Europe's Focus on SET May Not Work for U.S.

BY KATE JOHNSON

Montreal Bureau

LYON, FRANCE — Europe's focus on avoiding twins from in vitro fertilization may be inappropriate for the United States, suggests Dr. David Adamson, director of Fertility Physicians of Northern California.

Single embryo transfer (SET) has been mandated in many European countries as a means of virtually eliminating twins, but many studies show that in the hands of most fertility specialists, SET results in fewer pregnancies and babies than transfer of two or more embryos, he said in an interview at the annual meeting of the European Society of Human Reproduction and Embryology.

"We have to individualize our approach to each patient, and therefore I don't think [SET] should be regulated by government," Dr. Adamson said. "A twin outcome, while not optimal by any means—and we want to avoid it if at all possible—is not invariably a bad outcome, and very commonly it's been a good outcome."

Dr. Adamson touched on the root of the Europe-U.S. rivalry over IVF success rates. While experts at the meeting debated the often microscopic details of IVF, the big picture—the "take-home baby rate"—remained conspicuously out of focus. At a sparsely attended early-morning session, Dr. Jacques Mouzon reported the latest figures (2003) from the International Committee for Monitoring Assisted Reproduction: Europe's overall IVF take-home baby rate was 23% (per egg retrieval), compared with 38% for the United States, said Dr. Mouzon of Institut National de la Santé et de la Recherche Médicale in Paris.

Traditionally lagging behind the United

States in this ultimate measurement of IVF success, many European experts say America's higher "take-home baby rate" comes at an unacceptable price: high numbers of twins and triplets, who face poor health outcomes at a steep cost to society. In contrast, they emphasize their impressively low rate of multiple pregnancies.

The latest figures from ESHRE show that in 2004, across Europe, SET was performed in 19% of IVF cycles. Out of all IVF cycles performed, the twin and triplet birth rates were 21.7% and 1.0%, respectively, reported ESHRE spokesman Dr. Anders Nyboe Andersen of Rigshospitalet in Copenhagen. Elsewhere at the meeting it was reported that some individual European countries such as Sweden have a 70% SET rate and have reduced their twin rate practically to zero (OB.GYN. NEWS, July 15, 2007, p. 6).

In contrast, U.S. (2004) figures from the Society for Assisted Reproductive Technology show that SET, in women under age 35, was performed in only 1.2% of cycles, with the twin and triplet pregnancy rate clocking in at 32.7% and 4.9%.

Many experts acknowledge that cost plays a big role in the contrast between continents. National health systems cover IVF treatment in many European countries, which means they can mandate strict policies limiting the number of embryos transferred—and patients accept. In contrast Americans, paying out of pocket at \$9,000-\$15,000 per IVF cycle (including drugs and all costs), are not so keen to accept only one embryo per transfer.

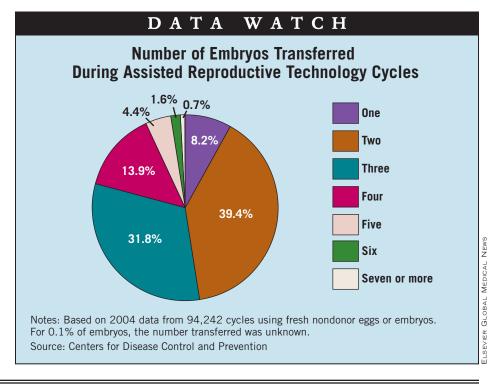
"There's no question that when patients are paying for it, they really are looking for success on the first cycle," said Dr. Adamson, who practices in Palo Alto, Calif. In

this context, an overenthusiastic use of SET to avoid twins may not be appropriate in the United States, not only because it may reduce the chances of pregnancy, but also because a twin outcome is not entirely undesirable, he said.

"One of my major arguments is you have to look at the benefits of having a child, and there's a benefit to having an extra child, especially if that child is healthy and even, possibly, if that child is not healthy," he said. "You can't just look at the costs of twins, which are clearly higher, and that the portion of twins that are healthy is a little bit lower, but at the end of the day most twin pregnancies end up with two healthy babies. Such twin pregnancies definitely create a benefit for the family, the children, and so-

ciety." Nevertheless, Dr. Adamson emphasized that the ideal outcome, and always the goal, is a healthy singleton pregnancy.

Studies have shown that getting two babies for the price of one IVF cycle is an attractive idea to many patients, regardless of cost, since for many the price of infertility treatment goes beyond money. "What we have to strive for is the best information so we can share it with the patients, and they can be well informed when they elect to undergo these procedures and decide how they want to invest their time, money, and emotional effort," Dr. Adamson said. "We have to try to find a balance. All reproduction is inherently risky . . . it's a question of balancing known risks and potential risks versus the expected benefit."



ART Twins Face More Umbilical Cord Problems Than Spontaneous Twins

BY KATE JOHNSON

Montreal Bureau

Lyon, France — Compared with spontaneously conceived twins, twins who are conceived through assisted reproductive technology have an increased rate of umbilical cord abnormalities, according to the first large study to assess this. And the incidence of such abnormalities increases with the invasiveness of the fertility treatment, said lead investigator Ilse Delbaere, a Ph.D. student at University Hospital Ghent, Belgium.

"The umbilical cord characteristics that have been associated with adverse outcomes are seen more frequently after ART [assisted reproductive technology]," she said at the annual meeting of the European Society for Human Reproduction and Embryology. "Considering the effect of cord

abnormalities in twin pregnancies after ART may further our understanding of the underlying mechanism responsible for adverse outcomes after ART," she suggested.

The study compared umbilical cord characteristics in 2,119 spontaneously conceived dizygotic twins and 2,243 dizygotic twins who had been conceived with ART. The incidence of velamentous cord insertion-which has been associated with preterm delivery, low birth weight, fetal growth retardation, and malformations—was 3.6% in spontaneously conceived twins but was roughly doubled (7.4%) in twins conceived with in vitro fertilization (IVF) and tripled (10.4%) in twins conceived with intracytoplasmic sperm injection (ICSI), Ms. Delbaere said. Moreover, the incidence of single umbilical artery (SUA), was significantly higher in twins conceived through ovulation induction (1.9% vs. 0.6%). It was also higher in IVF and ICSI twins, but the difference did not reach significance, she said.

The findings support the trophotropism theory that placental migration is more common in twin pregnancies because of competition for nourishment. ART twin pregnancies are particularly vulnerable because 80% of ART embryos implant near the transfer location, "which is not always ideal," she said. "The placenta may migrate to more favorable areas, turning an initial central insertion of the cord into something more peripheral." She hopes to follow up her research by adjusting for cord abnormalities in ART twins to assess whether adverse outcomes are still more common in them than in spontaneously conceived twins.

Less Aggressive IVF Protocol Cuts Multiples, Retains Live Birth Rate

A less aggressive in vitro fertilization protocol results in roughly the same rate of pregnancies leading to term live births as do standard methods, but with decreased multiple pregnancy rates and overall cost, according to Dutch researchers.

The cumulative 1-year proportion of pregnancies producing term live births was 43% in 205 women who underwent the less aggressive IVF protocol, compared with 45% in 199 women who underwent standard treatment, the investigators reported.

The women were randomized to one of two IVF strategies: standard ovarian stimulation with a GnRH agonist long protocol and the transfer of two embryos (standard treatment) or mild ovarian stimulation with GnRH antagonist cotreatment and single embryo transfer (what the researchers termed "mild" treatment).

The women were aged younger than 38 years and either had no previous IVF treatment or had borne a healthy child after previous IVF treatment, wrote Dr. Esther Heijnen and her colleagues at the University Medical Center in Utrecht, the Netherlands (Lancet 2007;369:743-49).

High-quality embryos that were not transferred were cryopreserved and thawed for transfer in a subsequent unstimulated cycle before the start of a new IVF treatment cycle. The average number of treatment cycles was 2.3 in the mild treatment group and 1.7 in the standard treatment group. Overall, there was no significant difference in discomfort between the groups, despite an increase in the average number of IVF cycles for the mild treatment group.

The proportion of multiple births per couple during 1 year of treatment was significantly lower with mild treatment (0.5% vs. 13%).

Despite a greater average number of cycles in the mild treatment group, total costs of IVF treatment per couple (regardless of whether pregnancy resulted) were significantly lower with less aggressive treatment.

-Kerri Wachter