

STAT

Human reproductive cloning: The curious incident of the dog in the night-time

By Henry T. Greely

February 21, 2020

[Reprints](#)²



Seven-month-old Dolly poses for photographs in 1997 at the University of Edinburgh's Roslin Institute, where she was cloned and raised. *Paul Clements/AP*

Gregory: Is there any other point to which you would wish to draw my attention?

Holmes: To the curious incident of the dog in the night-time.

Gregory: The dog did nothing in the night-time.

Holmes: That was the curious incident.

— Arthur Conan Doyle, [“The Adventure of Silver Blaze”](#)³

Sometimes what *doesn't* happen is as interesting as what does.

Cloning human embryos has been possible for nearly seven years. Yet as far as I know, during that time no one has made a cloned baby or, apparently, has tried to make one. And what I find most surprising is that no one has announced they *intend* to make one.

Why is this surprising? Let's go back almost 23 years to Feb. 23, 1997. On that day, news leaked out that the scientific journal *Nature* was about to publish a report of the birth of the first mammal cloned from adult cells — a [sheep named Dolly](#)⁴. The world was shocked, surprised, scared, titillated.

Creating Dolly meant taking an egg from one sheep, removing its DNA-carrying nucleus, fusing into the egg a cell from another sheep (in this case, from a cell line from a sheep that had been dead for several years), then hitting the resulting cell with a jolt of electricity. When this technique finally worked — the researchers tried it unsuccessfully 250 times — the resulting cell began to grow and divide. It was successfully implanted in a sheep's uterus and eventually became a healthy lamb.

Although this clone was just a sheep, the discussion turned immediately to cloned humans: cloned designer babies and armies of cloned warrior slaves. Governments around the world rushed to ban human cloning or to say that they had already banned human cloning, a procedure that had never been done or even tried.

[Related](#):⁵

[It's been 20 years since Dolly. Where's my clone?](#)⁵

At the same time, in the first years after the Dolly announcement, various people and groups said that they were going to clone a human. One of the first was the aptly named [Richard Seed](#)⁶, a physicist who, in spite of his well-covered announcements, seemed to have done nothing. Two OB-GYNs, Severino Antinori and Panayiotis Zavos, proclaimed their intention to create the first human clone within two years. Both said they had successfully started human clonal pregnancies, but neither one ever announced any births.

Most fascinating of all was the religious cult called the Raëlians. They announced that a religious command from aliens told them to go forward with cloning humans. In 1997, about three months after Dolly's birth was announced, the group created [Clonaid](#)⁷, an organization dedicated to that end. Led by biochemist Brigitte Boisselier, the Raëlians operated a laboratory in Nitro, W.Va., aimed at human cloning until [stopped by the Food and Drug Administration](#)⁸.

Undaunted, Clonaid moved its operations to the Bahamas. On Dec. 27, 2002, the group announced that the first cloned baby — named Eve — had been [born the day before](#)⁹. By 2004, Clonaid claimed to have successfully brought to life 14 human clones. These claims are widely disbelieved, in part because Clonaid did not allow independent testing of the babies, supposedly to protect the privacy of the babies and their families.

As far as we know, neither the Raëlians nor anyone else succeeded in using the Dolly process, technically called somatic cell nuclear transfer, to clone humans.

In the meantime, more conventional researchers were discovering just how hard it was to clone human embryos — or even nonhuman primate embryos. These researchers were not trying to make babies. They were trying to make cloned human embryos and, they hoped, keep them alive long enough to make human embryonic stem cell lines from them, cell lines that would be important for research and might be crucial for clinical uses.

If you could make cells, tissues, or organs from cells grown from an embryo cloned from a prospective patient, so the thinking went, those cells or their products should not trigger an immune response when transplanted into the patient. That could make these cells, tissues, and organs vastly important as treatments. But although researchers succeeded in removing the nuclei from primate (human and nonhuman) eggs and then fusing into them other cells with their own nuclei, the resulting cells would only divide a few times. These fused cells never survived long enough — about five or six days — to let researchers make cloned human or nonhuman primate embryonic stem cell lines from them.

In March 2004, Hwang Woo Suk, a South Korean scientist, and his colleagues [reported in the journal Science](#)¹⁰ that they had successfully cloned human embryos and had derived human embryonic stem cell lines from two of them. The next year [they reported](#)¹¹ having created 11 human embryonic cell lines from 185 eggs, using a wide range of sources for their body cells. This seemed to open the door to using somatic cell nuclear transfer to create human embryonic cells and from them create differentiated human cells and tissues from a patient's own body cells — or to make cloned babies.

Except it didn't. By December 2005, Hwang's work was shown to be [entirely fraudulent](#)¹². And although Zavos continued to talk about his efforts to clone humans [as late as 2008](#)¹³, people stopped listening.

[Related:](#)¹⁴

[Dolly the sheep died young, but her cloned sisters are still alive and kicking](#)¹⁴

Not all researchers interested in cloning were making big, unsubstantiated claims. Beginning shortly after the announcement of Dolly's birth, [Shoukhrat Mitalipov](#)¹⁵ and his team at Oregon State Health University worked on cloning, using more than 15,000 monkey eggs in an effort to make cloned non-human primate embryos. [In 2007](#)¹⁶, they reported making embryonic stem cell lines from monkeys, a finding that was [quickly replicated](#)¹⁷. They were not able, however, to make baby monkeys from those cloned embryos.

It took another six years for the Mitalipov group to report [successfully cloning human embryos](#)¹⁸, in that case from human embryonic cells, and making two human embryonic stem cell lines from those cloned embryos. The following year they reported having done the same with [cells from adult humans](#)¹⁹. Other laboratories quickly replicated their work.

Mitalipov was no fraud — his cloned human embryos were real. (Oddly, the secret ingredient that led to his success with humans was adding caffeine to the culture medium ... be careful with those double espressos!)

And Mitalipov made no effort to transfer human embryos made by cloning into women for possible pregnancy and birth. As far as I can tell, neither has anyone else.

But in January 2018, a Chinese group led by Qiang Sun and Zhen Liu reported the births of [the first monkey clones](#)²⁰. It was not an efficient process: About 80 cloned embryos led to six pregnancies and two live births. Even so, reproductive cloning had succeeded for the [first time in a primate](#)²¹.

For nearly seven years, then, the scientific community has had solid proof that human embryos can be cloned. And we have known for two years that cloned monkey embryos can yield cloned infant monkeys. So why has no one announced an effort to make cloned human babies? The laws have not changed substantially in the last two decades: Some countries banned human reproductive cloning — some before Dolly, some after, but generally before the announced cloning efforts of the early 2000s. Still, many countries have never banned it.

Other things, however, have changed in the cloning world. On the one hand, the value of using cloned human embryos to produce stem cell lines from an adult has been cast into doubt by competition from induced pluripotent stem cells (iPSCs). These were initially made by using several genes (now several proteins produced by some of those genes) to cause normal cells, usually skin cells, to become like embryonic stem cells. These stem cells, first made from mice by [Shinya Yamanaka in 2006](#)²² and then a year later from humans by both Yamanaka and [James Thomson](#)²³, can, like embryonic cells, produce all the cell types of a living human from cells carrying that individual's own DNA.

Like transplanting embryonic stem cells from cloned human embryos, transplanting induced pluripotent stem cells into a patient should avoid triggering his or her immune system. And making induced pluripotent stem cell lines is far simpler than making embryonic stem cell lines from cloned human embryos — no eggs, no embryos, no ethical or political concerns.

On the other hand, nonhuman cloning has become, to some extent, normalized. Several companies offer cloning services for pets — especially dogs — or for livestock. Indeed, the world's champion polo team has, for several years, [used cloned ponies](#)²⁶. The markets for these companies aren't huge, but the firms survive. And they claim that the safety and effectiveness of their methods keep improving.

And then there's CRISPR, the new kid on the block. After Jennifer Doudna, Emmanuelle Charpentier, and colleagues laid out in June 2012 the [potential use of CRISPR](#)²⁷ as a tool for DNA editing, visions of edited embryos and super-babies danced in their heads. The revelation in late November 2018 that Chinese scientist He Jiankui used CRISPR to [successfully edit embryos](#)²⁸ that led to the birth of two babies (joined at some point a few months later by a third) distracted attention from cloning. Why settle for a mere genetic copy of a living person when one could try to make a new and improved version?

All of which leads me to today. Where are the cloners who would be Richard Seed 2.0 or Clonaid 2.0?

I wish I knew.

It is now clear that many countries would treat human cloning as illegal in one way or another. But others, with bigger things to worry about, would not. And the perceived desire for cloned humans has not entirely dissipated. Couples grieving the loss of a beloved child (a favorite sympathetic example of would-be cloners) have, sadly, not disappeared.

Ambitious young scientists eager to make a splash with the firm if unfounded expectation that, even if initially rejected, they will ultimately be hailed as modern Galileos, have not disappeared either. Witness He Jiankui, although his [three-year prison sentence](#)²⁹, announced at the end of 2019, may have had a chilling effect on some of them, or at least might lead them to be more careful about where and how they operate.

[Related:](#) ²¹

[In a scientific first, cloned monkeys are born. Will they accelerate biomedical research?](#) ²¹

And those who could star in the favorite fictional plot — egocentric billionaires who want to clone themselves — have only increased in number and, it seems plausible, in revealed egocentricity. Some of these billionaires are [openly pursuing immortality](#)³⁰, so why not look into cloning?

Presumably, the Raëlians aren't interested, after having announced that they had successfully cloned 14 children more than 15 years ago. But it is a big world, with lots of unusual people. Why hasn't one of them yet followed in the footsteps of the many who, in the first years after Dolly, announced their intentions to clone humans?

Part of me would like to say that people have understood, from the writing of scientists, bioethicists, and other experts (mainly through journalists quoting those experts), that a clone would not be that special: It would never be an exact copy of a living or formerly living person. But as much as I would like to believe that, I doubt it. Recent years have not been kind to the idea that people listen to experts.

Is cloning passé, its moment in the spotlight having come and gone? If so, why?

I think this is a real mystery. It isn't a particularly important one, but it might provide some insight into public opinion, press behavior, moral panics, and other important aspects about social behavior in the face of startling discoveries in the biosciences.

At the very least it is a puzzle, one for which I invite solutions, total or partial, from Sherlock Holmes or any reader.

Henry T. Greely, J.D., is professor of law and professor by courtesy of genetics at Stanford University, where he directs the Stanford Center for Law and the Biosciences and chairs the steering committee for the Stanford Center for Biomedical Ethics.

About the Author [Reprints](#)²

Henry T. Greely

hgreely@stanford.edu³¹

[@HankGreelyLSJU](#)³²

Links

1. <https://www.statnews.com/category/first-opinion/>
2. <https://www.parsintl.com/publication/stat/>
3. <https://web.archive.org/web/20110116102811/http://etext.lib.virginia.edu/etcbin/toccer-new2?id=DoyBlaz.sgm&images=images/modeng&data=/texts/english/modeng/parsed&tag=public&part=1&division=div1>
4. <https://www.youtube.com/watch?v=tELZEPcgKkE>
5. <https://www.statnews.com/2016/07/05/dolly-cloning-sheep-anniversary/>
6. <https://www.chicagotribune.com/news/ct-xpm-1998-01-09-9801090042-story.html>
7. <http://www.clonaid.com/page.php?7>
8. <https://www.cnn.com/2001/HEALTH/06/30/clone.lab.txt/>
9. <https://www.newscientist.com/article/dn3217-first-cloned-baby-born-on-26-december/>
10. <https://science.sciencemag.org/content/303/5664/1669.abstract>
11. <https://science.sciencemag.org/content/308/5729/1777.full>
12. <https://www.sciencemag.org/site/feature/misc/webfeat/hwang2005/>

13. <https://www.wired.com/2009/04/cloneclaims/>
14. <https://www.statnews.com/2016/07/26/dolly-sheep-clone-aging/>
15. <https://www.statnews.com/2017/09/08/crispr-embryo-mitalipov/>
16. <https://www.nature.com/articles/nature06357>
17. <https://www.nature.com/articles/nature06456>
18. [https://www.cell.com/fulltext/S0092-8674\(13\)00571-0](https://www.cell.com/fulltext/S0092-8674(13)00571-0)
19. <https://www.nature.com/articles/nature13551>
20. [https://www.cell.com/cell/fulltext/S0092-8674\(18\)30057-6](https://www.cell.com/cell/fulltext/S0092-8674(18)30057-6)
21. <https://www.statnews.com/2018/01/24/first-cloned-monkeys-dolly-research/>
22. <https://www.nature.com/news/how-ips-cells-changed-the-world-1.20079>
23. <https://www.ncbi.nlm.nih.gov/pubmed/18029452>
24. <https://www.statnews.com/signup/>
25. <https://www.statnews.com/privacy/>
26. <https://www.sciencemag.org/news/2016/12/six-cloned-horses-help-rider-win-prestigious-polo-match>
27. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6286148/>
28. <https://www.statnews.com/2018/12/17/crispr-shocker-genome-editing-scientist-he-jiankui/>
29. <https://www.statnews.com/2019/12/30/he-jiankui-who-created-worlds-first-crispr-babies-sentenced-to-three-years-in-prison-for-illegal-medical-practice/>
30. <https://www.theguardian.com/technology/2019/feb/22/silicon-valley-immortality-blood-infusion-gene-therapy>
31. <https://www.statnews.com/2020/02/21/human-reproductive-cloning-curious-incident-of-the-dog-in-the-night-time/mailto:hgreely@stanford.edu>
32. <https://twitter.com/HankGreelyLSJU>
33. <https://www.statnews.com/tag/genetics/>

© 2020 STAT