you come forth with your empirical evidence that this can be duplicated, we have run it through these tests, including our discussion? Because I think there is a future for this research, and particularly here in this country. But we want to be sure that we can avoid the fraudulent practices up front.

Dr. BATTEY. I think that is an interesting suggestion that should be considered by those who are higher ranking than I am in the administration.

Ms. WATSON. Well, I throw that out for whoever is listening. Maybe it will get into the press and somebody will start considering it.

Thank you so very much, panel.

Mr. SOUDER. I want to also thank this panel. We will most likely have some written questions. Hopefully we can get a timely response. We will leave the record open longer than 3 days. But if we can't, my inclination will be to write that we could not get clearance of the Secretary of HHS, OMB, and the White House for the answers because we will try to keep the questions narrow enough. When this hearing book comes out, it should include a fair amount of data with that.

I also want to clarify two things that Ms. Norton said. She is correct that we do—in this committee, what I said is we look back on the past. We look in the past, at Katrina, at steroids, at whatever the issue is, to try to then develop and highlight what can be solutions that would then move to legislative committees. And so we have a future orientation by looking back on the past, and I didn't mean to imply we didn't have a future orientation.

The second thing, but I do think the record needs to reflect this: This committee does have jurisdiction over both the oversight on baseball, but also the legislation. There was a difference of opinion, which we have worked out, that if the steroid was overseen by the Office of National Drug Control Policy, it would be our legislative as well as oversight. If it is DEA, it is Judiciary. If it is FDA, it is Energy and Commerce.

The only question of where jurisdiction fell was on oversight, and that is really what we are battling over because we did have—in narcotics, we do have legislative as well as oversight. So I wanted the record to show that.

I once again thank this panel. Thank you for your time, and I look forward to continuing to work with you.

If the second panel could come forward.

Dr. BATTEY. Thank you, Mr. Chairman.

Mr. SOUDER. Thank you.

Our second panel is Dr. Richard Chole, Lindberg professor and chairman of the Department of Otolaryngology—the subcommittee stands in brief recess.

[Recess.]

Mr. SOUDER. The subcommittee will come to order.

Our second panel is Dr. Richard Chole, Lindberg professor and chairman, Department of Otolaryngology, Washington University School of Medicine, St. Louis; Judy Norsigian, executive director, Our Bodies Ourselves, co-author of "Our Bodies, Ourselves"; Dr. Diane Beeson, professor emerita, Department of Sociology and Social Services, California State University, East Bay; Mr. Richard

Doerflinger, deputy director of secretariat for pro-life activities, the U.S. Conference of Catholic Bishops; Dr. Debra J.H. Mathews, assistant director for science programs, the Phoebe R. Berman Bioethics Institute; and Joe Barden—Brown, excuse me, Parkinson's Action Network State coordinator of Texas.

If you will each stand—well, why don't I swear the four of you in, and then I will catch the other two, maybe, by the time we do the third one.

[Witnesses sworn.]

Mr. SOUDER. Let the record show that Dr. Chole, Judy Norsigian, Richard Doerflinger, and Joe Brown all responded in the affirmative. We will swear in the other two witnesses before their testimony.

We will start Dr. Chole. Thank you for coming.

STATEMENTS OF RICHARD A. CHOLE, M.D., Ph.D., LINDBERG PROFESSOR AND CHAIRMAN, DEPARTMENT OF OTOLARYNGOLOGY, WASHINGTON UNIVERSITY SCHOOL OF MEDICINE, ST. LOUIS; JUDY NORSIGIAN, EXECUTIVE DIRECTOR, OUR BODIES OURSELVES, CO-AUTHOR OF "OUR BODIES, OURSELVES"; JOE BROWN, PARKINSON'S ACTION NETWORK STATE COORDINATOR, TEXAS; DIANE BEESON, M.A., Ph.D., PROFESSOR EMERITA, DEPARTMENT OF SOCIOLOGY AND SOCIAL SERVICES, CALIFORNIA STATE UNIVERSITY, EAST BAY; RICHARD DOERFLINGER, DEPUTY DIRECTOR, SECRETARIAT FOR PRO-LIFE ACTIVITIES, U.S. CONFERENCE OF CATHOLIC BISHOPS; AND DEBRA J.H. MATHEWS, M.A., Ph.D., ASSISTANT DIRECTOR FOR SCIENCE PROGRAMS, THE PHOEBE R. BERMAN BIOETHICS INSTITUTE, JOHNS HOPKINS UNIVERSITY

STATEMENT OF RICHARD A. CHOLE

Dr. CHOLE. Thank you, Mr. Chairman. I am Richard Chole. I am a professor at Washington University, but I am not representing Washington University but rather myself as a private citizen.

I am a physician and a scientist. I have been funded for about 25 years by the institute, actually, that Dr. Battey directs. I am going to restrict my comments because of a lot of territory that has been covered already.

Biomedical sciences are on a brink of a real revolution in the development of our science. This is the era of regenerative medicine. This is an exciting area. It is not necessarily a new area, but it is the result of incremental change over several decades. These incremental changes continue to occur. This might in the future allow us to not only ameliorate and manage disease, but actually cure some diseases. Organ transplants are an example of the beginning part of that.

While the potential to help mankind is great, this new era poses some ethical and moral issues that we have never really encountered before that must be addressed not only by the scientists and physicians doing the research, but the public, probably more importantly by the public.

The source of these regenerative cells for regenerative medicine will come from a variety of sources, and I would like to briefly discuss a couple—make a couple of comments about these sources.

They might be embryonic, at the very earliest part of development. They might be fetal, at later parts of development. Or they may be adult, so-called adult, from the time of birth on. All of these sources of regenerative cells are called stem cells in that they can differentiate into any particular type of tissue. Some are more restricted than others.

Embryonic stem cells, as we have been referring to them, come from the very earliest human embryos, those from the stage of fertilization, the zygote, through the blastocyst, about 5 to 9 days. In order to get the embryonic stem cells from these early embryos, the early human embryo must be destroyed. And this is a human being at the earliest stage of developmental life.

Those inner cells, that inner cell mass, are the stem cells. They then are the ones that have been studied to lead to differentiation into different types of tissues. And indeed, scientists have been able to coax these cells to develop into a variety of types of tissues with potential uses for medical therapeutics.

Research into these cells has been incremental, and unlike the hype in the popular press, these have not been major breakthroughs but incremental, very small breakthroughs, showing some difference between experimental and control animals. The pitfalls of this type of research are that by definition, it requires the destruction of a living human being at the embryonic stage.

There are others as well. An embryonic stem cell is a different person. If you take the cells from that person and then put them into a different individual, there is a rejection process that goes on. That rejection would lead to the destruction of those cells unless the person was immunosuppressed by very powerful drugs.

These cells by nature are vigorous growers. They don't know when to stop growing in many cases, and most of this research has resulted in implantation of these cells where they will grow rather uncontrollably into tumors called teratomas. This particular question has not been answered.

These cells, once transplanted into an individual, may not—although they may function like a particular type of cell, may not be controllable. And in that environment, they may make too much of a hormone or not enough of the hormone. And there is no reason to—no evidence that these can really be controlled.

So those are some potential problems with embryonic stem cells. One of those problems, that they may be rejected, may be surmounted, scientists say, by cloning them. Cloning, as we have heard, is the placement of a nucleus from the body into an empty egg from an egg donor. This develops into a zygote and then a blastocyst.

If it were done in a human being, and it has never been done in a human being, this would recreate a living human being at the embryonic stage. The same ethical issues are faced by destroying this human being, albeit a cloned human being, if that were indeed possible. The advantage of this, theoretically, would be there would be no problem with cell compatibility. And I think that is why the excitement about this.

The difficulties are many. These cloned embryos are not normal embryos. Dolly was not a normal sheep. It took 250-plus times to get a cloned embryo from a sheep to become Dolly the lamb. These

cells have many, many different problems. They are defective embryos, and they are defective cells.

These stem cells in cloned embryos are defective stem cells. So they are not normal at all. They are defective. And the idea of using a defective embryonic stem cell that really can't be controlled for medical therapeutics is pretty conjectural thinking and far, far off from current scientific knowledge.

On the other hand, adult stem cells have their advantages and disadvantages as well. Adult stem cells, which are cells in our body—the most notable ones are in bone marrow, bone generation cells—have been shown to have more and more potential in development into specific tissue types. We have found recently that these cells can be caused to de-differentiate and become more like elementary stem cells, and can then be guided to develop into other types of tissue.

This line of research has great promise because it is taken from—the cells are taken from the individual, and there are no compatibility or rejection problems when the cells are given back. It also has great potential because of the variety of diseases that can be treated with it, and in fact, we treat many diseases with it in common clinical practice, and clinical trials in humans for lupus and heart problems and other problems have showed very promising results.

So the opportunities for adult stem cells are tremendous. There are disadvantages of adult stem cells, of course, in that they don't have all of the potential of an embryonic cell. But the problems can be overcome by further research into how these are developed.

I would like to just make a comment about this question of when life begins. It is my contention that life begins at the fertilization of the egg and the development of the zygote. Every, single person in this room was once a zygote, a unique zygote. From the time of the fertilization of the egg until this moment, it has been a process of your development. The genes were set. You are a human being at that point.

Medical science really has had little question about that, and I will read to you from a couple of textbooks that I took off the shelf at Washington University.

The first one: "The development of a human being begins with fertilization, a process by which the spermatozoon from the male and the oocyte from the female unite."

Another textbook: "Union of these gametes"—that is, the sperm and the egg—"during fertilization produce the zygote or fertilized ovum, which is the beginning of a new human being."

Another one: "Although life is a continuous process, fertilization is the critical landmark because under ordinary circumstances, a new, genetically distinct human organism is formed."

So, really, there has never been any question in the teaching in embryology and the textbooks, maybe until the current era—these may be changed—that life begins at that point.

Finally, I would like to make a comment about scientific hype and hype in the press about this.

Mr. SOUDER. You need to summarize. We let you go over 2 minutes.

Dr. CHOLE. OK. In the popular press, one might get the impression that paralyzed rats can walk again. This is incorrect. The studies have shown that when the experimental animals are compared to the control animals, both recover quite well in the experiments that she was citing, but the embryonic stem cell animals recover a little bit better. It is not the contrast that has been depicted in the popular press.

This drama to this field has led some scientists to assume the position of celebrity. Scientists are not prepared to be celebrities. The scientist's role is to use cold, dispassionate analysis for his or her data, and then present it in an honest way. This element of celebrity has led to some distortion, maybe the distortion that led to the big scandal in Seoul.

Thank you very much.

[The prepared statement of Dr. Chole follows:]

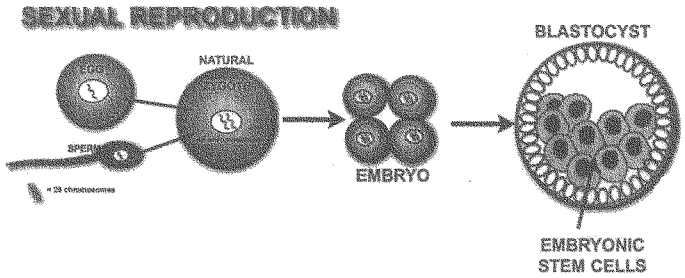
Human Cloning and Stem Cell Research

Richard A. Chole, MD, PhD
St. Louis, MO

Biomedical sciences are beginning a new era, that of regenerative medicine. This is not a new trend but rather incremental changes which will allow us to treat and possibly cure patients with diseases and injuries that have previously been managed or ameliorated. Organ transplantation is now performed throughout the country. The transplantation of regenerative stem cells is only beginning. While the potential to help mankind is great, this new era poses some new ethical and moral issues that must be addressed, not only by the scientists and physicians who develop these techniques, but by the citizens of our country. In order to understand the issues we face, decision-makers must have an understanding of the biology of stem cells and the beginning of human life.

Human Embryonic Stem Cells

Human embryonic stem cells are obtained from living human beings at the pre-implantation embryonic stage usually 5-9 days after fertilization. The tiny embryos (blastocysts) contain an "inner cell mass" which is destined to continue development. When these cells are removed from the embryo, the embryo is destroyed. These cells (embryonic stem cells – ES cells) are "totipotent" in that they can develop into all tissue types in the body.



Scientists have been able to coax animal and human embryonic stem cells to become numerous types of tissues in the laboratory. Since these stem cells are "programmed" by their very nature and/or definition to grow, they grow vigorously, even when separated in culture dishes in the laboratory. Because of their propensity to grow vigorously and to differentiate into various cell types, scientists have performed studies in animals designed to replace or regenerate missing tissues.

The Potential

- The hope in these studies is that the ES could be caused to differentiate and replace damaged or missing tissues in diseases such as diabetes, Parkinson's disease, Alzheimer's disease, spinal cord injuries, heart disease, etc.

The Pitfalls

- In order to obtain human ES cells, a human being at the embryonic stage must be destroyed.

- The ES cells are vigorous growers and when implanted into animals, their growth is often uncontrollable and results in the formation of tumors called teratomas. Techniques to suppress this tumor growth are under investigation, but a complete understanding of the early growth and development of the embryo is lacking at this time.

- Since a human blastocyst is a unique human being at the embryonic stage, its tissue type never matches another person perfectly. Just as in organ transplantation, transplantation of human ES cells into an individual would stimulate an immune response that would have to be suppressed using powerful anti-rejection drugs. To circumvent the rejection problem, scientists have suggested using cloned embryos which have a more perfect tissue match with the subject. (See cloning section.)

- Once transplanted into an animal (or someday into a human) transformed ES cells, although they may assume a new tissue type, may not function as they are intended. The control of the action of these implanted cells and their exact location will pose research challenges in the future.

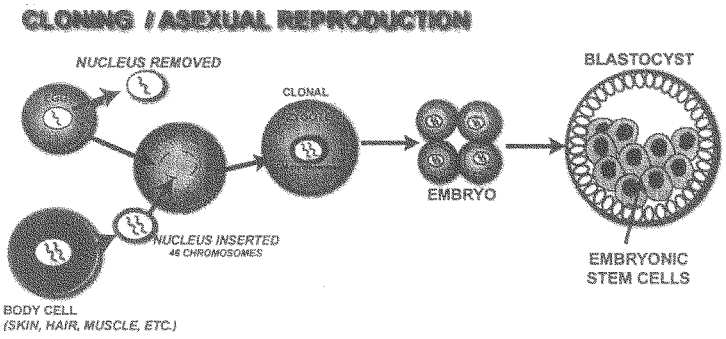
- There have been no successful human ES transplants.

Cloning to make Embryonic Stem Cells

In order to circumvent the inevitable problems of immune rejection of transplanted human embryonic stem cells, scientists have proposed to clone embryos so that their genetic makeup is identical with the subject being treated. Since a cloned human embryo would be genetically identical to the donor, immune rejection would not occur and transplanted cells would be free from rejection.

Cloned embryonic stem cells would be obtained from cloned human beings at the pre-implantation embryonic stage. These cloned embryos would be the source of cloned ES cells. The cloned embryo would be destroyed in order to obtain the ES cells from its inner cell mass. This is hypothetical; no one has been able to clone a human embryo.

The cloning process, as it is currently performed, is the process of somatic cell nuclear transfer (SCNT). This is the process that Ian Wilmut used to clone Dolly the sheep in 1997.[1] In this process, an animal (or young woman) is caused to hyperovulate by hormonal manipulation. Oocytes are surgically removed from her ovary and taken to the laboratory. In the laboratory, the nucleus from the oocyte is removed and replaced by a nucleus from a body cell (somatic cell) from the donor. The oocyte then functions like a fertilized egg (zygote) and begins the process of embryonic development. At the blastocyst stage, scientists can remove the inner cell mass to obtain cloned ES cells to use for research and potentially transplantation. Removing the cell mass kills the cloned embryo.



The Potential

- The hope in these studies is that the cloned ES could be caused to differentiate and replace damaged or missing tissues in diseases such as diabetes, Parkinson's disease, Alzheimer's disease, spinal cord injuries, heart disease, etc. without eliciting an immune response and rejection since the cloned cells are genetically identical (nearly identical[2]) to the donor cell.

The Pitfalls

- In order to obtain cloned human ES cells, a cloned human being at the embryonic stage must be created and destroyed.
- No one has ever cloned a human embryo, although there has been some success with cloning primate embryos.[3]
- Cloned embryos are defective.[4]

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[1] Schneike AE, et al Science. 1997 Dec 19;278(5346):2130-3

[2] In the process of SCNT some of the cell contents (cytoplasm) of the donor cell are mixed with that of the oocyte. Since cytoplasm contains some genetic material (mitochondrial DNA), the resultant cloned embryo contains cytoplasmic DNA from two individuals. This does not occur in nature. This adherent does not occur naturally.

[3] Simmerly C, et al Dev Biol. 2004 Dec 15;276(2):237-52.

- The pitfalls associated with the use of "natural" ES cells obtained from sexual reproduction apply to cloned ES cells also. (with exception of their tendency to be rejected)

When does human life begin?

One of the central questions that our society must answer in the stem cell debate is the question of when life begins. Biologically, there has never been a question as to when human life begins. A unique human being begins at the point where the chromosomes from the egg and sperm unite to form the earliest stage of human life, the zygote. One only has to look in a textbook of human embryology to understand this fact:

> "The *development of a human being begins with fertilization*, a process by which the spermatozoon from the male and the oocyte from the female unite to give rise to a new organism, the zygote."[5]
>
> "...Union of these gametes during fertilization produces a zygote or fertilized ovum which is the primordium or *beginning of a new human being.* (emphasis in original text) This highly specialized, totipotent cell marked the beginning of each of us as *a unique individual."*[6]
>
> "Although life is a continuous process, fertilization is a critical landmark because, under ordinary circumstances, a new, genetically distinct human organism is formed when the chromosomes of the male and female pronuclei blend in the oocyte." [7]

Human Adult Stem Cells

By definition embryonic stem cells are "totipotent" being able to develop into any type of tissue in the body. Stem cells have been identified in many locations in the human body which were at first thought to develop into only one or two cell types. However, it is now established that some adult stem cells have "multipotency" that they can develop into many types of cells. The scientific literature is now replete with examples of pluripotency of adult stem cells.[8,9,10,11]

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[4] "NT embryos appear inferior to fertilized ones due to spindle defects resulting from centrosome and motor deficiencies that produce aneuploid preimplantation embryos, among other anomalies including genomic imprinting, mitochondrial and cytoplasmic heterogeneities, cell cycle asynchronies, and improper nuclear reprogramming." Simmerly C, et al Dev Biol. 2004 Dec 15;276(2):237-52.

[5] Langman J., Medical Embryology, 4th edition. Baltimore: Williams & Wilkins 1981, p.
[6] Keith L. Moore & T.V.N. Persaud. The Developing Human: Clinically Oriented Embryology, 6th Edition, 1998
[7] Ronan O'Rahilly & Fabiola Muller, 2001 Human Embryology & Teratology, 3rd. Ed

[8] Krause DS, et al. Cell 105:369-377
[9] Jiang Y et al Nature 418:41-49 2002
[10] D'Ilppolito G, et al. J Cell Sci 117:2971-81 2003
[11] Zhao Y, et al PNAS 100:2426-32 2003

Unlike human embryonic stem cells, adult stem cells are in routine clinical use in the successful treatment of some malignancies.

Animal studies have demonstrated the regenerative potential of adult stem cells in retinal degeneration,[12] diabetes,[13] Lupus,[14] and many others. Positive clinical trials in human subjects using adult stem cells, including umbilical cord stem cells, have been observed in Lupus,[15] Crohn's disease,[16] myocardial infarction,[17] and many others.

The Potential

- The hope in these studies is that the adult multipotent stem cells can be removed from a patient, modified in the laboratory, and used to regenerate missing or damaged tissues.
- The potential for developing tumors is low.
- Implanted cells will not be rejected because, in most cases, they are the patient's own cells.
- Adult stem cells cannot become embryos; therefore, there are no ethical concerns about destroying human life.
- Primitive adult stem cells may have the potential of being "de-differentiated" to become truly pluripotent stem cells.

The Pitfalls

- Adult stem cells are not pluripotent and may not have the growth potential of embryonic stem cells
- Certain adult stem cell populations may not be accessible for clinical use (e.g. neural stem cells).

Scientific Hype vs. Reality.

Although there has been slow, incremental advancement of the sciences underlying stem cell research, unverifiable claims of successes by some investigators and gross exaggerations in the lay press have given people false impressions about the current state of the science of stem cell research and regenerative medicine.

The well publicized scientific fraud by Korean investigators is, of course, the principal example. Media exaggeration and mis-representation of solid, reputable scientific advances have also misled the public. Exaggeration of research findings in this field have led many people to false assumption that legitimate "cures" are available in other countries and would be available here if only restrictions were lifted.

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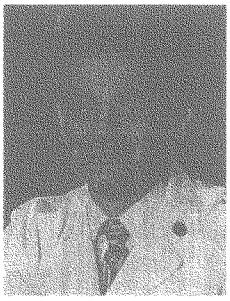
[12] Otani A, et al. J Clin Invest 114:765-74
[13] Sapir T, et al PNAS 102:7964-9 2005
[14] Burt RK, et al JAMA 295:527-535 2006
[15] Burt RK, et al JAMA 295:527-535 2006
[16] Kreisel W, et al Bone Mar Trans 32.337-40 2001
[17] Wollert KC, et al. Lancet 364:141-8 2004

Because of media hype about the significance of some findings, investigators may assume celebrity status which they are ill-equipped to handle. This celebrity status may impair a scientist ability to deal with research results in the cold, critical and dispassionate manner that is expected of all investigators.



Richard A. Chole, MD, PhD

Representing St. Louis Center for Bioethics and Culture
and Missourians Against Human Cloning

Lindburg Professor and Chairman
Department of Otolaryngology
School of Medicine
Washington University in St. Louis

Residence: St. Louis, Missouri

MD – University of Southern California
PhD – University of Minnesota

Research: Inflammatory bone disease. Continuously funded by NIH for 25 years
Medical Practice: Otologic and Neurotologic Surgery

Director of the American Board of Otolaryngology
Board of Scientific Counselors – NIDCD
Member National Advisory Council – NIDCD 2000-2004

Past President of the Association for Research in Otolaryngology
Past President of the American Otological Society

Board Member/Secretary – Missourians Against Human Cloning
Board Member – St. Louis Center for Bioethics and Culture