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# HJR 588: Medical, Ethical, and Scientific Issues Relating to Stem Cell Research Conducted in the Commonwealth

**August 17, 2005**

The second meeting of the Joint Subcommittee was held at the Fairfax County Board of Supervisors Auditorium and featured an impressive panel of experts.

## PRESENTATION BY DR. GARY S. FRIEDMAN

Dr. Friedman is a physician with broad transplantation experience, having directed a transplant program for 10 years and published extensively on clinical transplantation, transplant immunology, cellular pharmacology, and hematological issues in clinical transplantation. He is a founder of International Regenerative Medicine (a consortium focused on development of therapeutic applications of human stem cells), the Director of the Center for Regenerative Medicine in Morristown, New Jersey, and a trustee of the New Jersey Stem Cell Research & Education Foundation.

Dr. Friedman began by noting historical landmarks in transplantation, including the first successful kidney transplant performed in 1954 and the expansion of nonembryonic stem cells to include stem cells from umbilical cord blood in the 1980s. He also noted that the Organ Procurement and Transplantation Network (OPTN) was established by Congress under the National Organ Transplant Act (NOTA) of 1984; the United Network for Organ Sharing (UNOS) of Richmond was founded in 1984, and became the federal contractor for the operation of the OPTN; and NOTA included language that led to the formation of the National Bone Marrow Donor Program.

The bone marrow program was established to provide a data base of bone marrow tissue types in order to provide more access to therapies using stem cells for cancers and other disorders. UNOS, on the other hand, operates to provide solid organs on a need basis in an egalitarian manner. Dr. Friedman noted that physicians who perform transplants, solid organs or stem cells, are reimbursed for their services. He noted that federal law prohibits the sale of human tissue. Less than 20 percent of the people who are waiting for transplants actually undergo the procedure and time on the waiting list for solid organs has increased from one to two years to five to eight years in many regions.

## HIGHLIGHTS

- **Harvesting of bone marrow by transplant procurement teams, as well as the collection and banking of cord blood, would allow stem cell therapy to be available on a 24 hour basis to the many patients waiting for transplantation.**
- **Donor stem cells may migrate and reproduce in any part of the body of a patient receiving stem cell therapy; this phenomenon has been observed when embryonic stem cells are transplanted, but not with adult stem cells.**

**JOINT SUBCOMMITTEE STUDYING MEDICAL, ETHICAL, AND SCIENTIFIC ISSUES RELATING TO STEM CELL RESEARCH IN THE COMMOWEALTH**

## HIGHLIGHTS

- **The public wants stem cell therapies right now; however, the development of stem cell research, as well as potential therapies will take time.**
- **Dr. Friedman emphasized that the existing organizational structure for organ and bone marrow collection should be used for cord blood banking, as well as for the harvesting and banking of donor bone marrow to provide plentiful sources of stem cells for use in regenerative medicine.**
- **Internationally, there are probably over 250 validated embryonic stem cell lines, of which 22 appear on the President's list.**

Dr. Friedman became interested in stem cell therapy, because he felt that the life expectancies of patients waiting for organ transplants could be extended with stem cell therapy and that organ supply and demand issues could be ameliorated. He also noted that many uses have been found for stem cells that can be provided through umbilical cord blood. He expressed concern that procurement programs for solid organs do not include the recovery of bone marrow (which contains stem cells that can differentiate into blood, heart muscle, and other tissues) on a regular basis, because harvesting of bone marrow is not reimbursed. Dr. Friedman supports the harvesting of bone marrow by transplant procurement teams, as well as the collection and banking of cord blood. This would allow stem cell therapy to be available on a 24 hour basis in order to respond to the growing patient therapy needs of the many Americans waiting for transplantation of stem cells or solid organs.

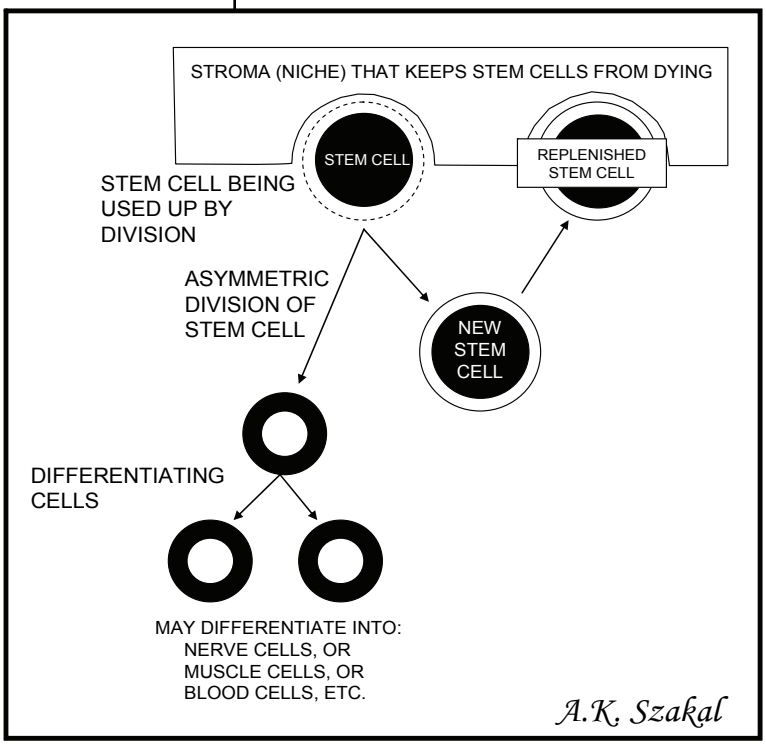
Dr. Friedman stated that using embryonic stem cells requires massive culture of the cells and involves risk of tumor development, specifically teratomas, or even malignancy. Donor cells may migrate and reproduce in any part of the body of a patient receiving stem cell therapy. This phenomenon has been observed when embryonic stem cells are transplanted, but not with adult stem cells. Because of this, care must be taken to avoid poor patient outcomes and litigation.

Dr. Friedman emphasized that he believes the existing organizational structure for organ and bone marrow collection should be used for cord blood banking, as well as for the harvesting and banking of donor bone marrow in order to provide plentiful sources of stem cells for use in regenerative medicine.

## PRESENTATION BY DR. JOHN D. GEARHART

Dr. Gearhart, one of the preeminent stem cell researchers in the United States, is the C. Michael Armstrong Professor, Medicine of the Institute of Cell Engineering, Johns Hopkins University; professor of gynecology and obstetrics and of physiology at the Johns Hopkins University School of Medicine; and holds a joint appointment in the Department of Biochemistry and Molecular Biology at the Bloomberg School of Public Health. He led the Johns Hopkins University research team responsible for first deriving human pluripotent stem cells in 1998. Much of his research has been focused on how genes regulate the formation of tissues and embryos, particularly in examining mental retardation and other congenital birth defects.

Dr. Gearhart began by responding to concerns about the formation of teratomas when embryonic stem cells are used in transplantation. He stated that he wanted to set the record straight, that "from the experimental side when you isolate derivatives, you don't put in a graphed embryonic stem cell. It will lead to a tumor...." He noted that the experiments




**Stem Cell Asymmetric Differentiation**

must be performed correctly, making sure grafts do not contain embryonic stem cells, because the capacity of the stem cells to divide and differentiate is a major safety issue. The Johns Hopkins program deals with various sources of stem cells, including adult sources, umbilical cord blood, embryonic stem cells, and stem cells derived from bone marrow. The research group seeks to address many stem cell biology issues; however, most of the research is preclinical and experimental. Very little of the research has resulted in clinical trials, which Dr. Gearhart believes is appropriate. He observed that the public wants therapies right now; however, the development of medical applications will take time.

Dr. Gearhart focused on the uniqueness of the stem cell—embryonic or adult—and its capacity to self-renew (i.e., it can produce another cell like itself and specialize into another cell type). Some stem cells can divide only once and others can divide many times, producing many different cell types [*See illustration previous page*]. This intricate and difficult problem is the central focus of stem cell science—trying to figure out which stem cells have the capacity for generating specific tissues. The only major clinical application of stem cells, at present, uses stem cells derived from bone marrow, which contains two kinds of stem cells—hematopoietic and mesenchymal. Dr. Gearhart noted that regardless of the source, certain criteria must be met in stem cell research: (i) self-renewal, (ii) stability, (iii) capacity to multiply and specialize, and (iv) reproducible results for quality control.

The Johns Hopkins research group is comparing various stem cell sources, which is the only way to find out what works. He explained that when you graft bone marrow, you are putting both types of stem cells (hemapoietic and mechenymal) into the individual, and the cells can migrate to any organ in the body and may contribute to a variety of tissues. To illustrate, he posed the question: "Are the cells functional in the tissues to which they contribute or are the cells simply residing in the tissue?" A neuron stem cell, for example, will only produce the type of cell from the brain region from where it is taken, but will not reproduce all other types of brain cells.

Internationally, there are probably over 250 validated embryonic stem cell lines, of which 22 appear on the President's list. Harvard University's Stem Cell Institute has developed approximately 17 embryonic stem cell lines. The number of stem cells being used in the United States is unknown, because private funds are being used to derive stem cell lines that are not eligible for federal funding. Dr. Gearhart emphasized that studies of adult and embryonic stem cells, thus far, in the Johns Hopkins laboratory research model, showed that embryonic stem cells work better .

Speaking to somatic cell nuclear transfer, Dr. Gearhart noted that scientists agree that reproductive cloning of human beings should not be allowed. The term "therapeutic cloning" has been used since 1999, and scientists regret coinage of the term. The actual process would be to match an embryonic stem cell line by doing somatic cell nuclear transfer from the patient to an oocyte and then generating a blastocyst. The resulting stem cell would be a precise match for the patient, eliminating host-graft rejection.

Dr. Gearhart concluded that studies of human embryonic stem cells will result in important drug developments, but the stem cell controversy will continue. Only further study of both adult and embryonic stem cells will reveal which stem cell source works better. The United States has lost the lead in stem cell research and therapy development to Australia, Singapore, Korea, Israel, and the United Kingdom. Many of our country's brightest students are looking for postdoctoral positions in these countries, because of the cutting-edge research and the availability of government and private funding.

## PRESENTATION BY DR. JONATHAN D. MORENO

Dr. Moreno is the Emily Davie and Joseph S. Kornfeld Professor of Biomedical Ethics and the Director of the Center for Biomedical Ethics at the University of Virginia; past president of

**JOINT SUBCOMMITTEE STUDYING MEDICAL, ETHICAL, AND SCIENTIFIC ISSUES RELATING TO STEM CELL RESEARCH IN THE COMMONWEALTH**

## HIGHLIGHTS

- **The United States has lost the lead in stem cell research and therapy development to Australia, Singapore, Korea, Israel, and the United Kingdom.**
- **The National Academies only address issues of national significance, mandated by Congress or the executive branch, or issues in which there is a perceived public need as expressed through the scientific communities.**
- **Guidelines are essential because there is public and scientific uncertainty about the appropriate procedures for conducting stem cell research.**

**JOINT SUBCOMMITTEE STUDYING MEDICAL, ETHICAL, AND SCIENTIFIC ISSUES RELATING TO STEM CELL RESEARCH IN THE COMMONWEALTH**

**HIGHLIGHTS**

- **The National Academies' position continues to be that human reproductive cloning should not be conducted.**
- **Compliance with the National Academies' guidelines are voluntary adoption of policies/ practices that are consistent with the recommendation and the imposition of appropriate institutional sanctions for noncompliance.**

the American Society for Bioethics and Humanities; a bioethics advisor for the Howard Hughes Medical Institute; and has published over 200 papers, numerous reviews, and six books on subjects ranging from human experimentation to clinical studies and practice. Dr. Moreno was co-chair with Dr. Richard O. Hynes of the National Academy of Science Committee on Guidelines for Human Embryonic Stem Cell Research.

Dr. Moreno's presentation was focused on the National Academies recently issued human embryonic stem cell research guidelines, now published as a book. He emphasized that the National Academies are not government agencies, although they are chartered by the federal government and 90 percent of its work is requested by Congress or the executive branch. The embryonic stem cell guidelines project was funded by two private foundations and National Academies' funds. The National Academies embryonic stem cell guidelines have no legal standing, only offer intellectual and professional persuasion. The Academies only address issues of national significance, mandated by Congress or the executive branch, or issues in which there is a perceived public need as expressed through the scientific communities.

Dr. Moreno cited the many reasons for developing embryonic stem cell guidelines:

- Significant public support for human embryonic stem cell research.
- Diverse funding available for stem cell research—private, federal and state.
- Scientific concerns relating to the hodgepodge of federal regulations.
- Lack of regulation of privately supported human embryonic stem cell research.
- Public and scientific uncertainty about the appropriate procedures for conducting stem cell research.

The purpose of the guidelines is to encourage responsible stem cell practices, including the use of stem cells derived from surplus blastocysts from in vitro fertilization clinics, stem cells derived from blastocysts derived from donated gametes, and stem cells derived from blastocysts produced using nuclear transfer. The guidelines address ethical and legal concerns and encompass policy issues relating to the use of human embryonic stem cells for research and therapy. Although the guidelines address human embryonic stem cell research and therapy, the recommendations could be applied to other human stem cell research, including adult stem cells, fetal stem cells or embryonic germ cells.

Among the issues addressed were donor recruitment (informed consent, compensation, conflicts of interest, confidentiality, risks of oocyte retrieval, and use of genetic information); stem cell characterization and standardization; safety in handling and storage of blastocysts and stem cells; sharing of materials between laboratories; appropriateness of and limitation on human embryonic stem cell research and therapy; and safeguards against exploitation or misuse.

Having already recommended in 2002, that "[h]uman reproductive cloning should not now be practiced. It is dangerous and likely to fail," the National Academies' position continues to be that human reproductive cloning should not be conducted. The recommendations include:

- Review by an Institutional Review Board, informed consent of all donors, severing donation decisions from all clinical decisions, prohibition of compensation or reimbursement to donors except for direct expenses, no commercialization (sale or purchase) of donated materials, and protection of donor privacy.
- Establishment of institutional oversight committees and an independent national panel to evaluate and revise the adequacy of the guidelines, as necessary. The institutional oversight committees, referred to as Embryonic Stem Cell Research Oversight (ESCRO) committees were recommended to include public and expert representation.
- Certain research with embryonic stem cells should not be permitted at this time, including in vitro culture of any intact human embryo beyond 14 days (a standard that has been accepted by most scientists), any research in which human embryonic stem cells are introduced into nonhuman primate blastocysts or in which any embryonic stem cells are introduced into human blastocyts, and that animals into which human embryonic stem cells have been introduced at any developmen-

tal stage should not be allowed to breed.

The mechanisms for compliance with the guidelines are voluntary adoption of policies/practices that are consistent with the recommendations and the imposition of appropriate institutional sanctions for noncompliance. The guidelines have been endorsed by the presiding or executive officers of many prestigious institutions and organizations, and hopefully, other states and entities will also consider adopting the guidelines.

## PRESENTATION BY REV. TADEUSZ PACHOLCZYK

Father Pacholczyk is the Director of Education at the National Catholic Bioethics Center in Philadelphia, an ethicist, and a Catholic priest for the diocese of Fall River, Massachusetts. Father Pacholczyk received four undergraduate degrees in philosophy, biochemistry, molecular cell biology, and chemistry from the University of Arizona; a doctorate in neuroscience, focusing primarily on cloning genes for neurotransmitter transporters that are expressed in the brain, from Yale University; and studied for five years in Rome conducting advanced work in theology and bioethics, examining the question of delayed ensoulment of the human embryo. He is frequently asked to speak regarding stem cells, cloning, and other biotechnologies, and has testified before the Massachusetts and Wisconsin State Legislatures and participated in a Pontifical conference on these subjects.

Father Pacholczyk's presentation focused on the moral arguments and ethical considerations raised by stem cell research, the proper direction for issues addressed by the legislatures in the future, and whether medical efficiency should trump and triumph over ethics. He began with a short vignette about a mother teaching her young daughters a lesson after not allowing them to see a movie which contained a little bit of immorality. The girls' mother showed them how a little bit of bad can ruin a lot of good by baking cookies with just a little of their pet rabbit's droppings in them. Dr. Pacholczyk applied the analogy to embryonic stem cell research and warned that in the same way that the rabbit's pellets ruined the cookies, society's attempts to cover up or ignore a little bad in something good is an effort to pretend that the "bad" does not really exist.

Father Pacholczyk posed the question, "What is wrong with a little bit of embryo destruction to help the greater good?" He asserted that everyone in the room came from an embryo and acknowledged that an embryo is a very small object. He insisted, however, that once everyone accepts the fact that they started out as an embryo, the focus is drawn to a discussion of whether all human beings are created equal, regardless of size. Thus, if all human beings are created equal, the size of the human embryo doesn't matter; consequently, the destruction of human embryos to help other humans is wrong. Father Pacholczyk disputed the argument made by those in favor of embryonic stem cell research that there are hundreds of thousands of embryos in a deep freeze in vitro fertilization clinics that will be thrown away if not used. He stated that it is important to realize that the "discarding versus using for research" argument is a lever to pry open the door to what he feels is the ultimate research goal--therapeutic cloning. Father Pacholczyk emphasized that discussion is very important and noted that, in his opinion, in vitro fertilization "slipped under the radar screen." He commented that the taking of a human embryo was "innocent life" compared with society taking human life as a matter of law through war and the death penalty.

Father Pacholczyk discussed alternatives to embryonic stem cell destruction, such as back-differentiating adult stem cells. Dedifferentiation (reprogramming of a specialized cell or tissue to a simpler, unspecialized form) of adult stem cells was postulated as a solution to the human embryonic stem cell controversy, because a human embryo would not have to be destroyed. The dedifferentiated adult stem cells could be differentiated forward in a new direction and have the potential to become many different types of cells.

Father Pacholczyk concluded by proposing that the United States should not be concerned with being at the forefront of stem

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## HIGHLIGHTS

- **Father Pacholczyk emphasized that if all human beings are created equal, the size of the human embryo doesn't matter; consequently, the destruction of human embryos to help other humans is wrong.**
- **The critical issue is for the country to lead in an ethical sense....and that we should take the high ground not run after the herd.**
- **There are current and potential problems with embryonic stem cells, which are difficult to establish, handle, and maintain and carry the possibility for causing tumors and tissue destruction.**

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**HIGHLIGHTS**

- **Adult stem cells are the most promising source for treatments, because they multiply almost indefinitely; provide numbers sufficient for clinical treatments; have proven successful in laboratory culture; "home in" on damage; and avoid problems with tumor formation, transplant rejection, and ethical quandary.**

cell research, but the critical issue is for the country to lead in an ethical sense. He fears that the raw power of science will lead to exploitation, and that we should take the high ground, not run after the herd.

## PRESENTATION BY DR. DAVID A. PRENTICE

Dr. Prentice is a Senior Fellow for Life Sciences at the Family Research Council in Washington, D.C., and an Affiliated Scholar for the Center for Clinical Bioethics at the Georgetown University Medical Center. Dr. Prentice held positions at the Los Alamos National Laboratory; the University of Texas Medical School at Houston; and the Indiana State University School of Medicine. Dr. Prentice is an internationally recognized expert on stem cell research and cloning and was selected by the President's Council of Bioethics to write a comprehensive review of adult stem cell research for the Council's 2004 publication "Monitoring Stem Cell Research."

Dr. Prentice began his presentation by discussing the current and potential problems with embryonic stem cells, noting that these stem cell lines are difficult to establish, handle, and maintain and carry the possibility for causing tumors and tissue destruction. Dr. Prentice presented the members with evidence that some adult stem cells show pluripotent capacity. Scholarly articles have shown that adult stem cells from bone marrow can form new neurons in the human brain and that bone marrow stem cells can go on to form all body tissues. Studies have shown that placental amniotic stem cells potentially form any type tissue without producing tumors. Human cord blood stem cells, which are young stem cells, have been shown to be pluripotent.

Dr. Prentice continued by describing studies from around the world in which adult stem cells have been demonstrated as being effective in tissue repair. The first clinical trials are under way to demonstrate that adult stem cells from brain, bone marrow, and umbilical cord blood provide therapeutic benefit after stroke. Clinical trials have been started in Australia and Portugal to determine whether adult stem cells are capable of re-growth and reconnection in the spinal cord.

In describing the current uses of adult stem cells, Dr. Prentice enumerated treatments for cancers, autoimmune diseases, anemias, immunodeficiencies, bone/cartilage deformities, corneal scarring, stroke, repairing cardiac tissues after heart attack, Parkinson's disease, growth of new blood vessels, gastrointestinal epithelia, wound healing, and spinal cord injury.

Dr. Prentice concluded by highlighting the advantages of pursuing adult stem cell research: adult stem cells are the most promising source for treatments; they multiply almost indefinitely, providing numbers sufficient for clinical treatments; they have proven successful in laboratory culture, in animal models of disease and current clinical treatments; they have the advantage to "home in" on damage; and they avoid problems with tumor formation, transplant rejection, and ethical quandary.

## NEXT MEETING

The September 21 meeting of the joint subcommittee will focus on stem cell research and related activities being conducted in Virginia. The materials distributed at the August meeting may be accessed on the study's website and audiostreaming is also available.

**HJR 588: Joint Subcommittee Studying the Medical, Ethical, and Scientific Issues Relating to Stem Cell Research Conducted in the Commonwealth**

The Hon. R. G. Marshall, *Chairman*

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