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HEALTH | NYT NOW

Fertility Clinics Scan for the Strongest Embryo

By ANDREW POLLACK JULY 11, 2014

Annika Levitt initially resisted the fertility clinic's suggestion that only one embryo — rather than the usual two or more — be transferred to her uterus because she was too small to risk carrying more than one baby.

"You go through all that and you put only one back in?" she recalled thinking, fearing it would lower her chances of becoming pregnant.

But her embryos had been tested for chromosomal abnormalities, giving a fair degree of confidence that the chosen one was healthy. "Knowing that it was the strongest of the strong was reassuring," she said. Ms. Levitt, who lives in Morris County, N.J., gave birth to a girl from that embryo and is now pregnant from another single-embryo transfer.

The chromosomal testing is one of the techniques now coming into use to help fertility clinics answer one of their most vexing questions: Which test-tube embryo or embryos will give a woman the best shot at having a baby?

Another new technique uses time-lapse imaging to study the development pattern of the embryo.

Both techniques can potentially provide more information than the approach now used to judge an embryo's fitness, which is to look at its shape under a microscope.

That could increase the sometimes frustratingly low efficiency of in vitro fertilization. And if clinics can be nearly certain that an embryo is fit, they might feel more comfortable transferring only one embryo rather than two or more, as is common practice. That would reduce the chances of

producing twins or triplets, which face greater health risks than single babies.

“What’s really good about this is we get high rates with singletons,” said Dr. Richard T. Scott Jr, clinical and scientific director at Reproductive Medicine Associates of New Jersey, where Ms. Levitt went.

But some experts say the new techniques, which can add thousands of dollars to the cost of in vitro fertilization, are being heavily promoted without data supporting that they truly improve pregnancy rates. For some women, they say, chromosomal testing, an invasive procedure, might even worsen their chances of getting pregnant.

“A significant portion of women may actually be hurting themselves by doing that,” said Dr. Norbert Gleicher, medical director of the Center for Human Reproduction, a fertility center in Manhattan.

The chromosomal testing is called preimplantation genetic screening, or P.G.S. This is different from a related technique called preimplantation genetic diagnosis, which tests embryos for specific mutations with the goal of preventing the birth of a baby with a genetic disease. With the chromosomal screening, the goal is mainly to improve birthrates, not influence the traits of the baby.

Ms. Levitt, who is 33, initially sought in vitro fertilization to avoid having babies with a genetic disease for which she and her husband carry mutations.

Despite some doubts, use of the new techniques seems to be expanding rapidly.

“We doubled the volume in 2013 over 2012,” said Dr. Santiago Munné, director of Reprogenetics, a laboratory that does embryo screening for fertility clinics.

Other laboratories that do this include Genesis Genetics, Reproductive Genetics Institute and Natera. Dr. Scott’s clinic developed its own test, which it also performs for other clinics.

Illumina, the largest manufacturer of DNA sequencing machines, is also making a push into the arena. It acquired BlueGnome, a British company

that sells DNA chips used by some laboratories to do the testing. Illumina also recently introduced a system that uses sequencing for embryo screening.

On time-lapse imaging, Auxogyn, a Silicon Valley start-up, just received clearance from the Food and Drug Administration to market a computerized system that predicts the fittest embryos. It will face off against Unisense FertiliTech, a Danish company that sells a time-lapse system called the EmbryoScope.

P.G.S. can add $4,000 or more to the price of a cycle of in vitro fertilization, which usually costs at least $10,000 to $15,000. Time-lapse imaging can add several hundred dollars to $1,500 or more. Insurance might not pay for such testing.

Even for younger couples, as many as half the embryos created in a test tube have chromosomal abnormalities, a major reason embryos fail to implant in the uterus or result in miscarriages. So it seems logical that weeding out the defective embryos would increase the chances of a successful pregnancy.

But that has proved illusory once already.

An earlier generation of P.G.S. was used for about 10 years — until a randomized clinical trial in 2007 showed that testing actually decreased the chance of getting pregnant.

How could that be? One likely reason was that the testing itself damaged some embryos. Also, the test could assess fewer than half of the 23 chromosome pairs, so it was not very accurate in determining if an embryo was normal.

Proponents of P.G.S. say that has now changed: The new techniques can assess all the chromosomes.

Also, the old technique involved removing one cell from a three-day-old embryo containing only eight cells. The new testing is generally done on five-day-old embryos, which have more than 100 cells. That makes it safer to remove multiple cells, giving a more accurate result than if only one cell is tested.

Still, critics say, if the test is at all inaccurate, some good embryos might be thrown out or defective ones chosen.

A study presented at the European Society of Human Reproduction and Embryology meeting on June 30 found that different testing techniques can yield different results for the same embryo, suggesting that not all the tests are accurate.

Also, some embryos die between Day 3 and Day 5 and lose the chance to be transferred. While those embryos might have been abnormal anyway, there is a chance that waiting five days to test could be costly, especially for older women, who produce fewer eggs.

Christine Peixoto of Lebanon, N.J., for instance, produced only one embryo that survived for five days and tested normal. But she failed to become pregnant.

The next year, at age 39, she had three 3-day-old embryos transferred, without testing. She gave birth to a girl.

Still, data is accumulating showing the technique can help improve pregnancy rates, particularly in younger women who produce more eggs and therefore more embryos to choose from.

One study involving about 100 women under age 35 found that 71 percent of the women in the group whose embryos were tested became pregnant compared with 45.8 percent of those whose embryos were selected based only on their shape.

For women over 35, who often need more help getting pregnant, a small randomized study by Dr. Scott's clinic and the Colorado Center for Reproductive Medicine found a higher live birthrate in those who had P.G.S. — 74.5 percent versus 53.7 percent in the control group. However, Dr. Gleicher, the critic, said the women in this study had a more favorable prognosis to begin with than many older women.

Use of time-lapse imaging presents a noninvasive alternative, in that it does not require removing cells from the embryo. Auxogyn's system, called Eeva, takes images of the embryos every five minutes or so for the first three days. It uses an algorithm to calculate a score on how fit the embryo is based

on the timing of certain events, such as how long it takes cells to divide.

"It improves pregnancy rates substantially more than anything that is out there, and without invasion," said Dr. G. David Adamson, chief executive of Advanced Reproductive Care, a network of fertility clinics, who has been a consultant to Auxogyn.

So far, however, there has been no published data showing that use of the system improves pregnancy and live birthrates. There is a study showing that the Eeva test is better than embryo shape alone in predicting which 3-day-old embryos will survive to five days in the incubator. Presumably those would do better in the womb as well.

FertiliTech's EmbryoScope leaves it to each clinic to analyze the time-lapse images. Niels Birger Ramsing, the company's chief scientific officer, said that clinics differ in how they culture embryos, so the timing of cell division events can differ. That makes it difficult to develop an algorithm that would work for all clinics, he said.

A version of this article appears in print on July 12, 2014, on page B1 of the New York edition with the headline: A Fitness Test, on the Smallest Scale.
