“We have been getting better at I.V.F. over the years, and as success rates go up, the number we transfer has to go down accordingly,” said Dr. Judy E. Stern, director of the human embryology and andrology lab at the Dartmouth-Hitchcock Medical Center in Lebanon, N.H. “Where three embryos used to work and give you mostly singletons, now we transfer two, because we’re making better embryos and more of them implant.”

The number of I.V.F. cycles in which four or more embryos were transferred has dropped sharply, to 21 percent in 2004 from 62 percent in 1996. Although the efforts have substantially lowered the rates of triplets born through in vitro fertilization, they have not made a dent in the twin rate. That is because many doctors and patients are reluctant to take the final step to ensure a single birth, a process called S.E.T., for single embryo

transfer. From 1996 to 2004, the rate of such procedures rose modestly, to 8 percent from 6 percent.

The American Society of Reproductive Medicine now recommends that women younger than 35 with a good prognosis have just one embryo transferred. Women under 35 make up 44 percent of I.V.F. cycles.

In women older than 37, who have a higher incidence of embryos with chromosomal defects, three to five embryos are still recommended, depending on the woman's age.

The main obstacle to single embryo transfer is its lower success rate. Some experts ask women to agree to two cycles, first transferring one fresh embryo while freezing the others. If the first transfer fails, doctors transfer a single frozen embryo, a much less costly and onerous procedure. That approach yields similar success rates to transferring two at once while drastically reducing twin rates.

With momentum building to transfer just one or two embryos, clinics focus on choosing the embryo most likely to succeed. Selecting embryos has traditionally been based on a visual examination of their morphology — shape, number of divisions and other physical factors. But morphology does not tell all, and many embryos that look great under the microscope have undetected chromosomal abnormalities like missing or extra chromosomes, called aneuploidy.

One method used to weed out unhealthy embryos is to leave the embryos in a Petri dish for five days, two more than usual, to allow more time for hidden chromosomal abnormalities to show up.

Other researchers are looking at the traits of women at high risk of having multiples. In research presented at the reproductive society's annual meeting last October, Dr. Stern linked a higher number of oocytes, or eggs retrieved from ovaries, with higher rates of single and multiple pregnancies.

"This will change our practice," she said. "If more oocytes are retrieved, we'll want to transfer fewer embryos."

Other experts are turning to preimplantation genetic screening to cull embryos without aneuploidy. The screening is used to select healthy embryos in families with histories of genetic diseases. Because one or two cells have to be removed for analysis, there is some concern that the process can damage embryos, lowering pregnancy rates.

In the complex, expensive and emotionally charged world of fertility treatment, doctors are sounding a call to arms to reverse the soaring rate of [multiple births](#).

But Dr. Sher, whose lab performs this procedure, has encountered the same obstacles as others. He has a very high twin rate, hovering around 60 percent, because although the

technique yields a higher success rate, women are refusing to have just one embryo transferred.

Many women in fertility treatment say that they simply do not view having twins as a risky situation and that they are willing, if not eager, to have them to speed the completion of their family, to avoid the high costs of future I.V.F. cycles or to ensure that their child has a sibling, among other reasons.

For a couple in Brooklyn who asked that just the woman's first name be used to protect their privacy, six years of infertility and several failed procedures was enough. When the woman, Marie, was 28, they requested that three embryos be transferred, even though their doctor advised transferring two.

"I wanted a set of twins," Marie said. "It is such a complicated and sometimes painful thing to go through I.V.F., and to have to go through it all again for a second child was just a waste for me."

In the third in vitro cycle, last June, Marie became pregnant, with triplets. At four weeks, she lost a fetus. At four and a half months, she lost the entire pregnancy.

She was devastated, she said, but she added, "I don't regret my decision."

Though it is widely accepted that carrying three or more fetuses can have serious complications, some fertility specialists do not view a pregnancy with twins as risky, as long as the patient is carefully monitored.

"Yes, twin delivery has more risk than singleton delivery, but with good obstetrical care and educated patients, the risk of twin delivery is minimally higher," said Dr. Norbert Gleicher, medical director of the Center for Human Reproduction in New York.

Carrying twins or higher-order multiples raises the risk of preterm births; low-birth-weight babies, with the possibility of death in very premature infants; long-term health problems; and pregnancy complications, including pre-[eclampsia](#), [gestational diabetes](#) and [Caesarean section](#). Studies show that 56 percent of I.V.F. twins born in 2004 weighed less than 5.5 pounds, and 65 percent were born prematurely, before 37 weeks of gestation.

Still, many patients take comfort in the improvements in neonatal care. The survival rate for newborns over 2 pounds 3 ounces is 85 percent. And many people just see the adorable twins cooing in the double strollers crisscrossing Central Park — not the ones that do not make it out of neonatal intensive care — or the fetus that was eliminated in a medical procedure called a reduction to improve the chance of survival for the remaining fetus or fetuses.

Along with changes to in vitro fertilization, experts say, physicians need to improve monitoring drugs used to enhance ovulation.

“The biggest problem with high multiples is coming from ovulation induction,” said Dr. Richard P. Dickey, chief of reproductive endocrinology and infertility at Louisiana State University Medical School in New Orleans.

If ovaries are too aggressively stimulated with hormones, a woman can produce a nest full of eggs and increase her risk of having triplets, quadruplets and even sextuplets. All ovulation-induction cycles should be closely monitored, and the cycles that produce too many oocytes should be canceled, Dr. Dickey said.

The biggest obstacles to reducing twins in infertility treatment are not medical, experts said, but the lack of insurance coverage, as well as pressure from patients to be aggressive.

“People have to recognize that there’s a connection between cost and how the treatment is going to play out,” said Barbara Collura, executive director of Resolve, a patient advocacy organization for people with infertility. “If you have \$10,000 that you’ve begged, borrowed and stolen for this one I.V.F. cycle, you’re not going to say, ‘Please just transfer one.’ ”

Even doctors in the vanguard of the trend face resistance from patients like Marie.

Despite her pregnancy loss, she said, “With all the hard work I put into getting pregnant, I’d just rather have a set of twins than a singleton.”

*This article has been revised to reflect the following correction:*

Correction: February 20, 2008

An article in Science Times on Tuesday about the higher risks involved in multiple births misstated the meaning of the term “vanishing twin.” It is a miscarriage of one twin, not a fetus eliminated in a medical procedure called a reduction.