Human Cloning Bid Stirs Experts' Anger

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Wednesday, March 7, 2001; Page A01

The bull was a born winner, naturally resistant to three bovine diseases, and a herd of genetically identical clones would be invaluable. Now, the first of those clones was just a month away from being born, but the mother mysteriously had become swollen with fluid.

"She got so big in the end that she aborted, and we lost that calf at eight months," said Mark Westhusin, the Texas A&M veterinarian who oversaw the 1999 effort. "That cow looked like she swallowed a 55-gallon barrel of water."

Westhusin has grown accustomed to such failures. He and other leading animal cloners know that behind the stunning stories of cloning successes in cows, sheep, goats, pigs and mice, 95 percent to 97 percent of efforts still end in disaster.

So while the prospect of human cloning raises countless ethical quandaries, it was cloning's dismal safety record that led experienced cloners to cringe in January when a team of fertility specialists announced it would embark on the world's first concerted effort to clone a human being.

That international team, which includes a maverick scientist-entrepreneur from Kentucky, will meet in Rome on Friday to further its plan, and scientists are fuming.

"What these guys are doing, or saying they're going to do, is just criminal," said Rudolf Jaenisch, a pioneer in cloning at the Whitehead Institute for Biomedical Research in Cambridge, Mass. "Serious problems have happened in all five species cloned so far, and all are mammals, so of course it's going to happen in humans. No question."

If the team really tries to clone a person, here's what to expect, several scientists said:

Almost all of the first 100 clones will abort spontaneously because of genetic or physical abnormalities, putting the health and lives of the surrogate mothers at risk.

Of the handful of clones that make it to term, most will have grossly enlarged placentas and fatty livers.

And of the three or four fetuses that may survive their birth, most will be monstrously big -- perhaps 15 pounds -- and will likely die in the first week or two from heart and blood vessel problems, underdeveloped lungs, diabetes or immune system deficiencies.

With access to an intensive care unit, perhaps one of those 100 clones will survive, scientists said. It will bear the hallmark of most animal clones: a huge navel -- a remnant of the oversized umbilical cord that inexplicably develops during most pregnancies involving clones.

"If there were cloned human beings, you'd be able to recognize them at the beach -- they'd be the ones with navels that are two or three times the normal size," said Michael West, president and chief executive of Advanced Cell Technology Inc. (ACT) in Worcester, Mass., a biotechnology company racing to perfect animal cloning methods.

Sometimes the fatal flaws in clones are obvious. In several instances, for example, cloned cows have been born with head deformities.

"They have a bulldog, squashed-up face or head," said Jon Hill, a veterinary reproductive physiologist at Cornell University and a leading expert in animal cloning. Those clones never survive.

Even when clones appear normal, they sometimes are not.

"Just before Christmas, we had a cloned lamb that was perfectly formed," said Ian Wilmut, co-creator of Dolly the sheep, the first mammal cloned from a single adult cell. But the lamb could not stop hyperventilating, and after a few days it was euthanized. An autopsy revealed malformed arteries leading to the lungs.

"What if it had been a child?" Wilmut asked. "Who would be responsible for such a child? What sort of life would it have, panting all of the time?"

"What's remarkable is when they are normal," Hill said. "We go, 'Wow, look at that!' "

Such tales do not fluster Lexington, Ky., fertility specialist Panos Zavos, who in January announced that he and Italian obstetrician Severino Antinori would embark on the first bona fide effort to clone a person.

Zavos, who has done research on cattle semen, owns two businesses in Lexington and runs a fertility clinic about which little is known because it does not participate in the national voluntary program through which success rates are published. He claims on one of his many Web sites to be a member of the prestigious American Society for Reproductive Medicine. The society says that is not true.

His Italian counterpart, Antinori, gained worldwide attention and some professional reprimands when he helped a 62-year-old woman become pregnant. He also raised eyebrows by placing infertile men's sperm cells inside the testicles of mice in an effort to enhance the cells' maturation before using them for artificial insemination.

When Zavos announced in January that he and Antinori would collaborate on a human cloning project, he said this month's meeting in Rome would include cloning experts from around the world as well as a Roman Catholic cardinal to discuss ethical concerns. "There will be Japanese, Koreans, Orientals, Greeks, Italians and some elite members from the Middle East Medical Society," he said.

But the program for the meeting indicates a significantly scaled-back affair. No cardinal is scheduled to appear. And several experts in the United States said that of the five speakers other than Antinori and Zavos, the only one whose name they recognized was that of Karl Illmensee, an Austrian who in 1979 claimed to have cloned several mice. The secretive work, which no other researcher was able to replicate, was ultimately discredited.

It's not clear whether the participants in Friday's conference will be directly involved in the human cloning effort, nor is it known where the work will be done. The Food and Drug Administration has said that no one may try to clone a person in the United States without its permission, but that it has no authority overseas.

Neither Zavos nor Antinori responded to recent repeated phone calls and e-mails from The Washington Post. But Zavos sought to reassure critics in January by saying that significant progress had recently been made in scientists' ability to select only those cloned embryos with the best chances of growing into healthy newborns.

"We have a good understanding of all the failures with animal cloning," Zavos said. "We can quality-control embryos now and screen them and make sure there are no defective genes."

Several cloning experts disagreed. Very little is known about what goes wrong in clones, experts said, and only now are researchers conducting sophisticated genetic experiments to understand what is going on.

Many suspect that the problem involves genetic "imprinting," a poorly understood molecular mechanism through which genes inside sperm and egg cells are turned on or off in preparation for early embryonic and fetal development. Problems arise in clones, it seems, because clones are not made from sperm and eggs, with their properly imprinted DNA. Instead, clones are made from a single adult cell, which is fused with an egg cell whose genes have been removed.

Although the fluids in the egg cell can largely reset the adult cell's thousands of genes to the proper "on" and "off" positions required for embryo development, the process apparently is imperfect. And depending on which genes are not properly reset, various abnormalities arise.

No test today is capable of determining whether a cloned embryo's genes are properly imprinted, so it's impossible to weed out embryos that are doomed to develop abnormally.

"That's still a scientific black box that we're trying to unravel," said Michael Bishop, president of Infigen Inc., a cattle cloning company in De Forest, Wis. "We want to be able to tell which embryos can grow to a calf and which cannot. We're getting there. But we're nowhere close to having that correct."

As a result, cloned animals continue to be born with serious problems such as those endured in 1999 by Second Chance, the newborn clone of a 21-year-old Brahman bull named Chance.

"Second Chance was in the ICU for two weeks, and we almost lost him from respiratory and cardiovascular problems; and then he developed juvenile type 1 diabetes, which we never see in cattle," said Westhusin of Texas A&M.

In other cases, said Hill of Cornell, "the mom can get so big they can tear the muscles in their belly wall."

ACT's West predicted that cloning efficiency will be vastly improved in a few years. And although he is opposed to human cloning on other grounds, he said those commited to cloning people should at least wait until techniques improve.

"We're talking about harming developing humans," West said. "Why not wait three years?"

The alternative to waiting is too horrific to contemplate, said Jaenisch of the Whitehead Institute.

"You can dispose of these animals, but tell me, what do you do with abnormal humans?" Jaenisch asked. "You probably keep them alive with medical intervention, and they'll probably be miserable; and even the ones that look normal probably won't be. It's an outrageous criminal enterprise to even attempt."