

desist from it. And as the stem-cell debate heats up in Congress, even outspoken opponents of embryo research have not mounted a national campaign to ban in vitro fertilization or to prohibit fertility clinics from creating and discarding excess embryos. This does not mean that their positions are unprincipled — only that their positions cannot rest on the principle that embryos are inviolable.

What else could justify restricting federal funding for stem-cell research? It might be the worry, mentioned above, that embryo research will lead down a slippery slope of exploitation and abuse. This objection raises legitimate concerns, but curtailment of stem-cell research is the wrong way to ad-

dress them. Congress can stave off the slippery slope by enacting sensible regulations, beginning with a simple ban on human reproductive cloning. Following the approach adopted by the United Kingdom, Congress might also require that research embryos not be allowed to develop beyond 14 days, restrict the commodification of embryos and gametes, and establish a stem-cell bank to prevent proprietary interests from monopolizing access to stem-cell lines. Regulations such as these could save us from slouching toward a brave new world as we seek to redeem the great biomedical promise of our time.

Zygote and “Clonote” — The Ethical Use of Embryonic Stem Cells

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Bioethics is a debate without rules about a future dimly apprehended — a debate that is ever in danger of slipping from judicious deliberations into secular sermons. I awoke to these facts soon after I had joined the President’s Council on Bioethics, when we began to discuss embryonic stem cells. The discovery of pluripotential, infinitely self-replicating stem cells early in the 1980s had lit up a whole domain of cellular and developmental biology and suggested therapeutic approaches to chronic, debilitating, and incurable diseases such as Parkinson’s disease and diabetes mellitus. But for some years, the U.S. government, knowing that harvesting the cells killed the embryos, would not fund research on stem cells that had been derived from human embryos.

On August 9, 2001, President George W. Bush made a thoughtful speech in which he proposed regulations permitting federal funding for research using stem-cell lines from human embryos that had been killed before that date. The National Institutes of Health, proceeding under this compromise, has

since made 15 to 20 human stem-cell lines available for federally supported research.

But as might have been expected, few serious participants in the debate were satisfied by this compromise. Most stem-cell specialists reject what they see as an arbitrary limit on their resources and programs — and, among other substantive objections, note that a boundary date for production eliminates the chance of improving the quality of stem cells.¹ People who recognize a gift of individual human

life in every embryo — an “end” in itself, not to be treated merely as a “means” — recoil at its destruction, no matter when or why it occurs. All the members of the President’s Council on Bioethics — whose formation President Bush announced during that same August speech — developed our views on federal funding as we gathered information and exercised (vigorously, I can attest) our human talent for disagreement.

The concern that shadows the free use of human stem cells derives from disquiet over their origins. If a source other than embryos can provide pluripo-



Blastocyst opened to reveal the inner cell mass.

Courtesy of Wellcome Library, London.

tential stem cells — and harvesting them requires no killing — then this shadow vanishes. Thus, we all celebrate the discovery of stem cells in umbilical-cord blood, bone marrow, and other tissues.

But President Bush charged our council with thinking through the possibility of "cloning" as another source of human stem cells. This process, better termed somatic-cell nuclear transfer (SCNT), carries the potential of producing a living replica (clone) of the donor of a somatic-cell nucleus. It involves calling into play the genetic material and mechanisms that are latent in all somatic-cell nuclei, allowing them, under certain conditions, to recapitulate embryonic development and produce stem cells.

Ultimately, the council was unanimous in many conclusions about cloning.² We rejected the use of cloning for human reproduction. We agreed that regulatory measures should be developed for stem-cell cloning to guarantee, among other matters, that only qualified laboratories would receive federal support for work with human SCNT.

We were divided over whether research should be put on hold until the regulations are in place. A small majority (11) of us favored a four-year moratorium on federal support to permit these regulations and oversight structures to be developed. A large minority (seven) of us believed that this work is so rich in therapeutic promise that it should proceed without delay, and regulations could catch up with it.

It seemed to me that most of our disagreements rested on different attitudes generated, interestingly, by the same view of SCNT. This view maintains that there is no ethically important difference between a blastocyst derived from in vitro fertilization and one derived from SCNT. Thus, if one holds that deriving embryonic stem cells from in vitro fertilization should be illicit, this conclusion would also apply to SCNT, and vice versa.

I, however, see a distinction between the two procedures that sanctions different practices involving their products. In my view, SCNT resembles tissue culture, whereas in vitro fertilization represents instrumental support for human reproduction. Specifically, SCNT is an engineered culturing of the nucleus of a somatic cell, accomplished by implanting this nucleus into an enucleated ovum, thereby forming a new diploid cell with the genetic characteristics of the "donor" of the nucleus. This new cell begins to replicate, following a developmental program that is latent in the genes of every somatic cell but

that has been suppressed since it was employed in the original embryonic development of the donor organism.

I argue that this process of SCNT, by causing the expression of an intrinsic potential for growth and replication that is found in every somatic cell, can extend and expand a donor's cellular mass into extracorporeal space, as any form of tissue culture does. The stem cells that issued from the process would, in this view, be licitly used as the donor allowed. To specify this fundamental difference between in vitro fertilization and SCNT, I suggested that, since we call the first cell produced by fertilization the zygote, we dub the combination of nucleus and enucleated ovum that launches SCNT the "clonote."

Thus, I argue that in vitro fertilization entails the begetting of a new human being right from its start as a zygote and that we should use it to produce babies rather than cells or tissues to be harvested for purposes dictated by other human beings. In contrast, SCNT is a biologic manufacturing process that we may use to produce cells but should not use to produce babies.

My distinction rests on the origin of cells in SCNT, not on the process's vaunted potential for producing a living replica (clone) of the donor, as with Dolly the sheep. My confidence in making origins rather than potential the crux of the argument rests first on a *reductio ad absurdum*: if one used the notion of "potential" to protect cells developed through SCNT because with further manipulation they might become a living clone, then every somatic cell would deserve some protection because it has the potential to follow the same path. But I became more sure of this opinion when strong testimony was presented to the council³ indicating that SCNT performed with primate cells produces embryos with such severe epigenetic problems that they cannot survive to birth.

I still support the call of the council's small majority for SCNT regulations that will ensure, among other things, that human ova are not wasted like cheap reagents, or women pressed into service in unsafe ovum-production lines. Also, because I see that my argument supporting SCNT as a source of cells might easily justify growing the blastocysts to more advanced stages so as to harvest organs or tissues, I support limiting the existence of the clonote to 14 days. When these regulations are in place, federal funding for biologic research on human stem cells derived through SCNT should proceed.

I continue to hold in principle — as do many Americans and governments of several Western nations — that using in vitro fertilization to generate harvestable cells and tissues represents a seriously problematic, life-disowning use of biologic science. But I also appreciate that practice with human embryonic stem cells has raced ahead of principle and that the President’s compromise — restraining the practice but not banning research that could bring great benefits — was a wise one.

I’m asked what I would say if some other country’s scientists, using methods unsupported in the United States, discovered a cure for parkinsonism, diabetes, or Huntington’s disease. But that’s easy. First, I’d celebrate. I’ve not spent 50 years working and praying for such a victory to meet it without a welcome.

Then, after we’d drunk all the champagne, I’d surely ask, “What price this glory?” If we could reap the benefits using adult stem cells or SCNT, I’d lose no sleep over the methods that revealed them. If the therapies depended on trophic factors that we could

extract and synthesize, I’d salute them. If the only effective therapies came with cells manufactured in factories where women were treated like battery hens, vats of sperm and ova bubbled and brewed, and human embryos were chopped and diced, I’d fret — as I fret over any product made under inhuman conditions.

But, even for bioethics, such matters lie too far in the future. The method I followed in arguing for SCNT remains compelling. Know the technical features through and through when working out the rightness or wrongness of a medical procedure. “God is in the details,” noted the architect Ludwig Mies van der Rohe. Never has that truth echoed more loudly in the arena of biologic enterprise than it does now.

1. Gearhart J. New human embryonic stem-cell lines — more is better. *N Engl J Med* 2004;350:1275-6.
2. Human cloning and human dignity: the report of the President’s Council on Bioethics. New York: PublicAffairs, 2002.
3. Jaenisch R. Testimony: President’s Council on Bioethics, July 24, 2003. (Accessed June 22, 2004, at <http://www.bioethics.gov/meetings>.)

BUSINESS AND MEDICINE

The Business of Stem Cells

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On February 12, 2004, a team of Korean scientists made global headlines. Using somatic-cell nuclear transfer (therapeutic cloning), they removed the nucleus of a human egg cell and replaced it with the genetic material from a single adult cell. They then stimulated the newly transformed egg cell and prompted it to begin dividing. Several days later, they had produced a line of human embryonic stem cells — the first ever created in a laboratory.

Scientifically, the impact of this procedure was immense. The Korean team had demonstrated the practical ability to manufacture stem-cell lines from scratch. They had shown that it was physically possible to grow stem cells from the genetic material of a single person and then — theoretically at least — to produce other cells or tissues that would match those of the original donor perfectly. From these identical matches could come whole new ways of treating human illness: nerve cells for patients with Parkinson’s disease, brain cells for patients

with Alzheimer’s disease. Accordingly, the Korean success was greeted with scientific delight and a flurry of accelerated research activity. In Canada, a parliamentary committee voted to legalize the use of excess embryos for stem-cell research. Sweden announced that it would support the cloning of embryos for therapeutic purposes, the United Kingdom authorized a private firm to begin deriving embryonic stem cells, and Singapore forged ahead with plans to spend \$300 million on Biopolis, a cutting-edge science park focused on stem-cell technology.

In the United States, by contrast, recent policy has moved sharply in the opposite direction. Following an August 2001 announcement by President George W. Bush, federal funding for stem-cell research has been restricted to roughly 19 stem-cell lines — those created before the President’s announcement from embryos donated after in vitro fertilization. No federal funds may be used to investigate other lines or to create new ones. Although