

CLONING'S SLIPPERY SLOPE

BY STUART NEWMAN

How embryonic cloning leads to human cloning

Advocates of research using cloned human embryos claim that the path to curing many of humankind's most terrible afflictions will be found through the production of embryonic stem cells that are genetically matched to prospective patients. But what is not generally appreciated is how, by simply following the logic of scientific and medical reasoning, the way would be paved for a "Brave New World" in which cloning technology will eventually be extended to produce even fully-developed clonal humans.

More than two decades of work on mouse embryo stem cells has yielded just a handful of published studies showing modest therapeutic results – in all cases less than what has been achieved with grafts of non-embryonic cells, including "adult" stem cells. Despite great efforts, embryo stem cells rarely become just one cell type or coherent tissue, but differentiate instead into disorganized mixtures of cell types. Most importantly, they are genetically unstable; when placed in adult mice, they produce tumors. Similar technical obstacles and risks would pertain to the use of embryo stem cells in human patients.

These problems may be overcome by additional research. But this would undoubtedly take many years, and technologies, like water, tend to follow the path of least resistance.

Embryo stem cells are derived from embryos that are less than two weeks old – often described by advocates of experimental cloning as "a clump of cells in the bottom of a Petri dish." But scientists at Johns Hopkins University have isolated a different kind of human stem cell. These "embryo germ cells" are derived from embryos eight to nine weeks old and, like embryo stem cells, can differentiate into all cell types. Most importantly, when transplanted into experimental animals they do not cause cancer.

On purely scientific grounds, embryo germ cells show greater promise than embryo stem cells. If they were derived from clonal embryos they would be ideal candidates for the proposed regenerative therapies – and if the supporters of experimental cloning were candid, they would also be advocating research into sustaining clonal embryos for eight to nine weeks so that genetically matched embryo germ cells could be harvested. Such embryos could, of course, no longer be characterized as clumps of cells in a Petri dish.

Some supporters of the use of later embryos may reason that it is better not to raise all these possibilities from the start: once we have clonal embryos for a while and have become used to the idea, who would turn a deaf ear to calls by patients for even better therapeutics? And once stem cell harvesting from two-month clonal embryos was in place, who could resist the pleas to extend the time-frame so that liver and bone marrow could be obtained from six-month clonal fetuses to cure victims of life-threatening blood disorders such as beta-thalassemia, or

so that brain lining cells could be harvested from near-term fetuses to treat people with Parkinson's disease? Earlier this year a Massachusetts company reported a "proof of principle" in which tissues from clonal cow fetuses were shown to be tolerated as grafts by their adult genetic prototypes.

All of this makes perfectly good scientific and medical sense. The only thing that stands in its way are standards of social acceptability concerning the uses to which developing human embryos and fetuses may be put. These, of course, may be quite different from views on the acceptability of ending a pregnancy when a woman decides to do so. Regarding utility, some may draw the line at the clump of cells; others at the two-month embryo; still others somewhat short of full-term. A prominent British biologist has advocated producing headless human clones for spare body parts. Few engaged in the current debate would go along with the more extreme possibilities – but what about future generations, growing up in a world in which clonal embryos are routinely produced for spare parts?

An example of the medical incentives to bring full-born clones to term can be discerned from a mouse study recently conducted by researchers at MIT. These investigators started with a strain of mice lacking a gene needed for functioning of the immune system and used nuclear transfer from these mice (i.e., cloning) to make embryos and then embryo stem cells. They corrected the gene deficiency in some of the stem cells and then employed a method which allowed them to produce complete embryos containing only the corrected cells. The resulting mice were genetically identical to the nuclear donor, but with a repaired gene. These germ line-modified clonal mice were then used as bone marrow donors for the original impaired mice.

Large sectors of the public have already accepted the idea that a couple can have a child to provide tissues for another, sick child, and this has actually been done in several well-publicized cases. The MIT study shows that, in principle, you can make the second child by cloning the first, with genetic corrections. This provides a motivation for full-term cloning that would not be viewed as sinister; indeed, it would be welcomed by many – and the technology exists to bring it off. Once the cloning of human embryos is underway, the spread of the technology will make it all but impossible to stop short of any of these applications.

Many supporters of research and "therapeutic" cloning, particularly those in the Senate, the scientific societies, and patient advocacy groups, have condemned the prospect of full-term cloning and stated that it should be banned. In this they have the support of the majority of Americans and of all international groups that have considered this issue. But the examples above show just how short-lived any such half-measure is likely to be. □□■