Bioethics Research Library at Georgetown University

https://repository.library.georgetown.edu/handle/10822/503786

Transcripts of the President’s Council on Bioethics (PCBE) Meetings 2001 - 2009

The Bioethics Research Library is collaborating with Georgetown’s University Library to digitize, preserve and extend the history of Bioethics.

Please tell us how this access affects you. Your experience matters.

Visit us at https://bioethics.georgetown.edu/.

Interested in learning more about President’s Council on Bioethics? You can visit their website as it appeared on the last day of its charter. There you can learn about the council members, browse their reports, and locate background materials. The website is hosted by the Bioethics Research Library and can be found at:

https://bioethicsarchive.georgetown.edu/pcbe/

Materials produced by the President’s Council on Bioethics are government documents and in the public domain. When citing this document please note the source as Bioethics Research Library and the appropriate Digital Georgetown hyperlink

Collection Permanent Link: hdl.handle.net/10822/559325
Meeting Transcript
April 25, 2002

Hilton, Crystal City
2399 Jefferson Davis Highway
Arlington, VA 22202

April 25, 2002

COUNCIL MEMBERS PRESENT

Leon R. Kass, M.D., Ph.D., Chairman
American Enterprise Institute

Rebecca S. Dresser, J.D.
Washington University School of Law

Elizabeth H. Blackburn, Ph.D.
University of California, San Francisco

Daniel W. Foster, M.D.
University of Texas, Southwestern Medical School

Francis Fukuyama, Ph.D.
Johns Hopkins University

Michael S. Gazzaniga, Ph.D.
Dartmouth College

Robert P. George, D.Phil., J.D.
Princeton University

Mary Ann Glendon, J.D., L.L.M
Harvard University

Alfonso Gómez-Lobo, Dr. phil.
Georgetown University

William B. Hurlbut, M.D.
Stanford University

Charles Krauthammer, M.D.
Syndicated Columnist

Paul McHugh, M.D.
Johns Hopkins University School of Medicine

Gilbert C. Meilaender, Ph.D.
Valparaiso University

Janet D. Rowley, M.D., D.Sc.
The University of Chicago

Michael J. Sandel, D.Phil.
Harvard University

James Q. Wilson, Ph.D.
University of California, Los Angeles
SESSION 1: STEM CELLS 1:
MEDICAL PROMISE OF EMBRYONIC STEM CELL RESEARCH (PRESENT AND PROJECTED)

CHAIRMAN KASS: Well, I would like to ask Dean Clancy to officially open the meeting, please.

MR. CLANCY: This meeting is lawful.

CHAIRMAN KASS: Thank you very much. Apologies to our guests and to members of the audience for the late start. Council Members had to take an oath of office, which should have been administered to us before our very first meeting.

That has been done and we are now legal in every respect. Welcome to this, the third meeting of the President's Council on Bioethics. We are expecting colleagues Krauthammer and George today, and Stephen Carter will not be with us, and Bill May will join us tomorrow.

I would like to introduce a new member of our staff, Judy Crawford, who comes to us as the office manager. Judy, would you please rise so that the council members can know you. We are very delighted to have Judy with us.

We reconvene as the debate about the cloning legislation heats up around us, a debate that we did not begin and do not control. We are in the midst of our own careful and thorough investigation of the ethical, social, and policy implications of human cloning seen in its larger scientific, medical, and human contexts.

We have chosen to proceed in a deliberate, collegial, wisdom-seeking, mode in keeping with our charge to inquire fundamentally into the human and moral significance of developments in biomedical science and technology.

The most challenging aspect of our inquiry to date has been the moral significance of cloning for biomedical research, a topic discussed for the first time at our last meeting, and to which we return later today in the hope of making progress and clarifying the contested moral issues at stake, and in articulating the best possible moral arguments for and again the conduct of such research.

On behalf of the council, I would like to thank the staff for its superb work in advancing our inquiry, and on behalf of the staff, I would like to thank council members for their thoughtful comments and responses. We are in your debt.

The agenda for this meeting brings us into some new, but not altogether unrelated, areas of inquiry. Stem cell research, a topic of our first three sessions today.

Second, the question of therapy versus enhancement as a goal for the uses of biomedical technology, and third, possible regulation of biomedical technology. These topics have been selected with a view to initiating one of our obligatory future projects, stem cell research, and exploring two possible future projects for the council for the rest of our two year charter.

As everyone knows, in his speech announcing the creation of this council, President Bush charged us with monitoring stem cell research, embryonic and non-embryonic, human and animal, in order to assess their progress in gaining knowledge and beneficial therapies, and in due course to offer guidelines and regulations for the conduct of such research.

As I indicated at our first meeting, we have begun to collect data that will enable us to describe, assess, and compare the successes achieved with both embryonic and non-embryonic stem cells.

As we are doing this, however, it seemed desirable for council members to learn firsthand, and from some leading researchers in the field, about the scientific and therapeutic promise of stem cell research present and projected; embryonic and non-embryonic.
And it also seemed desirable to explicitly begin a disciplined conversation about the ethical issues of embryonic stem cell research. Our first three sessions today constitute the official thematic beginning of our project on stem cell research.

We have of course already been deliberating about some of these matters in our discussion of human cloning for biomedical research, a topic that first arose for us as a crucial side question of the larger subject of human cloning to produce children, what to think about it, and what to do about it.

This is therefore a useful juncture at which to indicate the distinction, as well as the connection between these two topics. Many members of the public, including many of our elected officials who are in the process of making policy in this area, as well as some members of the media, have conflated the issue of stem cell research and the issue of cloning.

The issue of cloning comes first to attention as an issue of the ethics of producing children by novel technological means, and the issue of cloning, insofar as it has captured the public attention, is primarily about what to think about the asexual production of new human beings who are going to be genetically virtually identical to already existing individuals.

And the issues there are in the first instance the questions of the ethics of, crudely speaking, baby-making. That is quite different from the question of the ethics of embryo research.

Virtually all embryonic stem cell research now under way, both in humans and in animals, involve cell lines developed from embryos, whether inner-cell mass, or from the gonadal ridge of donated fetuses, that originate from the sexual union of egg and sperm, and very often in the human case using excess embryos produced in in vitro clinics and in all cases from material not produced for the sake of the research. The question of Federal funding of this research that President Bush resolved last summer, this was the question that was resolved last summer, and the research in this area proceeds not only with Federal funding under the guidelines that the President established, but also in the private sector.

The two topics, however, intersect and overlap because cloning to produce children necessarily proceeds through the production of cloned blastocysts, which offer special opportunities for embryonic stem cell and other research.

Some proposals to curtail cloning for providing children would do so by curtailing the initial steps, thus interfering with the possibility of using cloned embryos for research.

And this has given rise to arguments for and against cloning for biomedical research proper. This is where the intersection can be made explicit, and that is where we now are.

In order for us in the other project to continue to make progress, and therefore in order to see what value added might derive from working with embryonic stem cells extracted from cloned blastocysts, one needs to know something about what it would be added to. That is to say, to work on ordinary embryonic stem cells. And in order to see more clearly what the ethical issues are that might come from the question of producing cloned embryos for biomedical research, it would be helpful for us to know something of the ethical issues of experimenting on human embryos of sexual and not clonal origin, and of using extra embryonic — using the extra embryos or fetuses not created for experimental purposes so we can see what different questions arise here.

To help us with our scientific and medical education, we are very fortunate to have as our guests and presenters this morning two distinguished researchers, one who is a pioneer in isolating and characterizing human pluripotent stem cells, Dr. John Gearhart, the C. Michael Armstrong Professor of Medicine at Johns Hopkins University, and the Director of the Institute of Cell Engineering.

And second a person who is a pioneer in work with human multipotent adult progenitor cells, Dr. Catherine Verfaillie, a Professor of Medicine and Director of the Stem Cell Institute at the University of Minnesota.

Each of our guests in separate sessions will make formal presentations, roughly 30 to 35 minutes, after which time we will have a chance to ask questions about the scientific, technological, and clinical aspects of these areas of research.

This is our chance to learn about the wonderful prospects of these investigations. However, let me say that because our guests are here not only as scientists, but also as our neighbors, in a morally aspiring human community, we will perhaps try toward the end to elicit from them their own thoughts about the ethical issues in their own work.
But the purpose of these sessions is primarily our own education about the scientific and medical aspects. With that I would like to turn the meeting over to Dr. Gearhart, and to thank him very much for joining us this morning.

**DR. GEARHART:** I am certainly grateful to have this opportunity to share with the President's Council my knowledge in a very tiny area of biomedical research, and it is currently quite tiny, but if you read and believe the press, it is obviously going to expand enormously.

Much has been written and much has been said about stem cells, and it seems every morning in the paper there is some article relating to it and continuing the debate.

In the scientific literature, we see virtually in every issue of leading journals a paper dealing with stem cells. An age old dream I think of mankind or humankind has been to replace damaged or diseased tissues with functional ones, new ones, and wouldn’t it be nice to be able if you had a damaged liver or kidney to take one off the shelf if you know what I mean.

And this dream I think is going to become a reality, and with some of the advances in biomedical research, and one of the ones that we are going to talk about today, I think this will provide the starting material that will lead to this reality.

The concept behind cell-based therapies — and this is what we are talking about here initially — is a very simple one, and I think that that makes it attractive, and it makes it understandable to the public. And that is that if there is a tissue deficit, why not just replace the tissue. Now, it is easy to say, and it will be difficult to do, but the concept is an easy one.

Cell-based therapy has also been called regenerative medicine, and there are many rubrics for this today. The power of this technology is derived from information inherent in our genes and in our cells, and the recent isolation of these embryonic type stem cells I believe is going to provide the enabling material as I mentioned for this to go forward.

Stem cells are going to serve several purposes, the first of which could be as a direct source in transplantation therapies. That means specific cell types will be grown in culture, such as heart muscles, nerves, et cetera, and transplanted to patients for function.

Or they will be genetically engineered to do exactly what we want them to do and transplant it to patients; or they will be used by our tissue engineer colleagues to construct tissues and parts of organs, which would then be transplanted to patients.

Stem cells will also be used as a source of information, basic science, and this is really where we are at currently. That could be applied to a patient's own cells, such that we could remove cells from a patient and alter them in some fashion to produce the cell types that we want, and then transplant them.

Or ultimately I feel that what we are going to be able to do from the information that we are going to learn on stem cells is that we will be able to work in vitro with patient cells to get them to perform in a manner that we want without taking them out and putting them in culture. This, I believe, is the future. The scientific challenges to attain our goal of producing safe and effective therapies are formidable. It will take the efforts of many scientists and clinicians, in a variety of disciplines, to bring this endeavor to fruition.

Now, the stem cells that I am going to talk about today interestingly really do not exist naturally. That is, they don’t exist in embryos or fetuses. They are artifacts of culture.

But we take tissues from embryos and fetuses and they undergo a type of transformation in culture to provide these stem cells. And this source obviously brings with it a number of ethical concerns.

I, as an investigator, who has had to cross this bridge 9 or 10 years ago when I began this work, believe that the ethical issues are manageable.

I also believe that it is the responsibility of scientists to candidly and in a timely fashion present the social implications of their research and its technological applications; to provide assessments on reliability, and to participate in the establishment of ethical guidelines and to work within those guidelines.

For the past 9 years at Hopkins, we have been in compliance with all institutional, State, and Federal policies in dealing with the cells that we work with.

It has not been easy because the landscape has changed in 9 years, and every year there have been
new concerns raised, and new issues that had to be addressed, and I think we are keeping up with it. I should tell you also up to this point in time that no Federal monies, no public monies, have gone into our research effort. Now that Federal policy has changed, we do have applications pending before the National Institutes of Health.

I also want to point out something that may be surprising to most of you; that in our laboratory at Hopkins that we just are not concentrating on an embryonic or fetal source of stem cells.

We are studying stem cells from adult sources, umbilical sources, et cetera. This is the only way that we feel that you can have a scientific advance, and that is to be able to compare and contrast the different sources of stem cells.

So side by side, in the laboratory, in experimental paradigms, we are using stem cells from a variety of sources, and this is what I think has to happen to assess which of these sources are going to prove the most effective for any specific type of therapy.

Another thing that I want to point out to you is that the work on the human cells, I do have the questions that came from your committee in hand, and many of them are asking what is the status of certain types of work.

I just want to point out that this work has been ongoing for a period of 2-to-2-1/2 years, and although we feel that we are making progress, we certainly are going to come up with, well, I don't know as answer to some of your questions.

I just want to let you know that we don't have all the answers to this, and we are very, very early in all studies of stem cells, be they from the embryonic or adult sources.

I would tell you though that to date the work in our lab and others on embryonic stem cells and the results of that work is certainly consistent with the idea that this is going to prove to be a productive line of research.

Well, it is interesting that very few people know you and what you are about, and I think it is important to point out something. My interests, or my research interests for decades, have been in the area of developmental genetics and development biology.

I have been labeled as a human embryologist, and my interests certainly are in the area of how an embryo goes from a single cell to a multi-cellular integrated organism.

And this is where our research has been in the past 25 years, and I have carried this a step further. We are very interested in congenital malformations and birth defects.

I have had a program project through the NIH for many, many years dealing with Down's Syndrome, and we are very interested in trying to determine what the mechanism is that underlies many of the unusual anatomical neurobiological consequences of this extra chromosome in human beings.

And this is essentially how I got into this work. We wanted to have in the laboratory a source of cells in addition that we could study at the site or level of the impact of these extra genes.

And this obviously is a goal, along with a number of other genetic-based diseases and malformations in the human being. So this is what led to our getting into this area of research.

Now, I have to say up front that we are now required by our university to reveal where our monies come from, and these are the sponsors of our research, and there is one sitting in the middle there that I also have to show to you that I am conflicted.

And which means that to the sponsorship of this private company, we have received money for research, for which licenses have been negotiated between Hopkins and Geron, and that I am a stockholder, albeit a few hundred shares of something that is trading now at — and I hate to think about it.

It is not in our possession as you know. It is held in escrow. But nonetheless we do have this arrangement with this company. So I would tell you that this is not the motivation, this connection.

Without the sponsorship of this research, this work would not have gone forward over the past seven years. We are not in this business as individuals to make money.

Well, having said all of that, let's talk about stem cells. The first thing I want to give you is a little bit of a primer on stem cells so that we are talking the same language, and you have an understanding of
where I am coming from.

Well, what is a stem cell, and basically a stem cell is a cell that has two properties. It has a property in that it has a capacity for self-renewal, which means that the cell can divide and produce more cells like itself.

And it has some type or some degree of differentiative capability, which means that it can go on to specialize into a single cell type, or it can specialize into a number of cell types.

And in a developmental sense, if we over time at what our research has told us about stem cells, they fall into a number of categories. Early on in developmental practices, we have a cell that is totipotent.

It can renew, and it can form virtually every cell type that is present in an embryo. As development proceeds, its developmental capabilities become more restricted until we get into different lineages, specific lineages, and its ability to divide also becomes more diminished over time.

This has been the classical picture of development. Now, what has happened over the past couple of years interestingly is we find that these restrictions in developmental capability are much more plastic than we had thought.

So out here where we thought that these cells are highly restricted, perhaps they aren’t so, and when you remove them from the organism and culture them, they have capabilities of forming other cell types, and Catherine will be talking to you about some of these issues.

Well, we are going to be talking about embryonic stem cells, and what is it about them. Well, interestingly, we know that these cells are capable of producing virtually every cell type that is present in an embryo, a fetus, or an adult, except one.

And that one happens to be the trophoblast cell, which I will tell you about in a moment. So we consider these cells to be totipotent.

They don’t have the ability in and of themselves to form an embryo or an individual, okay? They have this other property of self-renewal, which basically with respect to embryonic stem cells means that they will expand indefinitely, and grow indefinitely, and this is a very important property.

It means that within the laboratory from a very few cells that you could grow a roomful of these cells very easily. But there is an issue here that we don’t know much about, and that is obviously there is a finite probability that at every cell division that a genetic mutation will appear.

And there was a paper published recently that indicated that indeed this is the case, and the types of mutation, although the mutation frequency and the mutation rate is greatly — by several folds lower than in normal somatic cells, mutations do occur in these cells, and they are of the nature of making these cells susceptible to formation of tumors.

The uniparental disomy appears and it is a condition about which we should be concerned. And up until this point, in the mouse where these cells were first isolated, and for that work the person who did this, Martin Evans, was awarded the Lasker Award last year.

We know that these lines forming whole animals, which is what they have been used for up to this point, in genetic mutations is getting genetically defined strains of mice.

That there comes a time when these cells are no longer productive in doing this and that they lose some quality. So we know that there is going to be a half-life to the use of these cell lines for whatever reason.

I just want to point that out, although they do have this replicative ability. Well, where do these totipotent cells come from, and two major sources. The first is this pre-implantation stage which we are going to talk about, and the second are from specific cells within the fetus.

I also have on this slide, and by the way, I have given you two handouts. One is the slides in the presentation, and another in a fairly recent Nature review of this material, that you can refer to.

I want to point out another source of a cell that is very similar to these two that we have isolated, and that comes as a stem cell for a specific type of tumor called in the old days teratocarcinoma, and now called mixed cell carcinomas.

These stem cells, referred to as embryonal carcinoma cells, were first isolated back in the 1970s
when I worked on this, and we thought that these would be the answer to finding cells that would produce a variety of cell types that we could work with within the human.

And I should tell you that at this point in time that there is a clinical trial going on at the University of Pittsburgh using embryonal carcinoma cells that have been selected for a neural lineage, and so that in culture you can derive neural cells and that these have been placed in the brains of 12 stroke patients.

It is a cell that is very, very similar to the two that I am going to talk about. Well, the first source that you are aware of comes from these structures here, which are pre-implantation stage human embryos, and I am sure you are familiar with this.

And where that structure consists of two groups of cells; this outer layer called trophectoderm, and an ectopically placed inner group of cells called the inner-cell mass. It is from this group of cells here that the embryo proper is derived, and it is connected ultimately to this outer layer, which develops in the placental tissue by connecting stock in an umbilical cord.

These cells may number only 15 or 20 in an embryo that may consist of perhaps several hundred cells. And in work in the mouse, and subsequently done in humans, first by Jamie Thomson, was that these cells were isolated, placed in a culture condition, which then permits their growth and their conversion into an embryonic stem cell.

This process of conversion can be highly inefficient, meaning that you would need a large number of blastocyst and inner cell mass cells to derive a few cell lines.

In some people's hands, it can be more efficient, but there is an issue with that. A second source of cells with the same features was identified in the early 1990s, first by Peter Donovan at NCI.

And what they were attempting to do were to culture long term cells that are called primordial germ cells. These are diploid cells that are present in an early embryo that eventually give rise to egg and sperm.

And they isolated, and this is superimposed upon a human fetus, they isolated from the gonads, the gonadal ridges, these large cells, which at the time of isolation in humans are about 20,000 of them present in a gonad, and placed them in culture and essentially ended up with the same type of cell.

This is what a human EG culture looks like, this clustering of cells and I want to point out that there are cells in the background here which are the so-called feeder layers.

All of these cell lines are derived on feeder layers, and all the lines that were approved by Mr. Bush, and all the lines that we have, are derived on a mouse feeder layer, and this is a point of contention, meaning that we are concerned now about the fact of any endogenous viruses being transferred from other animal tissues into the human cells.

And the FDA must deal with this at this point in time, but we do not have permission on the use of Federal funds to derive new lines, avoiding this issue of other animal products.

But they are grown on feeder layers. They are established and grown on feeder layers of other species. If we compare different properties of these cell types, and I bring this up — some of these are of no value to you immediately, but these are the criteria that one must use to say whether or not you have a cell line.

It is very important, and of the 80 some lines that are now purported to be available, I can guarantee you in talking to many investigators from around the world that only a handful of these are bona fide cell lines, and/or available to investigators.

Now, this may beg the point and that that may be enough to serve the purposes in the immediate future. But really the majority, the vast majority of so-called lines available do not meet the criteria that are now used to say whether or not you have a cell line.

Now, how do we — we are very interested then in two things here. One is the basic science aspect of this, and of course what is driving all of this is the hope for some type of transplantation therapy.

Let's talk a minute about the basic science. What we have in the laboratory now are cultures of cells in the plate that can form any cell type in a human body.

Now, the argument is have we demonstrated that you can get out of these all 200 and some cell types? No. You only find what you are looking for.
What we have found though are a large number of cell types that are present in the human body within these dishes. The problem at the moment is getting homogenous population of pancreatic islet cells or blood cells, or muscle cells.

This is the real part of the scientific struggle here, and coming up with the paradigms to say can we take a cell that can form any cell type, and get it to form but one cell type.

And to do this we have to rely upon our knowledge coming out of molecular embryology as to the genetics and what not involved in any type of cell specialization.

And this is really the limiting issue at this point in time, getting these purified populations of cells on demand. There are strategies that are used that we do pretty good at, and we will take the initial populations of cells, and we can change feeder layers, and we can change growth factors, and we can put them in different types of cultures and force them then to begin to specialize.

But they are mixed cultures, and within the same dish you are going to find neurons and muscle, et cetera. And we must then go another step and begin to sort out either through procedures called flow sorting based on what is on cell surfaces to get then pure populations of hematopoietic stem cells, muscle cells, or neuro cells.

And this works fairly well. We can get cultures of dopanergic neurons that are 80 percent pure, and we can get cardiac muscle that is 97 percent pure, et cetera.

But we are a long way from isolating in a homogeneous fashion the various types of cells that we would like to get. Some of them are doing well at and others were not.

And it is going to require an extensive amount of research to achieve this. Now in going to transplantation therapy — we are going to jump a little bit ahead here, and if we start, this could be ES.

If we start with this population, we do not transplant into anybody, or into an animal at this point, one of the stem cells. You don't do it. The reason that you don't do it is this.

These stem cells are capable of forming a variety of tissues, and they will form tumors, and these tumors are these mixed germ cell tumors that contain a variety of cell types.

They are called teratomas in the old literature. Monster. I mean, they are contained in a mixed array, and you can see teeth, sebaceous glands, hair, bone, parts of the gut, et cetera.

So what you have to do to make this work is you want to at least get cells that you have treated somehow in a dish into some of these more defined lineages that are away from this capacity to form tumors.

So that we then begin to select tissues downstream, all right? Part of the problem, and you will read this in the literature, is how good your selection is, is also indicated by whether or not when you take myocardiocytes that you say, oh, these are all 100 percent myocardiocytes, you transplant them into the wall of the heart, and you end up with a teratoma.

This happens, and we are into the central nervous system, and you end up with a teratoma within the brain. So getting rid of those initial stem cells are essential, and we have ways of doing this genetically, but I just want to point out that this is an issue.

To say nothing about the fact that we do not know whether any cell downstream here has the capacity to revert. We know very little about that at this point in time.

So let me give you an example. There are many of these coming out in a number of laboratories, most of them in the mouse in which lines have been derived in different lineages, and they have been transplanted into animals to show proof of concept, and that you can isolate a specific cell type, and you can transplant it, and it will function within the transplant.

I would like to give you now an example from our work at Hopkins. It is an unpublished work, and it is now under review, but I think it is important because it really illustrates several points that are critical here.

We have taken our human cells and grown them under culture conditions that would select for specific types of lineages, and whether it is neural, or whether it is muscle, et cetera. And now we have, I believe, in our laboratory over a hundred a hundred lines like this, of the human lines.
And in the one example that I want to present to you, which was done with members of our department of neurology, and in collaboration with our lab, is a model, using these cells in an animal model of the motor neuron disease.

And in this study, these animals are treated with a virus that destroys lower motor neurons, so that animals become paralyzed, and they are paralyzed because they lose the big nerve muscles that in your spinal cord hook your muscles up to the central nervous system.

So that in a period of 10 days following the injection of the virus into the brain, the animals become paralyzed, and we have gone to great lengths to show that it is really the ventral roots that are involved.

You wipe out these neurons and these animals never recover. They never recover. So what we have done is to take our human neural cells out of this and infuse it into the spinal cords of these rats, and to look then for the recovery of motor activity.

This is a rat out for a mid-morning stroll, and this animal is infected with the virus, and it is a virus that really leads to an encephalomyelitis, and within a period of 10 days the animal is paralyzed.

We can document exactly what this paralysis is about. The virus is cleared, and shortly thereafter we will put a cannula into the lumbar region of the animal, and infuse 300,000 cells into the cerebrospinal fluid, and these cells will float all the way up to the hind-brain.

And then we monitor the motor activity of these animals, and within a period of a few months, we begin to see animals that can now place their limbs underneath them, and that can draw them up, support some weight, and begin to push off.

And at the high end, within a several month period, we can have animals that are now walking. And the issue is why are they walking. And what we have learned, although it is not as you can see a normal gait, et cetera, and we have really documented this as well, they are walking.

And why are they walking? Well, initially what we felt was this. This is a panel showing cells within the ventral horn of those animals and I want you to look at this cell here.

This cell, based on its marker, and based on its physical characteristics, and molecular characteristics, is a human motor neuron cell that has been specialized out of these neural precursor cells, that has sent an axon out into the periphery at least two centimeters.

And we have been able to cut the sciatic nerve out on the limb of this animal, place a dye at that site, and that dye is picked up by that axon, and brought back to the cell body that extended the axon.

And it comes back, and this is the green stuff here, and it comes back then into the cell body of the human motor neuron. We have gone on to document how many human cells are present, and what they are as far as the phenotype is concerned, to see — you know, yes, they are forming glia, and they are forming a variety of cell types within the ventral horn of that animal.

Interestingly, and one of the safety issues that we find is that 50 percent of the cells don't do anything. And we are a little bit concerned about that.

I mean, is it good to have all these cells in there that aren't doing anything, but this is an issue that we have got to resolve. Well, it turns out that this is only part of the answer. It turns out that the human cells at the same time are producing growth factors that rescue and enhance the regeneration of the animal's own cells within the ventral horn.

And so this has led us then to set up experiments to try to figure or try to determine what growth factors it is that is causing the growth of axons in those mice and in rats in the ventral horn, and it may be that eventually we can use just the combination of those growth factors to elicit this response. We don't know.

So these cells are serving in a dual capacity, which is somewhat exciting. We have taken the human cells and we now have grafted them into monkeys. They were in monkeys for over a year.

This was a safety study to in fact show that we are not getting tumors formed. I think you can appreciate one of the major issues here that we are going to be faced with, with this type of approach, is animal experiments are of a very short duration. Mice and rats are for periods of several months.

Monkeys we can go much longer. How much data is going to be needed to convince the FDA that this is a safe approach, and this is something that is being debated now within the FDA and it is a
difficult issue.

But here we show human cells, and that is these blue ones that have been in this monkey, and in this case for 180 days, but we are now out a year, and we can show that these cells are forming specialized structures and they are non-tumorigenic.

The next phase is to look at a graph model here that is functional.

CHAIRMAN KASS: Can I just ask a question?

DR. GEARHART: Sure.

CHAIRMAN KASS: What has been injected here?

DR. GEARHART: Oh, I’m sorry. These are the same — what has been injected into this monkey are the same cells that were injected into the rat. The same cells. They were human cells —

CHAIRMAN KASS: Neural precursors?

DR. GEARHART: Neural precursor cells. The same cells, the same culture cells. A major issue that we must discuss and that we are concerned about is graft rejection. Obviously, anything that you grow up, unless it matches the patient, is going to be subjected to that, and now we get into an area which Dr. Kass has mentioned earlier.

But what are our options here? What are the options of being able to grow these cells into any of these lineages and then to transplant them and not have rejection?

Well, there is a long list, and it starts with, well, maybe what we ought to do is derive hundreds of ES and EG cell lines, and then you would have a best match for a patient. Not very practical.

Can we use the patients own cells, and you will hear about some of this shortly. Should we use immunosuppressive therapies. We would like to get away from that.

Can we use what the tissue engineers are referring to as sequestering grafts, and what this is, is you can take grafted cells and put around them matrices that will not permit other cells to touch them, but yet they can produce products, or they can function in a graft.

So you are trying to hide them from the host immune cells. How effective that is going to be, we don’t know.

Can we perhaps come in and genetically modify, which is easy to do in these cells with the histocompatibility genes, so we can make them more like a patient that is going to receive these cells.

Or is it possible that we may end up being able to produce cells that may be universal donors. Again, we are trying this, and at the moment it is speculation.

Clearly the one thing that has worked is the issue of nuclear transfer therapy, the so-called therapeutic cloning, in which as you know the argument is to take a cell from a patient, and fuse it to an enucleated egg, derive a blastocyst, recover the inner cell mass, culture it out, and then these embryonic stem cells would match the genome of the patient.

Is this a pipe dream? The answer is no, and I will give you an example of that in a moment. To get around some of the issues with the human cloning, embryonic cloning in humans, you have seen reports in the Wall Street Journal and other places which I can confirm are real, in which there are attempts now to take human cells, human nuclei, place them for example into rabbit eggs, enucleated rabbit eggs, and grow up a blastocyst, and generate stem cells that have human nuclei and rabbit mitochondria.

And the argument has been made here that, well, these cells would be perfectly fine for an autograft, and this isn’t accurate. We know that mitochondria produced polypeptides that are integrated into the cell membrane, and are actually considered to be minor histocompatibility antigens, and will be recognized and rejected by the host from which the nucleus came from.

So this really is not getting around the issue of the graft stuff at all using other animals, and we are a little bit concerned about how this is being handled.

So, let me give you an example, and one which you should read these papers if you haven’t from Rudy Jaenisch and George Daley at MIT, using the nuclear transfer therapy, or the therapeutic
cloning, to do two things.

What they did was to take a mouse that had a genetic mutation in genes that are important as far as the immune response is concerned. And they took cells from this mouse, took the nucleus out of the cell, and placed that nucleus into an enucleated egg to produce a blastocyst from a cloned embryo.

They took the inner-cell mass cells out of that, and generated embryonic stem cells, that then are the same genome type as this animal, and then went in and repaired genetically the mutation within those cells.

And then differentiated these cells into the hematopoietic stem cell component, transferred them back into this animal that had the mutation, and the transplant took, completing the whole hematopoietic system, and in rescuing that animal.

So this is a proof of concept kind of experiment, and I urge you to read it. It is an extremely powerful illustration, not only of the therapeutic cloning end of things, but also the ability then to come along and correct the genetic mutation and the reference was given to you.

Another argument has been made that we should be using perhaps just eggs that have been stimulated to form embryos, and these are parthenotes.

And the argument here has been that we can then use these directly into the female from which the eggs were taken. I just want to point out that in my opinion that this is going to have very low usage.

You are going to have to recover embryos or eggs from patients, post-pubertal, and pre-menopause. The window is going to be fairly short, I think, for many of the therapies that you would want to effect.

And the other issue is that we don't know much about cells that are derived this way, and how viable, and how functional they are going to be. But this has been used or promoted also as a source, and this is an illustration of where you take those cells.

All of this type of technology, I just want to let you know, and I know that you are grappling with this, but even within the field of the scientists are beginning to argue about what is an embryo and what isn’t an embryo.

So any arguments that you have within your council on this, I will tell you is also being held among biologists. I think that my own personal feeling is that anything that you construct at this point in time that has the properties of those structures to me is an embryo, and we should not be changing vocabulary at this point in time. It doesn’t change some of the ethical issues involved.

What are some of the problems here, and I will summarize this a little bit. Current research. Well, we have to come up with better ways of having high efficiency differentiation protocols resulting in homogeneous cell populations.

We are dealing with growth environments, and genetic manipulations, and we are trying to define stages of cell differentiation within our cultures.

And assessing whether or not the differentiated cells that we are getting out are normal and completely functional. And this is in a dish.

And let me tell you that there are examples of where you can spend all of an effort studying something in a dish, only to find that if you pop it in an animal that it doesn't behave how you think it is going to behave. We have a lot to learn here.

I think you can imagine that what is going on in a dish is not exactly what is going on in a site where you transplant. The whole issue of grafting, and how you put it in, and the safety issues, and that cells migrate away, and they differentiate, and will they form tumors, and then the issue of the immune response.

These are all, you know, formidable obstacles that lie ahead. I mentioned to you that we can use cells individually, and have been used in a variety of paradigms in our collaborators of single cells, and the tissue engineers are now taking these different cell types and seeing if they can reconstruct or construct organal aids or tissues to do in-grafting, and thee has been some success with this at this point.

Finally, to me, the future is going to be that the basic science coming out of this is the most important element, and that from that information we are going to be able, I think, to take patient
cells, where appropriate, and I say where appropriate because if you have autoimmune disease, or in
cases where you have an injury, spinal cord injury, or stroke, or heart attack, and you don't have time
to take that patient's cells, you are going to have to come up with different paradigms.

But I think we are going to be able to eventually coax a patient's own cells to behave in a manner that
we want to, but we are going to learn this I think through the study of stem cells.

The last thing I will say is I know that you want to ask, well, what is the future going to bring, and I
am concerned about predicting the future. I can't even do this on a three year NIH grant and this is
what is expected of us.

You know, what is going to happen here. I certainly think that everything that has happened up to
this point is consistent with success in this area, and I could get into more predictions in a moment.

But we are always asked when is this going to happen, and it is going to be I think based on specific
cell types, and on, and on, and on. But the predictive thing is very, very difficult.

Well, I thank you for your attention, and I hope that this was enough of a primer to add more meat
to your discussions. Thank you.

CHAIRMAN KASS: Thank you very much.

(Applause.)

CHAIRMAN KASS: We were only physically in the dark, but we are grateful for your
enlightenment, Dr. Gearhart, and the floor is open for questions, and comment, and discussion.
Don't forget that you have to turn your microphones on to be heard. Jim, go ahead.

DR. WILSON: Dr. Gearhart, do you foresee that it will ever make a difference whether cells that are
transferred for human cell regeneration come from cloned eggs, or from the retrieval from IVF eggs?
Does it make a difference what the source is?

DR. GEARHART: Well, I think in the short term that it will. I think the only way we have around
the immune rejection story at this point is from cloned embryos.

For a patient in which you can predict ahead of time is going to need stem cell therapy and you have
the time and money available to do the cloned approach.

I would like to think that this is going to be a transitional period, and that we will not have to rely
upon this in the long term, and that we will be able to take for any specific disease a stem cell, or a
derivative of a stem cell that may come from the adult source, the umbilical source, the fetal source,
or embryonic source.

I mean, whichever presents, and that we will have ways of dealing with this graft rejection story
other than through the cloning of human embryos.

DR. WILSON: If I could just supplement my question with a related one to which you referred.
What is your current assessment of the value of adult stem cells, as opposed to embryonic ones, as a
source of organ regeneration currently?

DR. GEARHART: Oh, I think it is a very viable option and I think NIH should fund it. I think that
from what we see in the work, and Catherine will present a nice overview of this, that this is going to
be a good source of stem cells.

They have some issues that they have to overcome, issues of expandability, and plasticity, that we
feel are — that have not been demonstrated as well as embryonic stem cells, but I think that
eventually we will be able to overcome this.

But I think part of the knowledge of overcoming it is going to be coming from our studies of cells
that have those capabilities, and being able to transfer that information to those other cells.

So I think we are going to come up with — I believe that in the stem cells, cell-based therapies, that
we are going to identify certain adult sources that are going to be good for some diseases, some
injuries, and embryonic sources for others.

So I think we are going to mutually proceed on this and benefit from it.

CHAIRMAN KASS: Please, Elizabeth.
DR. BLACKBURN: Dr. Gearhart, you can give us I think a unique perspective on the comparison between adult, and embryonic, and fetal stem cells.

And in particular many of us read the recent papers, the scientific peer-reviewed papers that came out with respect to the adult stem cells, and the interpretation of their plasticity being cast in some considerable doubt by the observation that there was cellular fusion of those cells which had led to in these particular cases examined a mistake in interpretation of their plasticity.

And I wondered if you could give us your perspective on that aspect, which extends Jim's question somewhat.

DR. GEARHART: I will do so in the face of Catherine sitting back here, who is —

DR. BLACKBURN: Yes, I am going to ask her, of course, about this, too.

DR. GEARHART: — actually done those experiments. Clearly the most difficult experiments that we have had to address and interpret are those utilizing adult stem cells that have been placed into the blastocyst of mice to create chimeras.

And in those chimeras, we see that the descendants of those adult cells gave rise to many, many lineages within the embryo, and this was really the issue. How did we explain this.

And from the studies of Austin Smith and others that you are referring to, the implication was that when those cells were transplanted into that blastocyst to generate the chimeras, that a subset of these cells fused with the hosts own cells and it was those fusion products then that gave rise to the variety of lineages.

At the moment that is an implication, and that has not been demonstrated in the embryo. It has been demonstrated in the dish that they had that capacity.

So we are now waiting and putting pressure on Catherine, and Freizen, and others to look into those animals to see if they can recover those specialized cells that were derived from or that had the adult phenotype if you know what I mean, the marker, to say are you truly of the adult stem cell lineage, or do you have other markers present, other chromosomes present, that come from host cells.

So until we see that data — you know, I will wait. That is something that can be looked at scientifically, and that is as far as I would go with you, Elizabeth, at this point.

It is an interesting observation, and we will see if it actually is the answer.

DR. BLACKBURN: And just to extend on what you said, I think what it does now do is to demand that the onus be put on the researcher to show that there has been a plasticity or transdifferentiation, and there are other set of criteria, which would be karyotype and multiple micro-satellite, polymorphisms — sorry to get overly technical — and other genetic markers.

There are clearly tools in hand, and so it seems as if every experiment can in fact be subjected to those sets of analyses now.

DR. GEARHART: Right.

DR. BLACKBURN: And will need to be before we can get a good view of this.

DR. GEARHART: Right.

CHAIRMAN KASS: Rebecca.

PROF. DRESSER: I have four questions, and maybe if I say them all it will be possible to answer some of them together. One, I was wondering if the rats are being given immunosuppressants in this study.

And then you said a problem with the rabbit eggs is that the mitochondrial DNA might cause rejection, and so I wondered if that would happen with a cloned human embryo as well if the egg came from another person, and if you are trying to do a therapy that is compatible with a patient.

And let's see. The feeder layers, I was wondering if they have available feeder layers that do not come from animals or what the state of that development is.

And then finally what about the fact that if you are creating a blastocyst from a patient's cell, and if the patient, let's say, has cancer or some condition that could be related to genetics, would the stem
cells somehow perhaps be risky?

**DR. GEARHART:** There is no question in my mind that the possibility exists that if you are doing an egg donor, and nuclear transfer into an egg, that there possibly exists that that cell — the embryonic stem cells derived from that could be rejected. Absolutely.

Now, how do you test this? I mean, where do you test it. This almost comes under the same criteria that I have for anyone coming to — if I was on an IRB and they wanted to clone a human reproductivity, what data do you present before you permit it to go.

To me, it is one of these things where you need perfection before experimentation, or without experimentation, which is something in science is anathema.

**PROF. DRESSER:** Well, you could test that in an animal, right? I mean, you could at least see —

**DR. GEARHART:** Well, you can, and we could set it up in an animal, but the issue is — I mean, where you are very defined and to demonstrate it by doing it into a different strain of mouse. There is no question about it.

But whether or not that would carry over in polymorphisms that exist in human, again you are still faced with human versus rodent.

The feeder layer issue. It is one that is being taken on, and there is no banning of this type of work with private money, and clearly there are a number of investigators, laboratories, working on establishing feeder layers from human tissue that could be used, and I think that this is very important.

So those studies are certainly under way. We have used a variety of different human tissues as well to look at in our studies. Oh, the very first question that you asked. I'm sorry, it was again?

**PROF. DRESSER:** For the rats —

**DR. GEARHART:** Oh, sorry. We did animals that were immunosuppressed and animals that were not immunosuppressed. And we did not find a great deal of difference in the short term, although — I mean, as far as any type of destruction of cells and things like that, although clearly in the animals that were not immunosuppressed that you could see reactive cells present.

So clearly in the monkeys immunosuppressed, absolutely, and so we have done them both. And then the blastocyst question?

**PROF. DRESSER:** If it comes from a patient with a particular disease.

**DR. GEARHART:** Yes. Clearly where there is a genetic basis of any type of a disease, you would be concerned about reintroducing the same cells that were subjected to whatever the disease process was.

And I think that this carries over also into, for example, the diabetes work, where if you have an attack on insulin itself, you know, is this going to be a viable alternative, and there are some evidence now that you can alter the insulin molecule to make it not recognized by some of the autoimmune antibodies.

I should say that there are a number of laboratories — and this is one area that is being emphasized in the use of human cells, including our own, with Mike Shamblott, where we have lines that are — human lines that are insulin producing that you can pop them into animals, and demonstrate that they can produce human insulin.

And we are very encouraged by some of these early results. But I would still contend that we have a long way to go to carry that into some type of clinical application. We have a lot of questions to answer.

**CHAIRMAN KASS:** Janet.

**DR. ROWLEY:** Well, I, too, have multiple questions and I want to thank you for a very lucid presentation. That helps a great deal. I would like to first — and I think I will do these one at a time.

It is a substantial question as to what value the embryos that are left over from IVF can play in this whole process as compared with embryos that you develop for either a particular purpose, or just straight off.
And my understanding was that maybe some of the embryos were sufficiently mature so that maybe the cells derived from IVF would not be useful in developing, say, cells lines or things. And I would like your comments.

**DR. GEARHART:** One of my hats at Hopkins when I moved there in the late ’70s was to develop the IVF program. So we are very well tuned into the issues of IVF, and clearly in an IVF procedure the best embryos obtained are those that are used first in first transfers.

So that generally those that are left over are of the ones — we don’t want to call it a lesser quality, but at least as far as our eye is concerned, and how we judge grades of embryos, based mainly on morphology to be honest, and more currently we are looking at biochemical parameters that we can measure in the media in which these cells are growing that something has been secreted to have some kind of a measure.

And that clearly those that are the spare embryos generally are those of — let’s say, what we deem, and knowing what that means, of lesser quality.

So what does that mean? In most cases, they have not developed far enough along, which means that if they are left over that you take them back out of the freezer, and you try in your culture conditions to get them up to this blastocyst point.

If you can’t get them to a blastocyst stage, you can’t derive the cells. If there is no inner cell mass, you can’t do it. And you find that you are compromised there, and that generally these are not very good embryos.

So one could argue that overall that you would expect to have a low efficiency yield with respect to taking in embryo and deriving a line from spare embryos in an IVF program. That is in general.

**DR. ROWLEY:** Okay. You mentioned modifying the histocompatibility locus, and I would have thought that there is still so much that we don’t know about the MAC that that would — I mean, obviously anything can be done in the future with time, but do you look on this as practical?

**DR. GEARHART:** Well, back in the ancient days, in the early ’80s it seems in this field, Oliver Smithies and others did do knockouts of Class I and Class II genes, in an effort to determine whether or not this could prolong grafts into animals without those.

And that depending on the tissue or the organ, there was evidence that this indeed could be the case, and not that it was an indeterminate thing, but just by days, or weeks, or months, that this was the case.

What they didn’t know about at that time were NK killer cells, and those kinds of things, and the importance of other determinants which must be on cells. They wiped everything out.

So some labs are now taking a look at this to see if it is possible then to rebuild back some of these markets. But it is a matter of speculation at this point whether or not this could occur.

Now, what we can talk about I think is it possible to take using the act of transgenesis and things like this, where we could move big pieces of DNA; of taking part of a patient’s chromosome-6, you know, and cloning that into a stem cell after knocking out some of it, and we may get some degree closer.

But that says nothing about the myriad of other loci that could be involved as minor histocompatibility problems. So, some of it is speculation, but I think it is also testable at this point in time.

**DR. ROWLEY:** And my last question is coming back to the 80 plus cell lines, and you raised concerns, which many of us have, as to how useful some of those are going to be.

**DR. GEARHART:** Right.

**DR. ROWLEY:** Could you expand a little bit, in terms of whether you think they are really not going to be long term cell lines, and that is your concern, or whether there are other aspects.

**DR. GEARHART:** Well, I have many concerns, and I hope that I can get them all in. I mean, look, we were all thrilled when Mr. Bush made the decision to move forward with this and establish cell lines to permit the work to go forward. There is no question about it.

But as we looked into — and by looking into, it was a practical matter. Many investigators around the world, and I have close contacts with colleagues in Germany, and in France, and in England, and
Japan, and Australia, and on and on, as we compare notes all the time on our results of research, as well as on practical things like this, and on political issues.

I mean, there is no question that we have to keep abreast, and what happened, particularly from the German investigators, which is significant, as you know, in Germany, they are not permitted to derive cell lines.

And for a while they were not permitted to use those that were even derived, and recently their parliament voted to permit the use of existing cell lines as of January 2002.

But what happened was that when these investigators set about to import cell lines, and contacted the registry list at the NIH, which continues to grow each day, and more lines are added to it as you know, it turned out that many of the lines were not defined.

Someone just reported that they had a clump of cells growing in a dish, and they didn't have any of these parameters or very few of them done.

And this reduced the list substantially, quite substantially, down to — we are talking about, say, a dozen. And then the issue came up as to, well, are these — can they be imported without a stringent material transfer agreement, and with a reach through clause that would say that anything that you would do with those lines belongs to the person giving you the line.

And this reduced the line substantially. And then other lines are not available because if you needed to get them, you needed NIH funding, and only NIH funding. You could not use private funding with them, and on and on.

And so it drastically reduced down the number of lines that are practically available. Now, whether or not this will have a major impact, clearly the NIH is receiving grants, and we have been reviewing grants, and using the existing approved lines, the few that one can get.

And the work will go forward, and whether or not that will be sufficient, and we recognize that there is going to be a half-life to these lines for various reasons, and that there will come a time if it proves effective in the basic science part of this to move forward, that we should be looking at being able to generate new lines.

And the issue of the feeder cells is a major issue as well, and to begin to establish lines on human cells so that we are not faced with that anything that we derive from this now, and it is important to consider, has to be considered as a xenograft.

Although it is a human line, the FDA requires that if it has seen these other products, it has to be considered a xenograft, which sets up a whole new set of criteria for moving this into the clinical applications.

So I think there are reasons why we should eventually be permitted to derive new lines. Well, I'm sorry. We can do it now on private money, but anything that is derived cannot receive Federal money for support.

**CHAIRMAN KASS:** There are people waiting in line, but can I get a clarification on this question that came up in your answer to Janet about the durability and longevity of the lines, and on the one hand, one says that the embryonic stem cell lines, their great virtue is that they can be self-renewed indefinitely.

On the other hand, they have a half-life, perhaps because of accumulated mutations. Could you say a little more? I mean, some people claim these are eternal lines.

**DR. GEARHART:** Right.

**CHAIRMAN KASS:** And could you say something about the possible differences between human and mouse with respect to renewability, because I think it is an important factor.

**DR. GEARHART:** Well, the issue is maybe they are eternal, but can you still use them. They can still divide indefinitely, but they may not —

**CHAIRMAN KASS:** But they are no longer the same.

**DR. GEARHART:** Yes, they are no longer the same, and they may not give you the biologic properties that you need. Strangely enough, Leon, there have been very few publications up to this point, and up to this point there is one that I can cite for you, and I have it in answer to some of your
questions by Joe Stanbrook at — Peter Stanbrook, at the University of Cincinnati, in which he looked — these were mouse lines.

And he looked at the frequency and rate of mutation within several mouse lines, and contrasted those with several schematic cell lines that were in the lab as well.

And he found that indeed the mutation rates — and what you do is you pick certain genes to look at changes, and to look at chromosome lost or gain.

This paper was published in PNAS in the March 19th issue for those who are interested, and what he found was that the frequency and rates of mutation were orders of magnitude less in the embryonic stem cell line than in the schematic cell line.

And you are looking at a rate of generally 10 to the minus 6 frequency within any mammalian cell as it is divided. But what he did find, and that was a bit troublesome, was that the type of mutation that appeared in the embryonic stem cell one led to what is called uniparental disomy, which is a situation where you end up with homozygosity across a region, or across chromosomes or regions of chromosomes, that gets rid of really the dominant tumor suppressor genes, which then raises the issue that these cells may be more susceptible to tumorigenesis than others.

Now, that is the only report, and I will tell you that in several laboratories what is being done now with the human lines, and that is using express sequence tags, for example, and you can use 10,000 of them, they are looking at mutation rates at 10,000 loci, if you know what I mean, over time in culture passage, after passage, after passage.

So we will get information on this parameter, and how significant it is going to be, I don’t know, but one would predict that clearly there is going to be an accumulation of mutations within these cells.

CHAIRMAN KASS: Okay. Thank you. I have Michael — well, also, was that on this point?

DR. BLACKBURN: Just a very brief clarification. Did the absolute frequency of uniparental disomy go up? Was it an absolute frequency increase, or simply did it relatively increase as you looked at the whole spectrum of mutations in the mouse embryonic stem cells?

Do you see the difference that I am trying to get at?

DR. GEARHART: Yes.

DR. BLACKBURN: That if it were an absolute increase, that is a reason for concern, much more than if it were simply a relative increase in a number that has already gone down by —

DR. GEARHART: These numbers are rates, and so I believe it is an actual number. In other words, it was a real —

DR. BLACKBURN: An absolute increase?

DR. GEARHART: Yes, an absolute increase.

DR. BLACKBURN: So I just wanted to make sure that I understood the numbers here.

CHAIRMAN KASS: Michael Sandel, and then Frank.

PROF. SANDEL: I would like to go back to the adult stem cell versus embryonic stem cell question, and ask it in a slightly different, and maybe more pointed, form.

As you know, there are some people who regard embryonic stem cell research as morally objectionable. I am not asking you or trying to drag you into that debate. But I would like to know your view on the following scientific question.

If adult stem cell research in the best case scenario redeems its promise, what would we lose medically and scientifically if we ban embryonic stem cell research, or imposed a moratorium on it for a period of time, until we could assess what adult stem cell research could achieve?

DR. GEARHART: I personally think it would be a tragedy, and for the following reason, if this was to happen. I think the length of time that it is going to take to assess whether the adult stem cell avenue is going to provide the potential therapies that we are thinking about, is going to be years.

And I think for us to deny at this point any avenue that has the potential of the embryonic stem cell story is a tragedy to those people who need or who will need these cures.
And I think that it is a time element. If this could be done in a year, I would maybe listen to that argument. But it is going to take years to really assess any of these approaches.

And I really think they should move forward together. I think we are going to learn in both directions how to utilize information coming out of these studies that would benefit, for example, or enable us to understand more about the adult sources if this is going to be the emphasis, and to really make them effective in their use.

So I think that it wouldn’t be wise to put a ban on the embryonic source at this point, and wait until another avenue is assessed. The length of time is going to be too long.

PROF. SANDEL: Can you be more specific? Are there certain types of research avenues that you would associate more with embryonic stem cell research, as against adult stem cell research?

Is it likely that success is in particular areas, or is it just that you feel that as a general matter it is better to have more avenues rather than fewer?

DR. GEARHART: Well, I think that one of the messages that I hope that I can get across, and maybe Catherine will, too, is that we are in very early stages in all of stem cell research, no matter what the origin of the cells are.

And to make a judgment as to which of these is already more advanced than the other, it would be a tenuous one at this point, because you have got to remember that there are very few investigators actually working on embryonic stem cells at this point.

The list on the adult side obviously is larger. I mean, as far as investigators are concerned. And I don’t think that any of us are really showing dramatic — you know, utilization in the sense that we can say we are going to go to any clinical use of this.

It is going to take years for this to occur. We are in the very early stages and so I would be really hesitant to say that anything is demonstrating anything better.

All I would say about embryonic stem cells at this point in a very positive way is that we know that at this point that out of these cells we can virtually generate any cell type we want in dish and in large numbers.

That is the advantage of this approach. Now, whether this will be surmounted by other discoveries in adult stem cells to do the same kinds of things, I don’t want to predict. I hope that it happens.

You know, our — and I also want to emphasize that we — and although we are associated with the embryonic form, we are studying other forms as well. We are not foolish.

As a scientist, you know, you are not going to put all your eggs in one basket here. And so we are trying to move forward on a broad front, and I think that this would be the more rational way to proceed in this arena.
neurons, inner-neurons.

I mean, we all — I mean, human and rat, or human and mouse, depending on which one we did. We don't know the relative contributions. We can count cells, but really what is the functional basis of what occurred there.

We know that the human cells are also rescuing the other, but to what degree. This is where the hard work comes in. What was the mechanism, and what really went on or is going on in that ventral horn.

I can tell you in work that John McDonald has done at Wash U, in which they generate a contusion injury in the spinal cord of a mouse or a rat, and then infuse in mouse embryonic stem cell derivatives, and that he is faced with the same issue. He can see that these animals recover to a certain degree, but the mechanism of what is it, of what has really occurred there, is not known.

And I think what we are going to find is a demand that we come up with mechanism in some of these animal models so that we can completely understand what that therapy is going to be if you take it to a human.

And this is going to require a lot of work. Now, some of it you could argue is that you could do it all within animal studies. You know, mouse embryonic stem cells, and you don't have to put the human in.

But I think we are finding enough differences between species that it would warrant at least the study also of the human derived cells in the same paradigms to ask those questions.

PROF. FUKUYAMA: But I am just curious. Are you getting actual tissues in which you have cells from different species that are growing simultaneously?

DR. GEARHART: Oh, yes, absolutely. Yes, sitting in the same — well, you can see in the section here that might be 15 or 20 microns across, you see a mixture of the rat cells or mouse cells, and human cells, functioning.

You know — I mean, this isn't uncommon. We do interspecific grafts a lot in experimental things, and the question is when you do it, and we see, you know, human cells growing in animals very nicely. I mean, as long as there is immunosuppression and things like this occurring.

PROF. FUKUYAMA: But could you go the other way, also injecting stem cells from other species into human beings?

DR. GEARHART: Oh, yes. I mean, this is one of the issues with xenografts. You know, is this something — well, there is a report recently about chicken embryonic stem cells, and the fact that people who had derived these were promoting the use in humans.

Pig stem cells, you know, et cetera, and so it can be done, but a couple of issues, and one of them is the issue of the xenograft itself, of bringing in endogenous viruses, and is this a wise thing to do.

And the other thing that I would ask you, and I won't be flippant about it, is to say that if you — and one of the concerns that we have that maybe this council and others would take up, is long term in a neurologic sense.

If you are putting stem cells in, and you are putting them in between different human beings, what are you doing to that individual. And I would say to you that if you have a stroke, and someone comes along and says, well, we have pig, cow, mouse, human, take your pick, what would you select.

I am not being flippant about it, but I am just saying that I think that we know that human would be preferable at this point in time.

CHAIRMAN KASS: Could I ask a question, and just for clarification again also on your own experiment that you showed us. You said that some of the rats were immunosuppressed and some were not. Is that correct?

DR. GEARHART: Yes.

CHAIRMAN KASS: And were there functional differences in the results between those two groups, and would that bear upon the question of whether or not the major effect was owing to the action of the human cells, or a stipulation of the endogenous cells?
And lastly, if these animals had come to post-mortem was there a difference? Was there rejection in the non-immunosuppressed animals of the human cells?

**DR. GEARHART:** It is important to keep in mind the time frame that these experiments are done in. They are of very short duration relatively speaking, in a period of several months maximum.

In experiments that have been done in our laboratory, principally by Mike Shamblott, in taking human cells and grafting, and these are insulin-producing cells, and we have done it in a variety of tissues into rodents, you always see reactive cells, which means that you are eliciting an immune response.

Again, they are short term, and whether you are getting destruction, we see cellular debris, and we see this kind of stuff at these sites. I should tell you a little bit that may be enlightening.

When you do grafts like this, if we say we are putting in 300,000 cells or we are microinjecting in a lot of these cells, many of these cells will die at the time of injection, simply because you have taken them out of one environment and you put them into another, and you see a tremendous amount of cell death.

Very few of these populations of cells continue to divide. In other words, it may undergo one more round of division, and they sit there.

You do see when you come in finally to look at where is the human versus where is the rodent, and you use your human markers. You invariably find a group of cells that you can't phenotype, if you know what I mean, and to say what has happened here, and clearly there are cells being destroyed.

**CHAIRMAN KASS:** Fused?

**DR. GEARHART:** Well, we don't know that. And one of the arguments for many years has been that the central nervous system is an immune privileged site. I don't think anymore that this is something that is believed or subscribed to, and if you have the option of immunosuppression, or of getting around that, that that would be preferred.

And particularly when you are talking about a graft going into a human being that may be there for 20 years, as opposed to a matter of a few months. So I think that this is going to remain a major issue, and there is no question about it.

**CHAIRMAN KASS:** Thank you very much. Bill Hurlbut and then Paul McHugh

**DR. HURLBUT:** John, I hear you saying that we should pursue all lines of research, but I want to weigh the different options here and pursue the question of if the lines were restricted what would be gained or lost.

Specifically, I have several questions that hinge each on the other. First of all, the cells that were implanted or tested for their tumorigenicity effect that you spoke of in your paper were the so-called EBDs.

Were those derived only from embryonic germ cells; is that what is implied there?

**DR. GEARHART:** Yes. In our paper, we took the stem cell itself and plated it out in a variety of culture conditions, some of which are designed to enhance or select for certain types of differentiation.

And we referred to these as embryoid body-derived cells. They came out of this little cluster, and in our field it is essential that we take the stem cell off the dish, and let it form into a little ball, and which is just a multi-cellular structure, called an embryoid body.

Now, this was an unfortunate name that was given to it by a French pathologist back in the '30s, but as you can imagine, when someone in a political sense talks about an embryoid body, they conjure up embryos here.

But these are little clusters of cells, and within those or within that cluster, the beginning of differentiation begins. These cell-cell interactions are essential for this. We have not been able to mimic this in a sheep yet.

So what happens is you get within that ball a variety of cell types being formed, and all that you want to do is to disassociate that ball after a period of time, and select out only those that are going in the direction that you want them to go in.
So this is what we did in that experiment, and so we have now these EBD lines, and in these lines, in these human lines, and these lines have been placed in a large number of animals, in the grafts that we have used, we have never seen a tumor up to this point.

And it may be unique to humans, because human primary cultures are easy to establish and mouse aren’t. I mean, there is an issue here that we don't know that you can’t do the same experiment in the mouse.

So with our experience with the EBDs, we have never seen a tumor. Our experience in the mouse and using what we thought were equivalent lines, we have seen too many tumors with respect to grafts into the central nervous system.

**DR. HURLBUT:** Just parenthetically haven’t I been reading all along that embryoid bodies are also formed from ES cells?

**DR. GEARHART:** Oh, yes, absolutely.

**DR. HURLBUT:** But the point is that your particular lines don’t produce tumors, and the ones derived from the primordial germ cells don’t seem to produce tumors; whereas, the embryonic stem cell lines do?

**DR. GEARHART:** Well, the only comparison that we have at this point are mouse ES lines, in which we have derived different types of precursors under different conditions, have been compared to human EG lines that have been derived, or which precursors have been derived in a slightly different manner.

You can’t derive them both in the same way. We have seen nothing up to this point on human ES derived lines transplanted. We just have not seen any data on that.

So I don't want to make it clear that there is a difference between the derivation either from a germ cell derived, or an inner-cell mass derived line. Does that make sense? That comparison is not there yet.

**DR. HURLBUT:** Well, obviously what I have been getting at here is if in fact your cell lines are less likely to cause tumors, then does that imply that there might be some advantage to using your cell lines, and if so, would it in fact be the greatest advantage if a patient’s own cell line could be derived from primordial germ cells?

**DR. GEARHART:** Oh, boy, this committee would well, wow. Now, think what this means. It means that you would be generating an embryo, and having it implanted. Now, what you don’t know is that our fetal tissue comes from 5-to-9 weeks post-fertilization. These are therapeutic abortions.

And which means now that you are way beyond — I mean, the point of where a blastocyst is, and obviously way beyond I think anyone subscribing to that approach.

**DR. HURLBUT:** You told us that in your paper.

**DR. GEARHART:** Okay.

**DR. HURLBUT:** But is it true that maybe there would be some great advantage if we could find a legitimate way to harvest tissues generated from a specific patient at a later date?

**DR. GEARHART:** Right. Well, I think it would be terribly risky. We have been asked this question a lot though; is it possible to do a biopsy on a developing embryo, and to remove just a few germ cells.

I think at the stage that we are using these embryos are a matter of — or fetuses are a matter of maybe 6 or 7 millimeters in length, and to do the surgery on this I think would just be impossible without causing harm.

The other issue that I would contend is do you think it would be okay to go in and remove the germ cells from an embryo and let that individual go on and say, well, we have taken your germ cells. Now, we have another therapy for you.

And so I don’t think it is a very good thing to do.

**DR. HURLBUT:** And that is my final point, and I wanted to ask you personally in working with these cells, do you see 14 days as some kind of magic marker moment?
Do you see something crucial about implantation? And you spoke of keeping all options open.

**DR. GEARHART:** Right.

**DR. HURLBUT:** Why in fact do we allow abortion fairly late in term, and yet now we are speaking as 14 days as the sacred moment? I know that I am opening a very difficult issue here.

But in fact wouldn’t we gain a lot scientifically from extending that 14 day limit potentially if we could find a culture median that could sustain the embryo, or wouldn’t we gain a lot from implanting, even gestating and harvesting?

And why do we feel that we shouldn’t do those things? And I would also be interested in your personal response to these ethical issues.

**DR. GEARHART:** Wow, you have asked a lot. As you know, stem cells have been obtained from many stages of human fetal development, and have been found to be useful in generating various cell types in culture.

And if we look at a variety of studies, you can find it in the published literature. We have had a number of requests for fetal tissue at different stages, and I think legitimate requests of investigators willing to investigate cell lineages, et cetera, within the embryo.

So people have been thinking about it. I mean, there is no question about that. We have found it difficult enough to be fortunate enough to obtain the fetal tissue that we work with.

I mean, there is a consenting process and we have nothing really to do with other than to make sure that it complies with institutional, Federal, and State law.

To obtain viable tissue from abortuses of any kind is a major concern. When we started our studies, we looked into using spontaneously aborted material, which occurs across the board, but mainly in the early stages.

And we thought that this would be a good source. As it turned out, by the time that we were notified — and this occurs in outlying hospitals, and not at major medical centers, where investigators are — you know, a patient presents with a miscarriage, and it is taken care of in the ER.

And it turned out that it was very ineffective, number one. And, number two, and then I will get back to your question, we found that most of the material that did come to us had chromosomal abnormalities that made it less desirable for use.

Now, the issue of the 14 days, and what does it mean. Well, this was something that really came into play in the United Kingdom when they were trying to deal with this issue.

And it was decided at that point that at that stage the embryo still does not have a central nervous system. It can feel no pain, et cetera. And this was why basically that period of time was set to be able to grow them in culture, or to remove tissue.

We, as embryologists, argue the point all the time as to what is going on in these early stages, and we were always asked these questions. When do you believe personhood occurs and when is it established, and things like this.

To me that is not a biologic question. We don’t have a means of probing that. So I think that is why the 14 days was selected, and that’s why it is sort of adhered to in a sense.

Do I adhere to that? Well, to a certain degree, no. We take material that is later on, and it is cadaveric fetal tissue. I think that we should be able to utilize any tissue that comes out of abortion if the alternative is that it is just going to be disposed of, which is what happens.

The pathologist takes a look at it to make sure that all of the parts are accounted for, and there is an issue about being concerned about what is left in the uterus.

That is my personal opinion on that. But I don’t think that we should be going and establishing pregnancies, and to downstream then utilize that tissue.

I mean, to then stop the pregnancy and then to recover it. I mean, that is my personal opinion. I don’t think we should be doing that. As you know, years ago, President Reagan was faced with this, I believe, when he heard that families were establishing pregnancies so that regions of the brain could be harvested to treat Parkinson’s disease in the family.
And clearly we don’t subscribe to that in any fashion.

CHAIRMAN KASS: Thank you. We are coming up to the break and I have Paul McHugh, Mike Gazzaniga, and we are running a little late because we started a little late. We will take a break shortly. Paul and then Mike.

DR. MCHUGH: My point is very brief, John, because you have touched upon it in several places. But first of all, I want to thank you very much for that coherent presentation, and I especially thank you for showing us experimental data.

And that is what of course generates better questions to ask you. And it is really out of that experimental work that I did have a question. And that is what you showed us was fundamentally a xenograftic experiment using human tissue, human cells, in rats.

And the results were very interesting, and not only was there growth of cells, but you told us that there were trophic factors that were probably acting in this way.

And I then wondered, and you can answer this, why was it necessary to use human cells to demonstrate this phenomenon in a rat, and why weren’t you using rat cells to do rat experiments.

And if that is true, that you could do rat cells to do rat things and the like, the development of the question is would it not be wise of us to ask you all to go back and work with your rats and your mice, and your cats and your sheep, and keep going at it, and come back and tell us why you need human stuff to do this stuff, okay?

DR. GEARHART: Okay. We did it first with mouse cells. We don't have rat embryonic stem cells. We did it first with the mouse and it worked.

And in our exuberance, saying, well, would the human cells work, and they did. There is no question that I think that the mouse cells worked better, and the mouse cells were from these neural precursors that we had obtained that I had mentioned that we had this concern about tumors.

But they did work, and so the only two cell types that we have found at this point that work have very similar origins if you know what I mean.

Clearly the paradigm has to be extended to other sources of stem cells, adult and umbilical, and this is planned to say in this particular paradigm will it work.

So, Paul, the answer is that we did it first with the rodent cells, and we could pursue that. I mean, as far as looking for the growth factors and what not.

But we have changed almost completely to the human cells for trying to determine what those growth factors were that were secreted, but we could do that again with the mouse, absolutely.

CHAIRMAN KASS: Mike.

DR. GAZZANIGA: Just briefly, thank you again for a wonderful presentation. This moves to another level, and that is how big is the American biomedical engine.

And I ask that from the sense of having just taken a trip to China and Japan, and England, and you read that Sweden and Singapore, and India, and so forth, are going ahead.

If America dropped out of this for legal reasons that are on the horizon, how big an impact would that have on the overall resolution and development of these therapies?

In other words, if you just look across molecular genetics and microbiology now, and prior to this issue arising, what is the size and importance of the American effort?

DR. GEARHART: Well, I don't think that there is any question that the investigators funded through the National Institutes of Health, and our academic establishments here, are the engine that drives biologic research, biomedical research, in the world.

There is no question about it. I mean, the volume, the sheer volume of this, is enormous. And if you look at this compared to even in our country to what the biomedical industry, or I mean the private industry is putting into this, it is dwarfed by the Federal funding.

And this is really what is enabling and this is why I think the U.S. has been so far ahead. So it is essential I think to have Federal funding into this area really to reach our goals as quickly as
There is one last thing or one thing that I would like to say to the committee, and it is understandable, but when you are in and start in a business like this, you don’t know the impact of it.

The thousands of communications that we have received from patients, and patient-based groups, about our work and about moving the work along, not only is it emotional, it is unbelievable. I mean, from the standpoint of just pure numbers, sheer numbers.

It doesn’t just extend within the United States, but throughout the world. In 1998 when we published our paper, within a few days we had 10,000 e-mails alone about it.

And every day I still get hundreds of e-mails relating to this. It extends not only to bona fide — you know, many people don’t understand what this work is about.

They are contacting you for a brain, or a uterus, or from some countries we have had requests, hundreds of requests for penises, for example. And you are trying to figure out why — you know, what is the issue here.

We need education and we need informing to say that we are dealing really with cells and tissues at this point. That is what we are really about. It is going to be years away before it goes beyond that.

And so what I am trying to say is that there are requests throughout the world. So that is one issue. I mean, the pressure is enormous, and also people offering you large sums of money to provide them with cells outside of the arena that it should be done in. Do you know what I mean?

There is desperation, and you see this, and it is tragic, and as a researcher this is new to you. This is something that you are not accustomed to and never will be accustomed to handling.

So I just wanted to let you know what that pressure is like. It is enormous. I have boxes full of these things. I don’t know what I am going to do with them, but you try to respond.

There has been an issue with brain drain. We know that there has been one investigator from the University of California system that went to the U.K. and received one-and-a-half million pounds to pursue this work in the U.K.

Well, this happened here. I will tell you that — and I am talking to students in our own group, you know, go to Europe for your post-doc, and go to England for your post-doc if you want to continue in this thing.

And I think you will see more of this, and whether major investigators will leave, I don’t think so. I think we will get through this, and I hope that we will get through this period in this country.

There are many, many investigators, many investigators, and I can’t tell you what it is like not to be able to give a cell to the person next door to you because of a policy.

I mean, this is just an incredible situation. I think we will get through it, and I think we will be okay. But I am still concerned about it. Sorry for the editorial, but I think it is important.

CHAIRMAN KASS: Charles, did you want a quick word?

DR. KRAUTHAMMER: If I could just ask a very quick question. You said that you would oppose and you supported the opposition of creating a fetus for, say, harvesting the brain cells, and you talked about the example in the Reagan years.

On the other hand, there is no difficulty, at least in your estimation, of using tissue from a discarded fetus already aborted, and tissue which would otherwise be thrown away.

Would you apply that same distinction to the embryonic stage? In other words, you now use — you develop embryonic stem cells from discarded embryos from IVF clinics, and would you be equally opposed to the creation of embryos specifically for their use as sources of embryos using that same analogy?

DR. GEARHART: No, I would not be opposed to that. I don’t give the same moral status to that entity.

CHAIRMAN KASS: Well, we have — let me just make mention of one matter. Janet Rowley has
submitted in writing, and I would endorse, these questions if we had enough time.

We would like your comments on what kind of regulation you think might be or should be developed for this area, and what is the status of government support for what kind of research, and what are the limitations that are counterproductive.

If we could invite — if you would be willing, and these are hard questions and they are big questions, but if you would be willing to respond if we put these set of questions to you, and perhaps some others to you in a letter?

DR. GEARHART: Absolutely.

CHAIRMAN KASS: I think the committee would be very grateful for your help in thinking through the regulatory questions, which are at the moment not what we have here.

DR. GEARHART: Absolutely.

CHAIRMAN KASS: I just want to thank you very, very much, for an instructive morning, and also for the wonderful spirit in which you presented your remarks and engaged the questions. I am very grateful to you for coming.

We are running about 15 minutes behind, and we will reconvene at a quarter-of. We have an hour-and-a-half for the second session this morning as originally planned.

(Whereupon, at 10:33 a.m., the council was recessed and resumed at 10:49 a.m.)

SESSION 2: STEM CELLS 2: MEDICAL PROMISE OF ADULT STEM CELL RESEARCH (PRESENT AND PROJECTED)

CHAIRMAN KASS: Would the members please rejoin the meeting. While we are waiting in the hope that our straggling colleagues will arrive, a couple of matters of business.

If anyone has not turned in a request for a box lunch, please do so now, and that should be in front of you. We will have lunch in the room just down the hall where we gathered before.

The photographer who has been around here is doing individual photographs for the commission and he will want to take individual photos of members, and we can do that in connection with lunch.

And you will also have in front of you in addition to the materials that Dr. Gearhart provided us, which by the way is — and the lights were out and so you couldn't see, but one could recapitulate his talk with the help of the figures here, as well as checking his article in Nature.

But you also have in front of you a revised version of Bill Hurlbut's memorandum. This has been updated and corrected, and he would like us to substitute it for the one that was sent around earlier this week. Is that correct, Bill?

DR. HURLBUT: Yes.

CHAIRMAN KASS: All right. Well, again, it is a great pleasure to welcome Dr. Catherine Verfaillie, from the University of Minnesota. You have her curriculum vitae in the briefing book, which you can consult.

I won't waste any more of her time by reading from it, and just simply allow her to help educate us on the prospects of present and projected of adult stem cells for regenerative medicine.

DR. VERFAILLIE: Good morning. I would also like to start out and thank Dr. Kass and the council to allow me to present this information on new findings in adult stem cell biology which have been received with great excitement, and correctly so. If they are, and they are actually set upside down, the classical paradigms of biology, and so to be able to do that you have to have full proof to actually be able to be in a position like that.

If they are, and they are actually set upside down, the classical paradigms of biology, and so to be able to do that you have to have full proof to actually be able to be in a position like that.

As Dr. Gearhart already gave in his previous eloquent description of what stem cells are and what
they can do, and we will get back to that to some extent at the end, although we are far away from actually being able to use adult stem cells for clinical applications.

But what I would like to do is give you an overview of the greater potential of adult stem cells, which has always been termed adult stem cell plasticity, and what we do know and what we don't know.

And where this may actually lead us. Dr. Gearhart also indicated that embryonic stem cells in humans are fairly or very much in their infancy, the same as we are for adult stem cell biology, too, and so I don’t think we are anywhere close to be able to come up with new therapies at this point in time.

I would also like to reiterate that even though my laboratory and our group works on adult stem cells, we have actually actively pursued investigators in embryonic stem cell research, human embryonic stem cells, just so that within the same institution we would have laboratories that have one cell, and other laboratories that have the other cell, so we would be in a position to compare and contrast the potential of the different cell populations, and I think that is very important.

With that, I will actually start my presentation, and I will point out that the work was mainly funded through the NIH, since it is all adult stems that we are working on, and not embryonic stems. And also a number of foundations and one pharmaceutical company.

Dr. Gearhart already gave you an overview of where embryonic stem cells come from, and where primordial germ cells or stems come from. And I am going to reiterate that for you.

I just put up this cartoon that Dr. Weissman published two years ago in Science to point out a couple of things. During development, cells in the inner cell mass make sequential decisions, and each of these decisions is actually accompanied with gain of function, but also loss of function.

The gain of function is that the cells learn how to become a more specified cell type; and on the other hand, actually lose the potential to become other cell types.

And so the decision to be made is somatic or germ cell, and within the somatic lineage doing something that is called gastrulation, cells decide to become the different parts of our body, whether it is endoderm, which is the internal organs, mesoderm, which are limbs and soft tissue, and ectoderm, which really comprise the skin, the central and peripheral nervous system.

And within each of these groups cells again make decisions and learn how to become stem cells for specific organs. And the stem cells for specific organs that has been most well studied is actually the hematopoietic stem cell, which is currently extensively being used in clinical applications for bone marrow transplantations or peripheral blood stem cell transplantations, or cord blood transplantations.

And so that actually has set the paradigm on how we decide what stem cells are. Aside from hematopoietic stem cells or blood stem cells, we have a number of investigators who have identified tissue-specific stem cells in a number of different organs, including for instance the brain, which we until about 10 or 20 years ago thought was a final product when we were born.

But it is now clear that there are stem cells in the brain that can recreate neurons and other components. There is also stem cells in the liver, and stem cells in the gut, and there is stem cells in the skin, and so forth.

The reason why I put this slide up is actually to point out that these arrows have always gone down, and so we have always thought that each time a cell decided to learn something new that it lost the capability of doing something else.

And so if we envisioned beforehand that the arrows would be reversed, we thought that was possible, but we associated that with classical transformation, or actually cancer-forming cells.

So what do we know about hematopoietic stem cells and that is really the paradigm to which I am going to try to talk through the whole field of adult stem cells.

In hematopoietic stem cells, we can actually take a single mouse bone marrow cell that we characterize by proteins on the cell surface, and take that single cell, and for instance you can take it from a mouse that is engineered to fluoresce green under a specific light, and put that in a regular mouse, and ask whether they can reconstitute the blood elements of that animal.

And a number of investigators have actually been able to do that. You can take a single cell, and give it to a mouse that was lethally irradiated so it has no blood, and this cell can recreate the red cells,
the white cells, platelets, lymphocytes, for the lifetime of that animal.

And that is really the proof that you have a stem cell that can self-renew, and a single cell can make multiple different things, and it can repopulate functionally the organ that it needs to repopulate.

And so that is really the criteria that we have to hold ourselves to, to actually talk about stem cells, and if you talk about plasticity, you will have to hold us on the same criteria and showing that a single cell can now make two tissues, and that this cell can make two tissues from a single cell, and that these new cells can repopulate a tissue functionally in vitro.

Now, over the last 5 or 6 years, there has been an enormous number — well, not an enormous number, but probably 40 or 50 papers now that have come out in the scientific publications that have used the word adult stem cell plasticity.

And what is meant by that is that you take a cell that was supposed to be a one cell type. For instance, you take a bone marrow cell, or you take cells that are enriched for hematopoietic stem cells.

And it appears that some of these cells may acquire characteristics of cells outside of the organ where they came from. And so it has been shown for bone marrow cells, or cells enriched for hematopoietic cells, that if you transplant these into an animal that was irradiated, and you look in tissues outside of the blood, that you can actually find, for instance, skeletal-muscle cells, heart muscle cells, or endothelial cells, that are now derived from this donor hematopoietic cell.

There is also papers that have shown that if you take muscle from an animal and mix it up in the laboratory, and culture it for a few days, and then use the muscle tissue to give back to an animal, that you could reconstitute the blood system in that animal.

Now, if you think in anatomical terms, this is still within one of the three categories that I gave you at the beginning; mesoderm, endoderm, and ectoderm, and all of this is still within the mesoderm. So this is maybe not so hard to understand.

However, there is also papers that two different cells from bone marrow, hematopoietic cells, and zymogenic cells, which are cells that make bone and cartilage, can give rise to cells that appear to have neuronal characteristics, both neurons and glial cells, that support the structure of the brain.

And there is a number of studies that have shown that bone marrow cells can contribute to liver, skin, lung, gut, and so forth, and so you can pretty much put arrows in whichever way you want.

You know, people have published data that suggests that indeed this may be possible. So obviously this goes against our paradigms and this would say that either something strange is going on, and just something in the last few years is something that we have actually identified.

Now, if we want to talk about blastocyst, I started out with the paradigm of stem cells, and so there is multiple different possibilities here.

Either the bone marrow, which seems to be the organ that harbors the most of these cells, harbors many, many different stem cells, and it harbors the hematopoietic stem cells, but it also harbors the neuro stem cell, and the liver stem cell, and so forth.

And which that would not be bad, but that truly would not be a single stem cell that could be expanded and used to actually transplant patients with all kinds of different organ diseases.

A second possibility is that somehow the cell can be "de-differentiated" and redifferentiated, depending on the environment that it is put in, and that the hematopoietic stem cell can learn how to become a liver if you put it in the liver, or it can learn how to become a brain if you put it in the brain.

Or it could be that it is a remnant of embryonic stem cells or the primordial germ cells that you heard about from Dr. Gearhart that are left around in the body, and that under specific circumstances can be reactivated and contribute to tissues.

And the issue of fusion has been brought up because of the two papers recently in Nature, and the possibility is in theory that what we see is actually that.

For instance, a hematopoietic stem cell fuses with a liver cell, and now you actually have something that is a hybrid, but it has actually liver characteristics.
The other questions that I am going to try to address, and I don't have all the answers for this, is this actually clinically relevant? You know, if you transplant bone marrow into a patient and you find two liver cells that are derived from the patient, from the donor, it doesn't necessarily mean that that is going to help anybody down the line.

So the graft has to be robust and persistent, and there has to really be proved that we don’t just see cells that look like a tissue that they end up in, but they also have to function like a tissue that they end up in.

And then the question that I will bring back up at the end, the first question, what is plasticity, and will that matter from a clinical standpoint?

And so we started out in this field — I am a hematologist, and I do bone marrow transplantation as my clinical profession, and I have been interested in hematopoietic stems in the bone marrow.

And about six years ago somebody in our group asked me whether we could grow mesenchymal stem cells, which are cells that may grow on cartilage, to treat children with a specific genetic disease called Hurler’s disease.

And when we did this, mesenchymal stems we happened to find, and we went about trying to create these to be in compliance with GMP qualifications, meaning we were trying to remove all sera out of the system, and yet we were trying to use very well defined culture systems.

And so while we were doing this, we came up with a cell that you have heard Dr. Kass refer to as a multi-potent adult progenitor cell, because we don’t have a much better word for it.

And it will be appreciated as MAPC, and which appears to have a much greater possibilities than the mesenchymal stem cell possibilities. So we take these cells from bone marrow from humans, and we can also take them from mice and from rats.

And you place these in a culture system that is very well defined, and ingredients, and growth factors, and no serum, and low density, and we expand the cells as much as we can by splitting the cultures on a regular basis.

And if we do this, we have actually found that these cells appear to have an enormous growth potential. And so here on the left-hand side would be bone marrow from an individual, and we start with about 10cc's or a spoon of bone marrow, deplete all the blood elements from the bone marrow, and put it in a culture dish, and then grow the cells for long periods of time.

Classical adult cells would actually not expand much more than 50 times or 60 cell population doublings, just because we have a clock inside the cell that actually causes the cells to become senescent or old once they go beyond a certain number of cell divisions.

And so in the human system, as well as in the mouse and the rat system, we have been able to show that we can create or grow cells that do not seem to conform to this internal aging clock.

And the cells can go beyond that and the human cells are now close to a hundred population doublings, and in mouse and rat, over 150 population doublings.

If you look at the aging clock itself, which are the telomeres, the telomeres are long and they do not seem to shorten in culture, which goes again with the idea that the cells do not senesce in culture.

So in this respect, they have characteristics that are similar to what you would find in embryonic stem cells, but also this internal clock is actually not working.

The phenotype of the cell is strange, and it doesn't really fit anything in particular, but there is definitely no characteristics in these cells.

These cells are blood hematopoietic stem cells, and I am not going to go through all the details here, but if you do an extensive phenotype characterization of the cells, they don't look like blood.

They have some characteristics of embryonic stem cells, but there are a lot of other ones that they do not have. So they have some genes that are turned on that are present also in embryonic stem cells, which are the top two here, and then they have on the cell surface antigens that you really only find on embryonic stem cells, or primordial germ cells.

So in some respects again these cells have some features of embryonic stem cells, even though we got these from the bone marrow of humans, mice, and rats.
We then started trying to test initially all in culture dishes what these cells could do, and we asked whether they could differentiate in multiple different cell types.

And because our initial charge was actually to try to grow mesenchymal cells and make bone and cartilage, that is what we did first. And so what we showed in the culture dish is that if we switch the culture conditions around, and actually use ingredients that are no longer supported for maintaining the stem cells in an undifferentiated state, by actually switch them such that we hope that we can turn on the genetic programs to make bone or cartilage, and so forth, we could indeed do this.

And this is no different than the classical mesenchymal stems that have been described. So we can induce the cells to become bone, and if we say that they differentiated into bone tissue, it is actually a calcified tissue at the bottom of a dish.

We can induce the cells to become cartilage that looks like articular cartilage, even though it isn’t very well organized. And you can induce the cells to become lipid-laden lipocytes, and we can induce them to become skeletal muscle cells.

And these cells can actually fuse and make long muscle tubes almost, and we can induce the cells to express a number of muscle markers for the heart, even though we haven’t really seen beating cells.

And so we don’t really know whether these cells are heart muscle cells. So this is still not that strange, because there is this cell in the bone marrow that has been identified that can do this.

Now, we found three other lineages that are completely outside of the mesenchymal lineage, and some of this has been published, and most of it is actually in press currently.

One of the things that we found is that these cells can differentiate into cells that line blood vessels, which we call endothelial cells. And we have been able to show that these cells differentiate into cells that look like endothelial cells, but also function as endothelial cells.

And as shown in this picture here is actually a blood vessel from an animal that had a tumor underneath the skin, and we actually infused human endothelial cells derived from human MAPCs in this animal, and showed that these endothelial cells seek out the tumor and actually help create new blood vessels in the tumor, which the tumor needs otherwise it can’t grow.

And so this proves that these cells that are in the bone marrow can differentiate into cells that can make endothelium. More surprisingly is that the cells can differentiate into cells that look like neurons, look like astrocytes, and support themselves in the brain, and to some extent function like these cells in the brain.

And so we show here that they differentiated into cells that look like neurons and have electrophysiological characteristics like neurons.

And so this is the second major layer of the embryo, and then we also have been able to show that we can make these cells differentiate into cells that look like liver cells, and actually function like liver cells in a culture dish.

And so this would mean that this cell population, these MAPC cells, can actually differentiate into all of the major components of a human being, even though we only show a few cell lineages here.

I am not going to go through this in too much detail because it is highly technical, but essentially we have not been able to use genetic marking to prove that this could all be derived from a single cell, and we don’t depend on population of cells.

So this fulfills two of the criteria of a stem cell. A single cell can differentiate and grow for long periods of time, and can differentiate into multiple different tissue cells.

Two more sets of experiments were done to try to gauge the potential of these cells. The first one was done in an chimeric animal model, in which we took the adult cells, and injected even a single adult cell into the blastocyst of a mouse and asked what would happen in this mouse, and whether we would see contribution to some tissues, no tissues, or all tissues.

So we injected a single cell or we injected 10 to 12 cells, and shown here are two animals. The top one is obviously and the donor cells here have a gene that if you stain it correctly the cells turn blue.

So what we did is we let the animals get born, and we looked at the animals by genetic tools to try to figure out if there were donor cells in multiple different organs.
And we also then took the mouse and actually cut a thin slice through the middle of the animal and asked which organs would have blue cells contributing to the mouse.

The top mouse is an animal that if you looked in the tail by genetic tools that we couldn't find any donor cells, and the bottom mouse here, this is its head, and over here would be his tail, and you can see the spine, and the brain, and all the internal organs.

And you can see that the majority of all the tissues of this animal actually appear to be derived from a single blue adult cell that we have put into the blastocyst.

The efficiency isn't a hundred percent, and this is shown on the bottom here, and so if you look over here, and if you put in one cell per blastocyst, 60 percent of the animals will not be chimeric, but 30 percent or 40 percent of the animals will be chimeric to varying degrees.

If you increase the cell number the chimericism goes up. So this is probably not quite as good as embryonic stem cells, but it is a fairly significant degree of chimericism, and actually the frequency appears to be one in three cells.

So this would suggest that the cells can probably make under the right circumstances more cell types than we have been able to prove in a culture dish.

We can also ask if we now take these stem cells and give them to a mouse that is born, and we give here again cells from the donors' mouse, which again are blue, and we gave these to an animal that was either not irradiated or irradiated with a small amount of radiation therapy in the hope that maybe that would help the cells engraft.

We used an immune-deficient recipient mouse, just because we were worried that the new genes that are in the blue mouse might actually be a basis for rejection. So we don't know what would happen in a non-immunodeficient mouse.

If we do this, what we found is that we do find engraftment in some tissues, but not all. So, for instance, in the top panel, we see that there is engraftment between 3 and 9 percent in the hematopoietic system of this mouse, and we can find the cells, and the blood we can find in the bone marrow, and we can bind them in the spleen.

And if we look in these animals, we can also find over here, and what we did is we actually — the blue color, we used an antibody that is now green, and co-labeled it with a red stain that stains the specific tissue.

And you can see in the liver that there is areas in the liver where donor cells appear to be present. And there is areas in the guts, in the villae of the gut, where donor cells appear to be present.

And there is areas in the lung where donor cells appear to be present. The presence of these cells can be seen anywhere from four weeks after transplantation, all the way to 24 weeks, which is about six months, and the unfortunate thing with the mouse model that we use is that these mice usually die from lymphomas at an early age because of the deficiency that they have.

So we really have not been able to extend the cultures or have the mouse experiments beyond 6 months, and so we are actually trying to go further.

We transplant the cells in an animal that is 6 to 8 weeks old, and so it is not a very young mouse, and it is also not an old mouse. What we showed is that if you damage certain tissues like the hematopoietic system, and the gut system, that you have increased engraftment, which is consistent with the fact that these cells go to places where the repair might be needed.

However, we did not see in this mouse model engraftment in a number of other tissues, and mind you that we gave these cells IV to an intact mouse, which actually was not damaged in any way, shape, or form.

And we don't see engraftment in the heart, skeletal muscle, or brain, and these tissues do not proliferate. We also don't see engraftment in the skin and the kidney, and so these organs we didn't really see very much engraftment.

However, if you infused the cells directly in the muscle, which causes damage, and actually done the cells in response to the local cues within the muscle, appear to be able to differentiate into muscle cells.

So it appears that these cells have the ability and blastocyst experiment to give rise to many, many
different tissue types, if given post-natally, and we gave them as stem cells, not as differentiated cells.

They appear to be able to respond at least in some respects to cues that are present in certain organs to differentiate into the cell type that is specific for that organ.

We have looked carefully at the cells in culture and we do not see a significant number of gross genetic abnormalities. We have not looked with a very fine-toothed comb through whether there might be some minor genetic abnormalities over time and culture, and these studies are ongoing.

If we infused the MAPCs in animals, we really do not see any tumors, and so far we have not seen that there are tumors that Dr. Gearhart talked about, and we also have not seen any other tumors.

Obviously if these cells come from bone marrow there is lots of precedent on bone marrow transplantations, where actually if you do this, actually you do not cause tumors in patients.

So MAPC that we have identified in our laboratory seems to be a cell that is not senescing and that can be found in adult tissues of humans, as well as mouse and rats, and they seem to be capable of giving rise to cells from the three germ layers, and it can engraft in vitro in a limited number of tissues.

Now, what I cannot tell is whether these cells actually exist as such in a person, in a mouse, or in a rat, or whether our culture condition is actually such that it, quote, reprograms or dedifferentiates the cells that we take out of the animal, and that then acquire this much more greater potential, and I will come back to that in just one second.

So we now go back to my initial definition of what is plasticity, which is really at the bottom of all of the adult stem cell excitement. I mentioned initially that we would have to show that this is a single cell of a rat, and I think the majority of papers so far published have actually really not been able to prove that a single cell could, for instance, give rise to blood and muscle.

In vitro, we have evidence for that, and in the blastocyst injection, we took a single cell and actually found multiple different tissues. You could ask, well, does it matter?

Does it matter if there are multiple different cell types in the bone marrow, and I think ultimately from an FDA or regulatory standpoint, it will matter, and we will have to be able to say exactly what cells that we are using to be able to acquire a certain function in vitro, and so I think that will be important.

The second question is, is the differentiation or is the remnant ES, and again you could say, well, it probably doesn’t matter. But I think at this point in time, I don’t think anybody in this field knows whether these are left-over early stem cells like ES cells, or whether these cells are cells that can be reprogrammed, and redifferentiated, and dedifferentiated under certain circumstances.

Now, does it matter? Well, you heard from Dr. Gearhart that embryonic stem cells as such, and not necessarily the differentiated progeny, it will matter, and we will have to be able to say exactly what cells that we are using to be able to acquire a certain function in vitro, and so I think that will be important.

If it is dedifferentiation, it means that you reprogram or you change the genetic material in a cell. But if you do that, currently we have no proof that we actually change something and actually cause an oncogene or something like that to be activated, but that is definitely within the possibilities, and that definitely needs to be looked at carefully.

Is it fusion? All the in vitro work that has been published, including the data that I have shown to you today, I couldn’t prove beyond any doubt that that is not based on fusion.

Our in vitro data, we have never co-cultured things with anything. So we have single cells that are deployed that can do multiple different things, and so we can’t really ascribe that to fusion.

However, in vitro, I couldn’t prove it to you today, and we are doing studies to try to address this. I think that fusion might be the reason why some studies in which a lot of pressure has been put on to the system, which is essentially what those two papers had to do in vitro.

So we have a lot of pressure exerted to have that one cell survive after it fuses, and that is a possibility. Also, single cells that are found, rather than whole colonies, may also be the result of fusion, more so than experiments where you see huge colonies arise in an in vivo model.
And so I think we currently cannot exclude the possibility that some of the data is as a result of fusion. Some would say does it matter, and I think it matters a whole lot, even though some investigators say, well, if you fuse the cells and it functions properly, it probably doesn’t matter. But I think ultimately that we do need to make sure that we understand the whole mechanism underlying everything. And is all this plasticity clinically relevant?

And so the majority of studies published to date have actually shown the very low numbers of tissue differentiated cells can be found in multiple different tissues. A number of papers have been published, two in particular. The paper by Lagasse, et al., where they show that they could rescue an animal with liver failure by bone marrow transplantation, but they have significant degrees of engraftment. So that definitely was up to 80 or 90 percent of the liver could be replaced by bone marrow cells. And a paper by Don Orlic showing that if they injected stem cells into the heart that was infarcted that a significant amount of donor cells would be found in the heart. And in the data that I have shown you, that we have up to 5 to 9 percent of the differentiated tissue that seems to be derived from the graft. However, the majority of studies again haven’t really addressed the other question in plasticity, meaning is it in vitro functional differentiation?

And there is really only a single study that has been able to show that, and it is again the same study by Lagasse, et al., who showed that if you did bone marrow transplantation in an animal that had a failing liver, you could rescue the animal and take it off the drugs that kept it alive. Some studies have shown that there is functional improvement, although the mechanism for the functional improvement isn’t completely known, and that is to some extent similar to what you heard from Dr. Gearhart. And so there is a number of studies who have injected cells in adults in organs and have shown, for instance, that there was improvement in the neuronal function, and that there was improvement in heart function, although there is no proof that the cells, per se, were actually responsible for doing this. And the question will be is this acceptable from a clinical standpoint, and if you show only functional improvement without knowing the mechanism for knowing why we see functional improvement, and in the long term, again, that is not a tenable situation, and we really have to dig into this much further.

So what can adult stem cells be used for? Well, I think like embryonic stem cells, or primordial germ cells as you heard from Dr. Gearhart, the cells are good tools to study five basic principles in biology. And we can study self-renewal, and we can study differentiation and redifferentiation if that is indeed the case, and learn what the implications for that are. And actually try to understand how organs are being created, and what the genetic programs are that you need to turn on. The cells, like other stem cell populations, could be used for drug discovery, for drug toxicity screening. Adult stem cells could be used as systemic therapies, and currently systemic therapies are done with adult stem cells. Bone marrow transplantation is done every day in many, many institutions around the world, and so we can infuse these cells if we do not think that they make tumors. So since adult stem cells don’t seem to have that as their side effect, theoretically, we could genetically correct cells for patients who have deficiencies of certain enzymes. And the disease, and Hurler's disease would be one example, and a second possibility would be, for instance, in hemophilia, where you need to have a cell that produces clotting factors.

Or other congenital diseases, like Alpha-1-Antitrypsin deficiency, or it could be used for systemic cell therapy, which you would have to treat in many, many different places in the human being. For instance, muscular dystrophy. So if you had a stem cell that was able to engraft in most muscles, and you could genetically correct it, you could correct that disease in patients with that disease.
Systemic cell therapy may be more complicated with cells that have the inherent capability of making teratomas just because you would always run the risk that teratomas might show up.

And then again if this field progresses further, the same diseases that has been quoted for embryonic stem cell therapies would also be on the list here, and if indeed the cells can differentiate into functional neuron cells, they could be used to treat Parkinson’s disease and many other ones.

And since the cells can appear to be able to differentiate into functional liver cells, they could be used either in vivo to replace the liver, but also would be very useful to make bioartificial livers, for instance.

We have shown, and others have shown, that cells from bone marrow can contribute to new blood vessels, and so this could be harnessed to create new blood vessels in vivo, or actually the opposite; lower these cells with anti-cancer agents, and actually use them in a anti-angiogenesis approach for treatment of cancer, and then many other diseases.

Again, we are not anywhere close to being able to do this in any way, shape, or form, and a lot of basic research still needs to go on.

So the first point that was on my previous slide, we really need to spend a lot of time in trying to understand what these cells are and aren’t.

And at the same time, start thinking about how we might be able to scale these up under GMP conditions that conform with regulatory agencies, and we will have to ask the question, as with any other stem cell population, whether we will use the cells as stem cells, or as more mature cells that have been educated to some extent to become the final product are totally mature cells.

And then again perform large scale culture systems or develop large scale culture systems. And then the last question is whether we should use these cells in an autologous setting or in an allogeneic setting.

Obviously adult stem cells for a number of diseases could be used in an autologous setting. However, if they were to be capable of repairing hearts, and you have a heart infarct today, we would not have adult stem cells sitting around instead of your own to treat you at that moment in time.

So I think there are some issues, and Dr. Gearhart also brought up the idea that with diabetes, for instance, in Type-1, is an immune problem, and again autologous transplantation may not be the way to go.

I think that for adult stem cells, the initial trials may well be autologous, but that in the long term, to make it more cost effective and more available to many patients with certain frequent diseases, that it might have to be an allogeneic therapy, and then we are actually faced with the same questions that investigators that work with ES cells, and primordial germ cells are faced with. I think I will stop there. Thank you.

(Appause.)

**CHAIRMAN KASS:** Thank you very much, Dr. Verfaillie, for a clear, lucid, orderly presentation, and it is very helpful to us. The floor is open for questions, comments, discussion. Elizabeth Blackburn, please.

**DR. BLACKBURN:** Thank you. Could I just ask a couple of quick clarifications. Dr. Gearhart mentioned in response to Bill Hurlbut’s question the difference between fetally derived human cells and mouse embryonic stem cells with respect to their teratoma producing properties.

And I could not quite gather whether it is human embryonic stem cells that are also known to have any teratoma producing properties. Could you clarify that for me, because you also had mentioned this, and I wasn’t sure if you were referring to the mouse embryonic stem cell work or the human.

**DR. VERFAILLIE:** If you use either mouse or human embryonic stem cells without predifferentiating them into a committed progenitor cell, and you use the stem cells as such, they will form teratomas, because it is one of the tools that investigators use that an embryonic stem cell has that capability. So they will form teratomas.

**DR. BLACKBURN:** And then post-differentiation?

**DR. VERFAILLIE:** I think there is very little data on the human embryonic stem cells, post-differentiation in vivo, and whether there is still the tendency for these cells to make teratomas.
**DR. BLACKBURN:** And the second question, since I promised that I would ask you about, is the fusion issue, and which of course you have raised in your talk as well, but again a question of clarification for me, and maybe expanding on your point that you said, well, fusions are going to be problematic.

I mean, the thing that immediately occurred to me was that these fusions, as reported from the in vitro culture, and I believe from engraftment into mice, that they showed aneuploidy, which of course anybody being a hallmark of tumor cells.

So I wondered if those issues and perhaps others were things you could tell us a bit more about when you mentioned that you had concerns about the fusions.

**DR. VERFAILLIE:** Well, I think it is something that because of the papers that were published that elegantly showed that if you took a somatic cell, an adult hematopoietic stem cell or brain stem cell, and co-cultured it with embryonic stem cells, and then put quite a bit of selectable pressure on the system in the culture dish, they proved that an embryonic stem cell quality could be transferred to the blood brain stem cell.

And initially they interpreted this as being reprogramming of the cell. But then it turned out that there were four sets of chromosomes, and that the cells fused.

And they took these fused cells and gave them to — injected them into a blastocyst as hyperdiploid as cells with four sets of chromosomes. One group was not able to create chimeric animals, and the second group, under the direction of Dr. Austin Smith, were able to create chimeras in the mice that were what he calls unbalanced, meaning that he saw a contribution to tissues, and that four sets of chromosomes are actually tolerated.

For instance, the liver, where at least 50 percent of the cells, actually half, have two nuclei. So I think that currently no investigator who has worked with adult stem cells has set up the right experiment to actually be able to disprove that it isn’t fusion.

I would argue that the data that I showed today in vitro, where single cells make three layers of the embryo, and these were euploid cells, meaning that they had a normal set of chromosomes, and which done in human, mouse, and rat, at the single cell level, we can make the three major layers of the embryo.

So that would go against the argument that at least in vitro, that all of it is caused by fusion. In vivo, in our blastocyst experiments, 1 in 3 cells could do it, which is much higher than the one in a million cells that were quoted in the two papers that were in Nature, but which indicated that one bone marrow cell out of a million could actually make a fused cell population.

And I think one in 50,000 neural stem cells could actually cause fusion. So that was a very rare event; whereas, our events are higher. We are in the process of actually going back to these animals — that we have cryopreserved, to try to identify that since some of the transplants were done female into male, we should be able to prove that we do not find the y chromosome in the engrafted areas and in the chimeric areas, which would get at the question whether it is caused by fusion.

And so I think we really need to set up experiments where we have generic markers on both sides, meaning the donor and the recipient, so that we can prove beyond any doubt that the in vivo results would be the results from a fusion.

**DR. BLACKBURN:** Yes, I totally agreement with that. I think the in vitro, and I am very impressed by the in vitro results, and as you said, there are questions in vivo.

I think in-part my question was addressing this issue, and I was asking about the tumor forming ability or otherwise, because it was not exactly 4N. It was the median number of chromosomes was different from simply 4N, suggesting that there was aneuploidy, and for example, one might not find Y chromosomes, for example, because those had been selectively lost.

So one would probably have to do much more extensive genome-wide analysis of both of those to be sure that there wasn’t some genetic contribution from the recipient cells.

But I certainly am very impressed as you say with the in vitro results, and they seem quite unequivocal, and I guess which is the question that you are addressing, and we will find out as the in vitro —

**DR. VERFAILLIE:** Yes, and I think we need to set up the experiments where we have on multiple
chromosomes genetic markers. You know, sequences that we can distinguish the donor and recipient between. So these experiments need to be repeated.


DR. ROWLEY: Well, I would like to ask a question that will include both Elizabeth, as well as Catherine, because I was struck in the data that you presented on your human cell lines that you had passed for more than a hundred generations, that telomerase was still active.

And I just am curious about that, because many of us do believe that that is, if you will, the internal clock that limits the number of doublings that those particular cells can undergo.

And you derive these from adults, presumably young adults in human, but at least adults, and I am curious as to what you thought about the mechanism of preserving the telomerase activity, and maybe if Liz would have any further comments on that, because again one of the critical features and potential limitations of adult stem cells is the fact that they would have potentially fewer doublings than would those derived from embryos.

CHAIRMAN KASS: Could I ask as a favor to the non-scientists in the group if someone would just give an ABCs on the telomerase matter, and just very, very briefly, so that everybody can understand what the discussion is about. Elizabeth, or Dr. Verfaillie, if you could just give the barest —

DR. BLACKBURN: I am the worst person, because I will fall into expert jargonese and so I will try not to. So, telomerase keeps the DNA at the ends of chromosomes replenished, and such replenishment is necessary, because each time one of our cells divides, the DNA at the end of the chromosome is a little bit whittled away.

So, telomerase keeps putting back a little extra DNA on to the ends of the chromosomes each time on average a cell divides. So the issue that Catherine pointed out in her talk was that if you don’t have telomerase after a number of cell multiplications, that whittling away process would have gone too far, and that sends a signal to cells to cease dividing.

And so many, many normal cells in culture are characterized by the inability to keep on multiplying. Did that clarify the question? So many cells do not keep multiplying because they turn the cells’ telomerase off as part of their natural differentiated state.

Cancer cells, on the other hand, have telomerase, almost in a great majority of the cases, and very up-regulated, and cells of the hematopoietic system — and I will defer to Catherine on this — have an interesting intermediate situation, where they have regulated telomerase activity that is turned on in a natural and regulated way as the cells multiply in response to signals in the body. Is that fair to say?

DR. ROWLEY: Yes.

DR. BLACKBURN: So I think it is a very interesting question of why telomerases is turned on in those cells that are multiplying so well in culture, and has there been a selective event that has allowed those cells, that for some reason have turned their telomerases on in the culture conditions.

But those are the cells that are outgrowing perhaps others in the population, and perhaps that question might be answered by what is the clonal efficiency with which you get these lines growing out. You may already know this.

DR. ROWLEY: But can I intervene, because you assured that it was often turned on, and maybe these cells are identified because they never turned telomerases off.

DR. BLACKBURN: Yes, and I don’t know if that is the typical situation when one puts cells into culture, and I thought that they more often would turn off and an earlier subset would keep multiplying, and again I want you to correct me on that cell growth phenomenon.

CHAIRMAN KASS: Thank you.

DR. VERFAILLIE: So currently we do not know whether it is often turned back on in culture. If we look at the cultures, for the first 40 population doublings, the cells appear to grow slightly faster.

And then a second wave of cells grows out and it grows slightly slower. So initially we thought that maybe the more classical senescing cells were disappearing, and that those were the cells that were growing faster, and the you then select for the cell that has inherent — you know, has the system turned on to not be subject to the clock of aging.
The frequency with which we can grow out the cells from human bone marrow is we believe one in a million bone marrow cells. So it is a very rare event, and so it will be quite difficult to actually specifically ask whether it is turned on and then back off, or turned off and then back on, unless we can actually do some genetic trapping experiments to try to ask the question.

DR. BLACKBURN: I’m thinking of David Beaches’ experiments in which he was able to show that cells would spontaneously, if you keep them in culture, turn their telomerases back on, because that gives them some selective advantage.

DR. VERFAILLIE: Right.

DR. BLACKBURN: And so I was wondering if such selected advantages occur in your situation?

DR. VERFAILLIE: It could well be, and so the culture conditions are very particular, and so I didn’t go into too much detail.

But if you do anything wrong to the culture conditions, we cannot create the cell lines, and so it might well be that it is what we call in my lab a cultural artifact what we see, which would mean that these cells may not exist really as such, but actually are induced to become this long-term proliferating cell by the culture conditions that we put them under.

DR. BLACKBURN: Thank you.

CHAIRMAN KASS: Janet, again, please.

DR. ROWLEY: I have two more questions. One is a follow-up of a question that I asked you about a year-and-a-half ago, on whether out of your MAPC cells you can get hematopoietic tissue.

DR. VERFAILLIE: Well, I think I showed you in vivo that if you infuse the cells into mice that were either not irradiated or sub-irradiated, that the cells appear to be able to differentiate into hematopoietic elements that have red cell, and granulocytic markers.

In vitro, we have had more difficulty to try to do that, even though it appears now that we can at least get for people who don’t understand this, but what would be yolk sac hematopoiesis, even though we haven’t really seen hematopoiesis that would occur in the embryo proper.

But we can find cells that look like the cells that have been created at the earlier stages of development, where the initial one is made, which is in the yolk sac.

DR. ROWLEY: And the other question is more a more practical question. I don’t know precisely how many cells would be required to treat an adult patient with a particular disease, and are the number of cells required, or what kind of limitations, using your system, would be faced if you have not one patient, but hundreds or thousands of patients that could benefit from a particular therapy? Is this really going to be an applicable strategy?

DR. VERFAILLIE: I think it is a bit too early currently to really be able to answer that question. We have been able to take cell populations and have them undergo 80 to a hundred population doublings, which is really if you were able to do that and not throw cells away along the way, it is 10 to the 50th cells or something like that.

So it is an enormous number of cells that you can in theory create. What I didn’t go into too much detail on is that the way that we have to grow these cells is under very low density conditions, meaning that the cells have to be far away from one another, or otherwise they do not maintain their undifferentiated state.

Which is quite different from embryonic stem cells, which tend to grow in tight clusters. From a bioengineering standpoint, meaning scaling it up to making hundreds of millions of cells, will be a major bioengineering question of how we can actually adjust the system to be able to do that.

But on theoretical grounds, you know, if you could overcome all the bioengineering problems, you should be able to create enough cells to treat multiple individuals, rather than a single individual at a time.

CHAIRMAN KASS: Question. Robert and then Mike.

PROF. GEORGE: Just a very quick question of clarification in response to Janet’s first point. On this question of whether they were — whether the telomerases were turned off and then turned
back on in the culture.

If it is not that, and if that's not what is happening, the other possibility is that they were never off to begin with?

**DR. VERFAILLIE:** Correct.

**CHAIRMAN KASS:** Mike Gazzaniga.

**DR. GAZZANIGA:** Again, thank you for a very excellent talk and a cautious talk I thought. I thought it would be helpful for us to understand the new pressures of a biologist like yourself, which are the following.

Here you have this fantastically interesting finding, and up until 5 or 10 years ago, the normal way that such things would be treated is you publish the work in peer review, and then you make the stuff, whether it is reagents, or whether it is cell lines available to others for reproducibility.

And that is a normal sequence of events that we are all familiar with. And now we have the bio-med inserting itself into these laboratories, where all of a sudden it becomes proprietary goods from this work.

When the original media picked up on your story, and I guess it was The New Scientist, there was this cryptic little paragraph in there about how they had seen the patent on some of this work, which is a very complete description, and how does that — what is going on here?

How can — and this is where I would like to go obviously, and obviously it is good for everybody here to get these cell lines that you have out to other labs, and reproducibility, and then the process goes forward.

Are you constrained in some way, and has life been made complicated because you didn’t have full public funding and you had to use this other money, or was that your own? What is going on?

**DR. VERFAILLIE:** So the work was really done at the university with NIH funds and university funds, and so there was really no private funds, except for the small amount from the company that was listed in the beginning, has gone into the work that we have done.

And because of the possible importance of the observation, the university, as well as myself, thought we should get some kind of protection, even though I am not sure that you can truly patent stem cells, because all of us have them.

But just such that we would be in a position to work with biotech companies to be able to produce large-scale numbers of cells and things like that, which is hard to be funded to known private funds.

So there is patents pending on the cell population. Currently, that really has not precluded us of collaborating with other institutions, or investigators within the same institution.

So they have collaborations with 10 or 15 different groups within the U.S., or outside of the U.S., depending upon the expertise that we need, to try to recreate the cells in other laboratories, and actually use their expertise, since I am a hematologist, and not a liver physician or a neuro scientist.

And to actually be able to use expertise in other people’s laboratories to move the research forward. So there are some minimal ties attached to working with the cells, but I think it isn't overcomeable, and it really has not been an issue with other academic investigators to collaborate with them.

And teaching people from those labs to come and to grow the cells, and at least start working with the cells. But it is a very complicated and it is a — and I have had myself a lot of problems in trying to find the right patent between potential biotech interests and academic interests.

**DR. GAZZANIGA:** Right, and you are not alone in that dilemma. So are there other MPAC lines at other institutions now that behave like yours, or is yours still the Golden Grail here?

**DR. VERFAILLIE:** We have given out the mouse, and to some extent, human MAPC lines to other investigators who are now setting the lines back up. We are also explaining and teaching people how to create them from beginning bone marrow.

And I know that there is one group in Japan who I think pretty much as the system set back up from human bone marrow. You know, they still need to do some additional studies to prove that it is really MAPCs, but we trained a person from there for 3 or 4 months in my lab, and they went back to
Japan, and were able to it appears to recreate them.

**CHAIRMAN KASS:** Could I ask a couple of sort of semi-scientific and semi-practical questions?
How hard is it — I mean, you have just indicated that not many people have already been able to do this, but how hard is it to find these cells?

And by which I mean two pieces, and in how many individuals in which you look for them can you find them? And how hard is it to find — how rare are they, and how hard is it to find in any particular individual?

Both of these questions bear upon at least a preliminary assessment of how useful this might be clinically speaking down the road, although things could change where you might be able to enhance the yield.

But could you give us a preliminary sense of this?

**DR. VERFAILLIE:** I think we have studied now between 70 and 80 normal humans to try to identify the cells. The age range, the youngest donor was two, and the oldest donor was 55. The majority are young adults who want some money to donate bone marrow at the universities.

**CHAIRMAN KASS:** The two-year old?

**DR. VERFAILLIE:** No, the 20 year olds. The 2 year old actually did a bone marrow donation for a sibling who needed a bone marrow transplantation. So we have been able to create the cells I would say in about 70 percent of the individuals that we have looked at.

Whether that means that the other 30 percent didn't have it, or there was some technical issue that came about, and we were not able to create them, we start out with 10 milliliters of bone marrow, and we would usually find a few clones that can actually grow out.

And so really the frequency is quite low, and it is one in a million, and that is at least the estimate that we have right now. But there is lots of bone marrow and so one in a million isn't an impossible task to do it.

**CHAIRMAN KASS:** And could I also follow up on the question of these cells and their promise, assuming the best, and the embryonic stem cells, assuming their best.

This is not a question of whether one should prefer one line of research or another, or whether we should now go ahead with them. But is there anything specific that you could imagine could not be done therapeutically with these MAPC cells that you would then need cells derived from embryonic tissue to do?

Or is this in the rosiest division, is this really a substitute, and one that might even have the rejection problem solved if I am dreaming?

And this is not a question about whether the other research should go forward, but really what is the best promise of this research so that at least we can think about it?

**DR. VERFAILLIE:** Well, I think that the data that we have in vitro suggests that we can create cells of the three germ layers of the embryo, and so theoretically, you could envision that you might be able to make more than we have done so far.

We have made liver-like cells, and brain-like cells, and epithelial cells, and we have not tried all the other ones. In vivo, the blastocyst experiment, unless that is a fusion event, and if it isn’t a fusion event, would indicate that the cells hold the inherent promise of making all the different cell types that make up the tissues, the somatic tissues of an animal.

So again that would suggest that is under — that if we changed culture conditions further that we might be able to, for instance, create insulin-producing beta cells, which we haven’t done, or create two heart muscle cells that function like heart muscle cells, and don’t just look like it.

So if all these promises hold true, and if we continue the cultures and they can be expanded even further into 80 or 90 population doublings, and so there are lots of ifs here, they may be able to be used to treat a large number of diseases.

The problem at this point in time is that there is so many ifs that it is a very difficult question to specifically answer.
CHAIRMAN KASS: Of course, and I appreciate that, and on the question of the longlivedness, or the half-life of these things, you have gone through — in vitro is what? It is what?

DR. VERFAILLIE: From 80 to 100 population doublings.

CHAIRMAN KASS: And it is obviously too early to say how much longer, and whether those conditions are matched in vivo. But when the people say that the promise in terms of longevity for cells derived from the adults is really much less, is there anything to be said on that question of the basis of knowledge now had?

DR. VERFAILLIE: Human embryonic stem cells have been kept in culture now for 350 or 400 population doublings. So that is 3 or 4 times as long as the adult cells. So we are striving to go there, but we just need time to do that.

Are these cells going to be able to do that? As far as we can tell, after 80 population doublings, there is no shortening of telomeres, and so that means that there is at least another 50 or 60 left.

If for some reason telomerase is shut off along the way for reasons that we currently don’t know why that might be, then the longevity would be less than what has been shown for embryonic stem cells.

Now, for classical adult stem cells, if you take hematopoietic stem cells that make blood, but not something else, they would not go for 80 population doublings.

So there is something special about these cells, that they can overcome this senescent block at 60 or 70 population doublings, which is actually long for any other adult stem cell.

CHAIRMAN KASS: Thank you very much. Questions or comments? Janet again, please.

DR. ROWLEY: Coming back again to partly the real world in this iffy situation, and it is a question of the practicality for treatment for particular individuals.

It seems to me that the notion that you might be able to derive these MAPC cells from an individual who had some medical problem might have some limitations because it probably takes 3 to 6 months, or so to get enough cells to then be able to use them therapeutically in that individual, and that is always assuming that the individual has some kind of a somatic disease, and not the basic underlying genetic problem.

So then the way to get around that if it really is 3 to 6 months, and you don’t have that window of time, would be to do somatic cell nuclear transplant. Now, have you ever tried that in your MAPC cells?

DR. VERFAILLIE: In collaboration with Dr. Jaenisch, and two weeks from now we will try the mouse MAPC cells in mouse eggs, and ask whether the efficiency of nuclear transfer would be closer to what you would see with embryonic stem cells, and where the efficiency is much, much, much higher than if you use a classical adult cell.

And that might improve efficiency of making cloned embryonic stem cells.

DR. ROWLEY: But I am thinking of the other experiment. You have a patient who is desperately ill, and so you would have cells from that patient, and you would want to use the nucleus of the patient’s cells into your MAPC cells, and so that is a different thing.

You have got these cell lines, and how can you make them more compatible with the patient, and agreeing that you can’t get rid of the mitochondrial problem unless you do additional manipulations and strategies.

But have you ever tried to replace the nucleus in your MAPC cell with a nucleus from an adult somatic cell?

DR. VERFAILLIE: No, we have not yet.

DR. ROWLEY: Do you plan to?

DR. VERFAILLIE: We might.

CHAIRMAN KASS: We could always get everyone at the age of 15 to put away a little bit of marrow for the time that we might need it.

DR. ROWLEY: Another reason to save cord blood.
CHAIRMAN KASS: This is your chance, council members. This is a wonderful opportunity. Questions?

DR. ROWLEY: Well, I would just be interested from Catherine's point of view on her answers to some of the questions, to the two questions that I posed at the end to John Gearhart, and again give her the option to do this as a written response rather than a direct response, but I think it may be easier to — and the second question, which may be very simple to answer in terms of the kinds of restrictions that you find now in funding.

And I would assume since you are dealing with adult cells that there aren't any, but I would be interested in your perspective on the funding, in both government and other agencies.

DR. VERFAILLIE: Well, currently for the work that is ongoing in my group, which works with adult stem cells, actually the amount of funding that has become available through the NIH has increased dramatically over the last few years to support this kind of research.

So that has not been a problem. I have wanted to compare these cells carefully with embryonic stem cells, and so we are in a position currently to do this in a mouse, but mice aren't humans.

And so we have really not been able to do that until earlier this year when human embryonic stem cell research was allowed in academic institutions under NIH funding.

And as I mentioned, we had actually gone out and tried to recruit an investigator with that kind of expertise to be in a position to try to address some of the questions that have come up here, and are these cells going to be equipotent.

And I think to date, even though they are exciting and they seem to be quite potent, I can't really say whether that is the case. And so ultimately we won't be able to answer this question until we can truly compare them and not across country borders, but actually within the same institution, where people can look at the two cell populations at the same time.

And so in that respect, I think that the lack of funding for embryonic stem cell research in humans has made it impossible up until just recently to be able to do that.

CHAIRMAN KASS: Michael Sandel.

PROF. SANDEL: I wonder if I could put to you the same question I put to the previous speaker. Given that some people regard embryonic stem cell research as morally problematic, what would you think of the idea of imposing a moratorium on embryonic stem cell research until we could assess what might be achieved by adult stem cell research?

DR. VERFAILLIE: I think that my answer is very much in line with what you heard from Dr. Gearhart. I think that the main reason why we — to investigate in the field of embryonic stem cell — human embryonic stem cell research is to be able to compare and contrast the two cell populations at the same time.

I also think that what we did in our culture dishes to try to differentiate these MAPCs into liver-like cells or neuronal-like cells is really based on what has been learned from mainly the mouse embryonic stem cell field, where investigators have been able to take these cells and drive them in vitro to become certain cell types, even though that is not a hundred percent fool-proof, and it is not completely figured out how you should do that.

So I think if you have a number of different cell populations at the same time, we try to test all these different questions. What we learned in adult cells might be applicable to embryonic stem cells if they are the cells that ultimately will be the suitable source for our clinical applications or the other way around.

And so I think stopping research in one field actually will slow down research in the other field, and it would be either way. In other words, if you stop our research in adult cells, or embryonic stems, as I think what can be learned in the two systems should be translatable in the other system.

And so I think if you were to ban all embryonic stem cell research, it would really slow down the insight that could be gained in adult stem cell research.

CHAIRMAN KASS: Rebecca Dresser.

PROF. DRESSER: This is unfair, but I am wondering if you had any ideas about the cost of such a
procedure? I mean, just based on what you have done in mice, and you mentioned at the very end that to be cost effective that you would probably would have to just have a number of cell lines and not rely on the patient cell.

Is this going to be a very, very expensive technology, and where we have to worry about — well, if all these ifs work out, will we have to worry about who has access, or will it be comparable to the stem cell transplants that we do now with bone marrow now? Or what do you think?

DR. VERFAILLIE: Well, I think it will be relatively expensive if you do it on a single person basis, and you will have to create the cell lines from the beginning, rather than go going to a frozen stock of cells, where you have a very well-qualified product to start with and where you expand cells.

And so you might even have already committed cells frozen as well, and so the cost to get to that point would have to be incurred once rather than doing this over, and over, and over again.

The costs I think — well, it is hard to say, because I am not sure how much of the regulatory issues we have actually complied by at this point in time to actually truly gauge how much it would cost.

But I think that by the time that you do all the quality control tests for infectious agents and things like that, that amounts to quite a bit of money for each cell line that you try to establish.

And in the long term I think it would probably be more cost effective if you would have a therapy for heart infarcts that you could go to a limited number of cell lines. And to put numbers of them, I don’t really know.

It would probably be in the range of a bone marrow transplantation currently, which is quite expensive. So it is anywhere between $50,000 and $200,000 per patient.

If you had qualified cells that were frozen, and then you could expand them for a short period of time and do a limited number of tests at the end, the amount of cost incurred would really be all up-front, and then there would be a relatively small amount per patient.

PROF. DRESSER: I guess the other thing is that bone marrow transplants work fairly well with some illnesses and not with others, and would you expect to see those kinds of results with these kinds of therapies?

DR. VERFAILLIE: I think that would highly depend on the type of disease that you tried to treat. You know, you are all well aware of the treatments that have been used for Parkinson’s disease, which the trials that were done in Sweden have made little complications.

But when this was extended in multiple hospitals in the West, there were a lot more complications if it was done on a larger scale. So I think that depending on the disease that you go after that it may work better or worse, and it is really too early to be able to comment on that.

CHAIRMAN KASS: Bill, do you have a question?

DR. HURLBUT: Well, if we have time, I would like to ask a couple of scientific questions if that is all right.

CHAIRMAN KASS: Please.

DR. HURLBUT: Do I understand this correctly that you are saying that your MAPC is put into the blastocyst to perform more cell lines than do other adult stem cells?

I thought that adult stem cells generally formed lines in a blastocyst?

DR. VERFAILLIE: There are 3 or 4 papers published on adult stem cells into blastocyst experiments. There is one paper published by a German group, where they took purified hematopoietic stem cells, and injected them into the blastocyst, and what they were able to show was that the cells gave rise to some hematopoietic elements, and that they actually recapitulated the developmental behavior of hemoglobin, which switched at different stages of development during embryos, fetuses, and then adults.

They did not see any contribution outside of the hematopoietic system. The second paper is a paper from a Swedish group, where they had taken neural stem cells that have been cultured, and introduced them in the blastocyst, and as far as I know, they have never had animals been born alive.

And they saw a contribution to a few tissues, but not all tissues of the mouse fetus. And in the last
papers, we did a paper by Austin Smith, the one that reported on fusion, where they had taken
defused cells and given them to a blastocyst again, and it showed a contribution in one animal that
was born, and that was really only a single animal, to the liver and a few other tissues.

But it was not quite the amount of contribution that I showed in the picture here, where every single
tissue of the mouse appeared to be having a fraction of the single MAPC cell.

**DR. HURLBUT:** That is very, very exciting. Another question that I think might be of good general
interest to our council, but the question of whether transdifferentiation is occurring, or even the
process of embryonic stem cells just differentiating, it is always clouded by the question of how do
you know when there is actual differentiation taking place?

In other words, just because you follow one or two gene expressions, you don’t know, and one of the
problems with embryonic stem cell therapies will be to get the target tissues up to speed, like beta
cells producing enough insulin.

I know that there are advances being made on this, but can you just give us a general description of
how you identify when you are satisfied that a tissue has in fact been produced?

And maybe tell us a little bit about the — maybe we need a little education on messenger RNA
assays.

**DR. VERFAILLIE:** Okay. The criteria to say that you produced tissue I think needs to include that
you turned on the genetic program that is compatible with the tissue that you want to produce.

You find therefore proteins from the genetic program in the cells, and the cells have morphological
changes consistent with the cells that you are looking for, and the cells have functional
characteristics of the tissue that you are looking for.

So what happens in a cell is that in an undifferentiated state a number of gene programs are shut
down, meaning there is no transcription to the messenger RNA, and you will find no protein, and
therefore no function.

During a differentiation process, you come in with a growth factor or a cytokine, or a stimulus from
the outside, and you trigger a certain set of signals that then open up a new genetic program and the
first thing that happens is that you transcribe messenger RNA, that then gets translated into proteins
and/or sugars, that then supposedly give a new function to the cell.

So what we have been looking for in vitro, and that is where most of our work has been done
initially, is actually taking an undifferentiated cell and showing that a certain genetic program isn’t
turned on, meaning that you don’t find mRNA, and you don’t find protein, and you don’t find
function.

We then switch the culture conditions and add triggers by trial and error, to a large extent to try to
activate certain genetic programs. And if we do that, we look for protein and mRNA first.

So we look to prove that the genes are turned on, and then we look to prove that these gene products
actually give rise to proteins. We have gone to the next step also and actually tried to then take the
cells that we believe that are like brain or like liver, and started asking questions.

If it is a liver cell, it should secrete certain things. It should have the machinery to detoxify blood and
things like that. So we have been able to show that in the liver lineage, for instance, that we do turn
on the programs to make albumin, which is one of the major proteins that is being secreted in the
liver and is present in the blood.

These cells have, for instance, cytochrome P450, which is a massive machinery in the liver that helps
detoxify the blood components. And we can show that it is there, and it responds in the correct ways
as liver cells would do.

So that is what you do in vitro, and in vivo, it is a bit more complicated, and you really need to use
animal models where there is a disease. So you would have to show that the cells ingraft and you can
find the donor cells.

You would have to show that they turn on RNA and protein, and therefore have this genetic program
turned on. And then function, which means that if you take an animal that has a failing liver, and
you give the liver cells to this animal, the animal will now live without having drugs that keeps it
alive.
And so that would prove that the cells that you put in have actually acquired the ability to function like a liver cell. And so for adult stem cell research, very little proof of the latter is actually present.

For embryonic stem cell research in mice, there is a lot of evidence, and in the human embryonic stem cells, that evidence is just starting to become available, just like it is with adult stem cells.

**DR. HURLBUT:** Could I ask one last little question? How many genes are we talking about here; like hundreds, or thousands, and how many do you monitor in fact?

**DR. VERFAILLIE:** Well, we usually monitor between — well, there is probably hundreds of thousands that get turned on, and so using the new technologies, the array technology, and the proteomics technology, that is one of the things that we are looking at, because it will give us a much better insight in the whole programs that are being turned on.

We just pick and choose the ones that we think are known to be important at certain stages of the differentiation. So, for instance, if you go from a stem cell to a liver cell, we know that you have to turn on X number of genes that happen to be known to be turned on.

So we look at 2 or 3 that are early, and 2 or 3 that are in the middle, and then 5 or 6 at the end. We have not exhaustively looked at all of them yet.

But I think with the human genome being sequenced, we now have the tools in hand to now take cells created from stem cells and look at the whole program of genes that is present, and what we created in a culture dish, compared to what is actually present in real life in vivo, and get a feel of how closely we actually are getting to the real cell.

**DR. HURLBUT:** Thank you.

**CHAIRMAN KASS:** Could I — Robby, did you have a question? Why don’t you go first, because I have a couple of things as well. Please.

**PROF. GEORGE:** Actually, I just wanted to follow up the question that Dr. Kass asked earlier just for clarification, and I recognize that there is a great deal of uncertainty as to what the future holds in your area for research, as well as in embryonic stem cell research.

And estimating or evaluating what the prospects are therapeutically is a speculative business, but having all of that in mind — and I was not clear in responding to Dr. Kass whether you identified some areas in which knowing what we do know now about the differences between embryonic stem cells and the MAPC cells, it is possible to identify some areas where we just know that whatever the prospects are for MAPC cells that they won’t be able to do, or our therapies won’t be able to be developed based on them to do certain things.

And that there is at least a prospect of embryonic stem cells being used to do.

**DR. VERFAILLIE:** It is so very hard for me to answer that question, just because embryonic stem cells have been worked with for so much longer, and so investigators have been able to, for instance, make cells that secrete insulin to some extent on demand, which has not been accomplished with adult stem cells.

There is a little bit of evidence from pancreatic tissue itself that there might be precursors that can do that, but from MAPCs, for instance, we have not been able to do this yet.

It doesn’t mean that we can’t. I don’t know that answer. So there is a lot more experience with embryonic stem cells and there is a lot more — at least in the mouse system, there is a lot more known on how to try to trigger certain differentiation programs and whether the MAPCs will respond to the same extent and to the same degree.

And I think that currently I can’t really answer that question.

**PROF. GEORGE:** But asking if you look at it and not asking what do we know MAPC cells will be able to enable us to do, and have a prospect of doing, that embryonic stem cells have a prospect of doing.

But if we simply ask the question as do we know just on the basis of the facts of what we know about the differences, and that there are in fact some things that MAPC cells, no matter what, won’t be able to do. Or is the answer that we just don’t know?

**DR. VERFAILLIE:** I think we don’t know currently, and I can’t really answer that question,
because we just don’t know at this point in time.

**DR. FOSTER:** I just want to interrupt with this one point. Those questions are really hard to answer, but there is another whole area that is going to impact what you are going to use cellular based therapy for.

And that has to do with good vectors, retroviral gene therapy, and that you are going to accomplish with other diseases that you don’t have to use cells for at all.

I mean, the most recent thing in severe combined immunodeficiencies in humans, is you put a retrovirus in, and you put the common gamma chain in for about five cytokines, you know, for these kids. It was just in the New England Journal a couple of weeks ago, or three weeks ago, or something like that.

And they are now two years out, and so there are going to be a whole lot of diseases that you are not going to have to use regenerative therapy or cell therapy. You can’t predict those things either at this point.

So I think if you try to jump way ahead of what the basic science is doing, then you are prone to error, and I know everybody wants to know whether an adult cell is better than an embryonic stem cell, or something like that.

And I don’t think you can answer those questions, and one of the things that we have heard from both the investigators this morning is that they cross-fertilized with each other.

And so — I mean, that you could not have done what you are doing in the adult cells without what had already been done with the embryonic cells.

So I just would argue against trying to push investigators to say whether an adult stem cell can do this or do that at this point, because we have not even taken into consideration many other approaches to human disease.

I don’t mean to be fussy, but I do think that that is an important thing.

**PROF. GEORGE:** But I was actually asking — well, I think the question I asked was that it really is about what we know now. The question is do we know now that there are certain differences, that as a result of which the prospects for the one area are different from the prospects of the other. And I got my answer. Thank you.

**CHAIRMAN KASS:** Let me take the privilege of the Chair to expand in a way Dan Foster’s comment in a direction that he might not have intended.

**DR. FOSTER:** That does not surprise me.

**CHAIRMAN KASS:** Well, I mean, you are a genial sort, and I think you won’t — I mean, one of the things that one has to remember in this conversation is that wonderful as the stem cell approach is from whatever source to the treatment of these diseases, that is not the whole area here also.

And that the gene therapy is not the whole story as well, and there are preventive measures, and there are all kinds of other things. I mean, the conversation, because we are taking it up, gives it a certain type of dramatic focus and concentration.

But for the people who work in clinical medicine, they know that this is — that there are lots of ways to try to skin this cat. But I wanted to ask a couple of — to make a comment, and then ask a couple of questions.

You have talked understandably and very welcomed to us about your own very exciting work. There is a great deal of skepticism about many of the published works in using adult stem cells.

And unfortunately, for better and for worse, these reports are caught up in the political controversy that now surrounds us, with people on both sides having a stake in either making the results on one line of work seem better than the other, precisely because they are wed to an either/or choice.

Can you, abstracting from all the political considerations, and the various axes that various people are grinding on these poor cells, can you say anything at all generally about the kinds of initial reports of a clinical sort that we have had with alleged adult stem cells?

Because at least according to some accounts, these have been very exciting, and yet there is a great
deal of skepticism about whether these are in fact stem cells that are producing the results.

Can you tell the council anything at all about how we should at the moment regard the news that is coming out to us in this area? How should we receive it?

DR. VERFAILLIE: There have been several publications that came out over the last 1 or 2 years now, where investigators or clinicians have looked at individuals who were transplanted with classical bone marrow transplantations, and looked in tissues outside of the hematopoietic system to ask whether bone marrow derived of donor-derived cells could be found in different tissues.

And the reports that have come out have indicated fairly significant levels of contribution to certain tissues, meaning they have found cells in the heart, and they have found cells in skin, gut, liver, and so forth.

And we really have not looked in the same situation to see whether we can confirm these data or not. I know that some clinical groups have put in doubt to some extent the degree of contribution that has been reported, and it is not quite clear whether the 5, 10, or 20 percent that has been quoted in some papers is indeed actually going to hold up over time.

I think there is some contribution, and the question in my mind still is how clinically important is it what investigators have seen or what clinicians have seen currently.

If you go strictly by the term of stem cell plasticity, none of these studies really show that it was a single cell, or it was a blood cell that gave rise to these tissues, and it might still be that some contaminating cells were contributing to that.

And really none of these studies have shown that this has had any clinical impact on what was going on in these patients. And so they didn’t really show that you restored function of the organ that the cells were found in.

CHAIRMAN KASS: I was thinking of a recent report on the Parkinson’s cases.

DR. VERFAILLIE: Correct. So the Parkinson’s cases were — and that is with fetal brain tissues, and are those the reports that you are referring to?

CHAIRMAN KASS: Yes.

DR. VERFAILLIE: And so there has been a series of patients transplanted in Sweden with Parkinson’s disease, where one team of investigators in a non-controlled study, shows that implantation of the fetal tissue brain — fetal brain tissue into the brain of patients with Parkinson’s disease could rescue patients, and could actually correct the Parkinsonism.

And actually have now done so for some patients for more than 10 years. Now, these were highly selected patients, and done by a single group of investigators.

The same was done in the west in 3 or 4 institutions, and some patients got better and some patients did not get better. But I think that gets to the proof of concept that if you have the right cells, and if you can create the right cells, and if it is from embryonic stem cells, or adult stem cells, or from tissues itself, that there might be a way of correcting Parkinson’s disease.

But there is again — and I think it would behoove us to really look carefully at exactly what single cell or fused cells that we have to put into the brains of patients with Parkinson’s disease to try to correct the disease, and not over correct it as it was done in some of the patients in the U.S., where they had more side effects from the therapy than they initially had from their Parkinson's disease.

And so even though there is an enormous amount of pressure on all of us with stem cell research to try to come up with therapies yesterday, I have been very, very cautious in telling people that do the clinical work that you can’t just go around and take stem cells and put them in places in the hope that they will work.

Because we will get into situations like the gene therapy field, where a couple of awful problems have popped up, and have actually halted the clinical potential of these cells enormously.

CHAIRMAN KASS: Could I follow that up, because if there had been more time, I would have asked Dr. Gearhart this question as well, and you are a clinician who deals with patients that are also — now thanks to your new results, and I am sure that you are getting lots of calls as well.

There is an ethical dimension to this area that worries not so much about where you get the cells
from, but how we deal with the desperately sick patients looking for any sort of hope.

And let me say flat out that in-part to fend off the opponents, the people in the scientific community and medical community, has to some extent not been adverse to shall I say hyping the benefits here and possibly even taking rather cruel advantage of these hopes.

And from what I hear from you, and from what I hear from Dr. Gearhart, these therapies, there are lots of problems to be solved before these things will be made available.

And that is not to say that there isn't this enormous promise, but what can you tell us, or what advice would you give us about we could responsibly speak about this promise without behaving, let me say, unethically in dealing with the very patients who are coming to us for help?

And I think that's something that you have probably faced directly, and whatever help you could give us on that would be welcome.

**DR. VERFAILLIE:** Well, like Dr. Gearhart, my e-mail and phone have a lot of messages on them from patients locally, around the country, and around the world who want to bring a child or a parent with a certain disease, and want us to treat whatever disease you can come up with.

And we have to speak the truth, and even though we are excited about the work that we have, and for the work that people do in embryonic stem cells, at this point it is a promise, and I don't think there is any data to say that in the next 1 or 2 years we will actually be in clinical trials with any of this.

So we really have to tell patients, families, and whomever, that currently we are trying to cure mice, but a lot of mice have been cured with a lot of different things, and that doesn't necessarily mean that it will translate into humans.

And so we need to do the regular science that needs to be done to come up with a therapy that is both potentially useful and for certain not dangerous.

And so that the last part of that whole thing is really where everything sits. And so we could go ahead and do things now, but then run into major, major complication issues which would make patients way worse off than they started out.

You could argue that bone marrow transplantation, there was not a whole lot known when the first bone marrow transplants were done, and that is before I started in bone marrow transplantation, and probably some patients didn't fare that well either in the beginning.

But people ultimately still have to learn by doing it in humans, but we have to learn as much as we can in culture dishes, mice, rats, and larger animals before we proceed with therapies for things that are not immediately legal.

And so it is not because you are diagnosed with Parkinson's today that four months from now that you will die from your disease, which is different if you have a acute leukemia, where there is really no other solutions.

And so I also think it will have to be graded depending on the type of disease that you start treating.

**CHAIRMAN KASS:** And I have one last question, and I don't think we will have another opportunity in this discussion, but this comes to Rebecca Dresser's question about the costs, and how to think about this. And also about the applicability.

There was recently a meeting of the major biotech companies in Princeton, and our scientific director, Dick Roblin, was there, and they were discussing among other things the question of the solution of the immune rejection problem from all these various things.

And all of the ones that were present there are putting their research money not into somatic cell nuclear transfer to deal with the rejection problem, but into other means, for a reason that would have never have occurred to me until it came back from this meeting, which is to say that if you have highly individualized treatments, case by case, that at least under present regulatory systems, if you call these things products, each one of them has to be approved independently by the FDA before it can be used.

And so the question is whether or not — and in partly thinking about the cost and the scalability, and the things that might make things universally applicable, doesn’t it make sense more to be thinking more in terms of cell lines, whether embryonic or adult, and that could be made universally applicable, rather than trying to continue to think each person, his or her own replacement, given
these practical problems of scale and product approval?

I am not sure that the question was clearly put, but it bears upon the efficacy of this in terms of long term clinical use, and the questions of cost.

**DR. VERFAILLIE:** Ideally, it would be personalized therapy, and so you would create cells that are completely compatible with the person that you need to treat, except again in situations where there is an autoimmunity issue, which makes it complicated.

And if it is an autoimmune problem starting out, then cell therapy is probably not the best way to go about doing this. For instance, Type-1 diabetes would come to mind, where there is really a rejection of your own islet cells.

I think the costs — and I spoke to that just a little bit before — of creating everybody's own cell line will in the long term will be extremely high, and it will not be a therapy that is suitable for acute events.

So if you have an acute stroke, or if you have an acute heart infarct, and you try to correct that, there is no way that you can clone ESLs to correct that, or you could create MAPCs to correct that within the next one or two weeks.

It just takes too much time to try to do this. Then you could argue, well, I will store our own MAPC cell lines or own ESL lines just in case we need it, which definitely I don't think is financially tenable.

So even though the ideal situation would be to be able to make everybody's own cells, and I think in the long term if the cell therapies are proven to be, for instance, very useful in patients who have a severe MI that you can actually correct them almost immediately after the MI has occurred, or within the next few weeks after it has occurred, it almost has to be done on an allogeneic basis.

And in that case, trying to come up with wise ways of making the cells acceptable to the vast majority of patients, whether it is multiple cell lines and a minimum amount of immunosuppression, or establishing partial chimerism by creating both blood cells and heart muscle cells from the same cell lines, for instance, would be one way to get around that.

**CHAIRMAN KASS:** Thank you very much. Thank you very much for a wonderful presentation, and a very generous and full response to our questions. If we might take the liberty of just contacting you with some other things.

I know that your e-mail is full, and we will try to add very little, but as we go along, we might have some additional things.

**DR. VERFAILLIE:** That would be great. Thanks.

**CHAIRMAN KASS:** Thank you very much. Members are asked to go immediately from here to the other room, where they want a group photo, and the four or five of us who have not yet posed for our individual mug shots, are asked to stay. I think lunch will be served there.

We will reconvene here shortly after 1:30, and let's say about 1:35 or 1:40. (Whereupon, at 12:28 p.m., a luncheon recess was taken.)

**SESSION 3: STEM CELLS 3: ETHICS OF HUMAN STEM CELL RESEARCH**

**CHAIRMAN KASS:** Well, if I sing a song, or make some announcements, maybe we will get the full numbers, but this is the third of our three sessions on stem cell research, having spent the morning hearing two presentations on the science.

And we now turn in this session to ethical questions in stem cell research, and we are very fortunate to have as our guest Professor Gene Outka, who is the Dwight Professor of Philosophy and Christian Ethics at Yale University.

And for a long time one of our most careful students of the ethics of biology and medicine among many other things.

Apart from our interest in the merits of the case, a paper written on a subject of concern to us, I have confessed in the chairman's cover letter, in a sentence which has a missing word, that I have an additional purpose in mind here, namely as just as those of us who are not experienced in science,
need practice in grasping the concepts and methods of scientific analysis, so those of us who are not experienced in ethics would need some practice in working with the concepts and ways of ethical analysis. And Professor Outka's work is nothing if not careful, analytical and disciplined, and we are very thankful that he could be with us to discuss his paper.

All of us have had a chance to read it, and I exhorted you to read it more than once, and there is a lot packed in it. And Professor Outka is going to lead off with a few remarks, after which I have asked Michael Sandel to make comment that would open our discussion. Thanks very much, Gene.

DR. OUTKA: Well, it is a great honor for me to be here, and I enjoyed sitting in enormously in the morning sessions, and noted that although the focus was on scientific matters, moral matters also arose from time to time, as when Dr. Gearhart told us that he doesn't give the same moral status to the embryonic entity as he does to the fetus.

And I think that illustrates one of the claims that I actually make in the paper, which is that on this subject, whether we like it or not, we all have to be moralists in one way or another; that certain moral determinations are unavoidable.

And in-part that is because the moral positions that we take have such direct and sometimes colliding implications for the policy and political recommendations that we make.

And I contrast that with certain other cases where you could have some theoretical debates and disagreements might abound on that level, but you could when you turned to practical and political matters, you could come to some modus vivendi or something of the sort, where the theoretical disagreements don't translate into necessarily practical political disputes.

That is not the case with this subject I contend, and so we all have to be inclined to engage in moral reflection, and although moral reflection has its own esoteric features in the hands of at least some, I think that this session may be more egalitarian in a way, because I, like Samuel Johnson's dictum, that we are perpetually moralists, but we are geometricians only by chance.

And by that I take him to mean that moral matters, that there is a fundamental equality about our reflection on moral matters, and it does not require a special talent in the same way.

So that then leads me to say a few things about this paper, which we are going to discuss. I tried to do several different things in it, and I tried to give some kind of an account of some of the major points of disagreement, and I have a spectrum of views from the right to the center, to the left.

And I myself then plum for a particular region of the center, and along the way though I do try to show how debates about abortion and debates about stem cell research converge and diverge.

And finally I propose a nothing is lost principle, and let me say a little more about that, but I think probably the most economical way to proceed is simply to indicate for you some of the normative conclusions that I put forward in the paper.

And not tarry over the questions about whether I do justice to those either more conservative than I am, or more liberal than I am. Spokespersons for both positions can speak for themselves later on.

So let me just then lay out some of the claims that I make, and that will get us started at least. I make some claims about the status of human life from conception forward, and I argue that once conceived each entity is a form of primordial human life that should exert a claim upon us to be regarded as an end and not a mere means only.

And I say that it is one thing to allow that we need not yet ascribe full moral standing or equal protectibility to embryos. That is to say, I deny that abortion and embryonic stem cell research are morally indistinguishable from murder.

But I claim on the other hand that it is another thing to instrumentalize embryos through and through when what we intend in the actions we perform exhaustively concerns benefits to third-parties.

And I take that to be one indication of sheer instrumentalization, where the actions that we perform we can only justify, and justify exhaustively by virtue of benefits to third-parties.

That is to say that I deny that abortion and embryonic stem cell research are morally indifferent actions in themselves to be evaluated wholly by the benefits that they bring to others.

I then go on to conclude that to conduct research on embryos that creates them in order to destroy
them clashes directly with the judgment that entities conceived have irreducible value.

So that is on the one hand. I want to say that the case for sheer instrumentalization is to be resisted, but on the other hand, I also think that we don’t confront a single either/or as some conservatives and some liberals suppose, to the effect that we should forbid all embryonic stem cell research, or we should permit it all.

I consider instead a more nuanced possibility, or at least I think it is more nuanced, where we may distinguish creating for research and only employing for research.

And the latter of employing for research allows us to consider in vitro fertilization as a practice in our culture, and employing for research connects with the datum of discarded embryos, where I want to say that the original creation of embryos has a non-instrumentalist rationale, namely the promotion of fertility.

So that what we intend does not exhaustively concern benefits to third parties. But yet the aftermath allows us to pursue benefits to third parties when we may do so without from the start creating in order to disaggregate.

And the way that I try to speculate about the pros and cons of this conclusion is to invoke the nothing is lost principle, which I think illuminates a morally significant distinction between creation for research and employment for research.

The nothing is lost principle says that we may — that although it takes the prohibition against murder seriously, it allows two exempting conditions. The first is that the innocent — that some innocent will die in any case, and the second exempting condition is that other innocent life will be saved.

And applying that to the matter at hand, I say that we cannot choose whom we save in the case of discarded embryos. They will die if we do nothing.

And we cannot save them by killing others or letting others die. Yet, we may save others by virtue of the research. And yet on the other hand, and why this remains incurably in the middle, while the nothing is lost principle permits attention to the possible benefits to third parties from research on discarded embryos, it does not permit the concern about the status of embryos to recede to a platitude.

And where such concern never has efficacy and can always be trumped, and that is one of my tests about saying that a commitment to in this case embryonic life is serious only if it trumps something whenever there is a conflict.

It does not have to trump on all occasions, but it has to trump on some occasions. And where I want to say it trumps is where it disallows the creation of embryos only and exclusively for the sake of, and in order to, disaggregate them.

I speculate on some of the difficulties that this position generates and trying to face those I hope honestly. Some of the difficulties I regard as more demanding than others, but I do rehearse some of them.

But I think it would take us too far a field to review those now. So let me just content myself with having summarized that part of the case.

CHAIRMAN KASS: Thank you very much. Michael Sandel will lead us off with some prepared comments. Thank you.

PROF. SANDEL:

Well, let me first of all add my thanks for really a fine paper that has so many virtues of the best work in moral philosophy, and its close reasoning, and its careful reasoning, and in it directing our attention to some really central moral questions.

And it also has, the paper does, and the proposal of the appeal of staking out a middle ground, of trying to find an alternative to either/or positions, that it exudes the spirit of compromise, which is appealing in and of itself.

And more than that, the kind of compromise that it offers has a certain kind of intuitive appeal, which is faced with these hard moral questions about the status of embryos, it is on the other hand the goods to be had from research and possibly curing disease.
And the intuitive appeal is to say, well, the spares, the excess embryos left over from IVF clinics, they are going to die anyhow, and so we may as well get some good use out of them and do some good.

But we shouldn’t therefore consider it morally permissible to create for the sake of the research or curing of diseases new embryos. We should just use the spare ones and that is the nothing is lost principle.

There is something very appealing about that compromise and intuitively persuasive. But since I don't find it persuasive, I want to see if I can press a little bit and offer a concrete case to illustrate why I don't think the principle works, or is persuasive.

The first thing to notice — and this struck me I think only maybe in my second reading of the paper — is that the distinction, the crucial distinction is not as we might think from our common discourse about these subjects, between fertilized eggs left over from the — well, the distinction isn’t between the IVF fertilized eggs, or embryos, on the one hand, and cloned ones on the other.

To the contrary, the morally relevant distinction here cuts across the distinction that we are familiar with between the ones that come from the IVF clinics, and the ones that are created as clones.

Because the crucial distinction is why the embryo was created. So if we imagine an embryo, a cloned embryo, created for reproductive purposes, and then we consider it spares in that process, it would be all right to do research on those cloned ones, provided that they were created for the sake of reproduction.

But it wouldn’t be all right to use cloned embryos created for the sake of research. Likewise, it would be all right to use embryos created with sperm fertilizing an egg in an IVF clinic, provided that it was created for the sake of reproduction.

But it wouldn’t be all right to use an embryo created when a sperm is brought together with an egg in sexual reproduction in a clinic if the purpose of the clinic bringing the egg and sperm together was to create an embryo for research.

So the key here, and what is carrying the moral weight, is not how the embryo was created, but why. Scientists may use excess embryos, however created, provided that they were created for the sake of reproduction. But scientists may not use embryos created for the purpose of research or curing diseases.

Then the question arises why or the reason, or the motive for creating the embryo determines whether it is permissible to use them for research into diseases.

Now that is the heart of the question; why the motive matters, and why the motive for the creation makes a moral difference. And the way to explore this question would be to put aside cloning altogether.

Let’s imagine two cases; of traditional sexual creation of an embryo, or in a clinic, or in a lab. In case one, a woman comes to an infertility center and donates some eggs because she wants to help infertile couples have a genetically related child.

And the clinic brings together her eggs with donor sperm and creates some embryos, some of which are implanted, and some of which wind up being spares.

In case two, a woman goes to a clinic or to a lab, and donates eggs for a different reason. She donates them because she wants to support stem cell research to cure Alzheimer's and Parkinson's.

Her eggs are brought together with donor sperm, and made available to scientists who are engaged in this research.

In both cases, the motive of the woman who contributes or who donates the eggs is to advance a worthy end; helping an infertile couple have a genetically related child in the first case, and advancing scientific research in the other.

And in both cases, she contributes knowing that at least some of the embryos created from her eggs will be sacrificed, will be discarded or destroyed.

Now, according to the nothing is lost principle, what do we say about the availability of these two embryos, or sets, or batches of embryos for research?
Well, the nothing is lost principle in the paper tells us that it is okay for scientists to extract stem cells from the first batch, but not from the second. And the question that I have is why.

The answer that the paper seems to give is, well, in the first case, they are spares. They are excess embryos. But then it is not so clear to me what counts as spare.

Well, strictly speaking, a spare is an embryo not needed for reproduction that is going to die anyhow. So we may as well use it for some good. But by that definition of a spare, both batches of embryos are spares.

Once they exist, they both meet the nothing is lost principle. It is true that both batches of embryos that we have here are going to die otherwise, and we might as well get some good use out of it.

So that can't be — well, maybe that is too limited of an account of what you mean here by spare embryos, because by that definition they would both be spares, both batches.

So maybe there is a further condition of an embryo being a spare embryo; namely, that it had been created in the first place for the sake of reproduction. That would limit us to batch one.

But then the question is whether that condition adds any moral relevance or interest. The idea must be that the intention of the donor confers some morally relevant difference.

Moreover, a morally relevant difference that somehow filters all the way down to govern what a scientist may morally do. Well, what could that difference be?

How could the motive, the different motives in these that led to the creation of these two batches of fertilized eggs, or of embryos, how might that work? Why would the motive make a moral difference?

Well, there are at least two possibilities that I see from the paper. Maybe the motive makes a difference in the moral status of the embryos that result. Maybe it makes a difference therefore in the respect that the embryos are due. But why would that be?

How does the different motive in the two cases confer different moral status on the embryos in batch one than in batch two, such that the ones in batch one are properly open to use, to be sacrificed for a worthy scientific end, but not the ones in batch two?

There doesn't seem anything different in the moral status of the embryos in batch one and batch two. Well, maybe the difference then isn't in the moral status of the embryos that result from these different motives.

Maybe the difference is in the way that the scientist who would do the research is complicit in the destruction of the embryos that is a necessary feature of the research. But how does the motive that the donor had in creating the two batches change the degree of complicity of the scientist?

And here I am drawn to our Footnote 12, which cites our colleague, Gil, in a question that he put, which I think is a perfectly relevant question here if you are trying to work out some difference in the complicity.

Just because there are some embryos that somebody else has decided to destroy or to discard, why does that remove the complicity of the scientist who does the killing, and Gil's example, who is cited in the paper, seems to me to be a very good one.

If the Nazis decided to gather people in the concentration camps and had determined that they be killed, it wouldn't — that fact that they were going to die anyhow, wouldn't justify a doctor coming and yanking out their organs to save some innocent people.

He would not be less complicit or she, that doctor, in doing or in yanking out their organs to do a good thing simply because somebody else had decided that those people would already be killed, regardless of how you regard the moral status of the embryo.

It seems to me the degree of complicity isn't affected by the motive of the person who created the embryo in the first place. Well, the only other possible answer that I can think to the question why does the motive of the donor confer some morally relevant difference on these two batches, is — well, maybe to recur to the underlying intuition of the paper, which is that embryos should be treated as ends, and not only as means.

And therefore to sacrifice excess or spare embryos in connection with IVF is morally permissible,
because the donor didn’t know which of the embryos created would be sacrificed, i.e., treated as a means, even though the donor knew that some would be.

But even if that marks out a morally relevant difference for the donor, and the donor's willingness to sacrifice embryos for the sake of various ends, it is not clear how this makes the embryo that results more open to use by the scientist.

So my question is going back to these two scenarios, these two batches, created for different motives, to test my motive matters, is what moral difference does the motive make.

**CHAIRMAN KASS:** We have to decide on a procedure it seems after a wonderfully rich comment like that. The only fair thing to do is to ask Gene if he would like to respond now or later.

**DR. OUTKA:** Well, I think it was a wonderfully rich comment, and probably since it was a rather complicated one, it might be best at least to maximize the chances that I will forget less of it if I go ahead and respond now rather than wait, because there are a number of points that come up.

And I thank you very much for your care in putting these questions to me. I guess I don’t really want to use as you suggest — and I don’t use I think the language of motive. There is a wide question about why the embryo is created, but I don’t think that is satisfactorily accommodated by calling it a motive.

What I wanted to do was two things. I wanted to take seriously the notion of the injunction that comes to us in religious traditions, but also in some philosophical ones, above all, Kantian ones, that treating people as ends and not merely as means.

And I wanted to say that that generates a certain case for inviolability, and so I connected that injunction to the ethics of killing. So the first thing that we are talking about I think is more the morality of actions, rather than the morality simply of motives.

And I want to say that certain actions may be licit if one can say that the rationale for — let's say in the case of IVF clinics, being in the mess that we are in with respect to them doesn’t have to do with actions that we ourselves perform.

We are actually dealing with the after effects of an entire industry, and so that would already distinguish the status of what we are contemplating there from the status of contemplating a direct action ourselves when we do X in order to do Y.

And I want to say that a prime case for treating an entity as instrumental through and through is when we do X in order to destroy them for the sake of the benefits that destruction will bring to third parties.

I want to say that that is an instrumentalist action through and through. So I would prefer to use the language of ends and means, and the morality of actions, and specifically the prohibition against killing, rather than I think the language of motives.

And which does not seem to me to quite capture those points. Now, in regard to your very interesting example, of case one and case two, it would be the case that if a woman donates eggs for reproduction, she there is donating her eggs for an end that isn’t menial.

I mean, there she is donating her eggs for the sake of a couple who want a child, and so nothing that the couple contemplates, or nothing that she does contributes to a case for creating in order to destroy.

Whereas, if she gives her eggs to support stem cell research — and that is her only reason, so that she is giving her eggs in order to do that — there it seems to me that she runs the risk of violating the thing that I am objecting to, which is creation in order to destroy.

So the relevant fact is not simply that they are both spares. The relevant fact has to do with the morality of the two different kinds of actions.

And where the ends have to then be also distinguished, and you say that both ends are worthy. One is to help a couple, and one is to promote research. But I am precisely objecting to the second kind of so-called worthy end if it means that you may directly create a life in order to destroy it.

That seems to me to be a trumping action; that is to say, the objections against a trump, the good aim of promoting research. Whereas, nothing about helping a couple involves a creation in order to destroy. So it is not subject to the same kind of objections.
Now, you also then list some possibilities about how these different cases might be distinct. I think the batch one and batch two — I hope that I have given a different account of why I make a distinction between those two cases.

Your reference to Gil Meilaender is a very important objection to me in correspondence about whether or not nothing is lost allows to much or permits too much.

I strain there, and I grant that I strain, but what I want to argue is that in the case of embryos slated for destruction, and who are frozen in perpetuity, or eventually to be discarded, we have a peculiar condition of perpetual potentiality.

And that distinguishes them from some of the other possible uses of nothing is lost, which I disallow. So there the argument would be that they are the peculiar features of entities that are characterized as having perpetual potentiality that distinguishes them.

That is not certainly an adequate reply, but that would be the shape I think of my general response.

CHAIRMAN KASS: Michael, please come back and maybe one more round would help, and other people would like to get in on this.

PROF. SANDEL: Well, there are two issues here. The last point was an attempt to show that in the first case the woman who donated an egg to help a childless couple, that her act was morally permissible.

Whereas, the second woman's act was not morally permissible because it instrumentalized the embryo in a way that the first one didn't. Now, that is one issue, and I would like to come back to that issue maybe later.

But even if you are right about that, it still would be true that the nothing is lost principle, from the standpoint of the scientist, must regard both batches of embryos as spares in the relevant sense that they are going to be discarded or destroyed anyhow, and why not derive some good from them.

So even if you made out the first distinction between the acts of the woman donor, and there are questions about that, but independent of that, still how does that limit or change the scope of the scientist's responsibility, such that — there are certain eggs or the eggs in batch one, because they were not conceived instrumentally, are open to use.

Whereas, the eggs in batch two, the embryos in batch two, because they were conceived instrumentally, are not open to use. Why is that?

DR. OUTKA: Well, the key thing there I think I think is that I was talking about the rationale of in vitro fertilization clinics by and large, and rightly or wrongly, characterize that rationale as being able to sort of claim that.

Their dominant aim was to address the problem of infertility, and not to provide embryos for research. That is the overall generalization, and I know that there are a lot of questions to be raised about that, and at the very end of the paper, in the last version of the paper, I raise some of those questions myself.

But nonetheless I would stick to that. So I would think that your second case, your second batch, would not come up very much. I mean, I am obliged to you for thinking that it might. I guess I was talking about in vitro fertilization with that overall rationale.

You are talking about women who would donate their eggs simply to support stem cell research, and they would do that independently of whatever the scientist did.

And I would agree that in such a — and I think they are pretty rare cases though, that scientists would not be complicit.

PROF. SANDEL: They are rare only because IVF happened to get going sooner, and it has generated a hundred-thousand of them. But once stem cells get going, there is no reason to think that there won't be a hundred-thousand of those out there.

DR. OUTKA: I doubt it very much. I mean, there are lots of questions actually about the pressure placed on women to donate eggs, and the morality of egg donation is actually I think a really important subject that has not been discussed by ethicists.
But the important point here is that since you don’t have such a class, what I am objecting to are researchers, scientists, who become complicit because they themselves do the creating.

PROF. SANDEL: Through cloning, but morally speaking, what do you say about the case where a lab takes or invites women to donate eggs, whether it pays them or asks them to donate them for the purpose of stem cell research?

DR. OUTKA: If it is inviting them, I would have to look at that. To the extent that it takes initiative, to that same extent it becomes more complicit, and therefore more subject to the objection that I am raising.

PROF. SANDEL: But you would agree that from the scientist’s point of view how it got there, whether it was from someone who gave it for reproductive purposes, or from someone who gave it for stem cell research purposes, from the scientist’s point of view, do you think that makes a moral difference?

DR. OUTKA: Well, I do if they are inviting a woman to donate eggs so that they may take those eggs and fertilize them in order to destroy them for the sake of, and so yes, then they are complicit.

PROF. SANDEL: Well, the lab. I am assuming the lab does and then the scientist goes and gets the — whether the scientist, or whether she goes to the lab and says give me some of your spares from reproductive donations, or says give me some of your spares from people who actually wanted their eggs to go to this purpose, do you think that makes a moral difference?

DR. OUTKA: I think it is worse whenever there is an active role played in an action which I regard as disallowed for reasons given. Now, there are a lot of nuances here, and I know that there are a lot of conservatives who think as I say in the paper, there will be some colluding going on between people who run in vitro fertilization clinics, and scientists who want spare embryos.

And I agree that there is a kind of performative problem there, and I tried to discuss that. So I am not saying that there aren’t shades here, but the spirit of the paper is this. That we do have an action where we are creating in order to destroy something, and that does seem to me that it should give us pause. It is not the same, and it won’t simply be justified by saying, well, look at all of the third parties who are going to benefit.

If that is what we are saying about it, and we are creating in order to destroy for that reason, then let’s say it very clearly. But let’s say that we are then treating some entities totally instrumentally, and make no bones about it.

That is the first part of the spirit of the paper. The second part is to say, all right, it is the case that there are enormous benefits to be derived from embryonic stem cell research.

Let’s see whether or not we can mount a consistent moral argument that will allow us to draw on some of those, but to keep some limits, so that we are not simply tolerating anything, or losing all of our criteria for distinguishing.

That is the spirit of the paper. Now, some of these cases will involve as I say gray areas, but I don’t think that those gray areas by themselves will invalidate that two-fold part of the case as such.

PROF. SANDEL: Just a brief reply. If doing something to help a third-party is instrumentalizing, then all of the embryos in batch one are also morally impermissible because we are imagining a case where the woman goes to the infertility clinic to donate her egg for the sake of a third-party, for the sake of another couple having a child.

So that is doing a good thing for a third-party, and so that is instrumentalizing isn’t it in just the same way as the second case?

DR. OUTKA: But there is no killing involved. She is donating her eggs in order that they may take those eggs and fertilize. That is life enhancing. This is as I said —

PROF. SANDEL: Provided that there are no spares that are destroyed.

DR. OUTKA: No.

PROF. SANDEL: The issue arises only because — if it were a one for one, if there were no spares, no excess, then the issue wouldn’t arise. We are talking about the woman making the donation to help the third-party have a genetically related child, knowing that there will be some fertilized egg,
some embryos, that will be sacrificed, discarded, as a consequence of her doing that.

**DR. OUTKA:** But you know how long, and perhaps too long in the paper, that I agonized about precisely that recognition. That that is a case where we foresee under present circumstances that more embryos will have to be created for promoting this end of conception, and fertilization, than we would like.

But we say that we foresee that, but we don't directly intend it, and there is still a claim that I think needs to be — I would still want to try to make, which is that there is a morally relevant difference between foreseeing the inevitability of excess embryos, and lamenting that, and wanting it over as soon as we can, et cetera.

And creating again in order to kill, or to destroy, and I still think that there will be a difference there.

**CHAIRMAN KASS:** There is a long queue that is prompted either by the paper or the comments. I have Jim Wilson, Mary Ann Glendon, Alfonso Gómez-Lobo.

**DR. WILSON:** Let me begin with the language of motive, because though he may not have intended it, I think Professor Outka has in fact used the language of motive on page 24, where he talks about creating an embryo exclusively for research, the motive of the person.

Or creating it exclusively for fertility, the motive of the actor; and then again on page 35, creating for research, motive, and creating for baby creation, motive.

I think it is well to get the word motive out of our language. I hope that Mary Ann Glendon will forgive me if I use an inept legal analogy, but in the criminal law, we don't ordinarily determine guilt or innocence on the basis of the motive.

The man lies in wait to kill a woman, and shoots her from a distance, and approaches closely to make sure that she is dead, and finishes her off with several bullets to the head.

We don't ask in the court whether he did it to collect her insurance or to prevent her from carrying on her experiments in dogs, since she happens to be a biologist at a local university laboratory.

We might take motive into account in the sentencing decision, but that would be up to the probation officer. It seems to me that to modify the circumstance that Michael laid out for you and with which we have been struggling, suppose now the woman donates eggs in an IVF clinic, and they are all fertilized.

And suppose before picking the egg she wishes, she does what I think is in fact not impossible, and may indeed be commonplace, she has each fertilized egg tested for its likely hair color, or intelligence, or sex, or whatever of the embryo that will be produced.

And having selected the egg she wants and has it in place, she looks at the other people and says kill the rest. In fact, particularly kill those two. One is going to have Down's Syndrome, and the other one is going to have cerebral palsy.

Doesn't that put the IVF eggs in exactly the same position as the eggs created by a woman who has done it solely for the purpose of creating somatic cell nuclear transfer for the purposes of biomedical research?

In fact, does it make it worse, because now not only are the eggs that she has picked out with the doctor's consent going to be destroyed, they will not be destroyed in a way that will help anyone else.

So that to me the leftover egg solution to this problem doesn't work. The leftover egg solution doesn't solve the moral difficulty.

**DR. OUTKA:** Shall I try to respond to each of these as I —

**CHAIRMAN KASS:** Well, I think that these are all solid, and —

**DR. OUTKA:** Oh, yeah, very solid. I am indebted to you all, and let me say though that I think the statements that you read really are precisely about motive.

Let's maybe use the language that is closer to what I actually use in the paper, which is intention rather than motive. Now, I have always been drawn to an old assumption about the doctrine of double effect.
I am not sure that it is going to work, but I have always been fascinated with this claim, and I think there are some cases where it worked, but it doesn't always work.

And that is that certain action descriptions entail certain intention descriptions. Now, that is much closer to the timbre of my argument than the language of motive, because what I want to say is that an action, where you actually create in order to destroy, if you describe that action, it is hard to avoid identifying one intention.

And that intention is to destroy, and so I don't — I am going to continue to try to try to resist of saddling me with the language of motives here, and I don't think the statements that were cited really do that.

Let's think about intentions with respect to actions more than about general motives. With respect to your case, Professor Wilson, of all of the eggs fertilized. That it seems to me is — I have gotten a little bit of a bee in my bonnet about this.

The suppose this or suppose that, as a kind of test for measuring the adequacy of an argument, this hypothetical case that you cite is I think not at the moment within the realm of possibility.

So I am not sure that I have — that I am obliged to respond to it in precisely the terms that you have set it out. The fact of the matter is that we do have a situation where one of these embryos is going to be chosen to be implanted and brought to term, and the others will not be.

That is the datum that we are dealing with in trying to make moral sense of, and I would have to stick with that one, rather than speculate on all of the eggs being fertilized, and then if she chooses only one, rather than all of them, she is guilty for what she does to the other.

I think that changes the terms of the example so far that it is not any longer precisely comparable as a test of what at least I want to argue.

DR. MCHUGH: Leon, I have to interrupt just for a second. I just don't understand when you say the intention, or any intention, is in order to destroy. Nothing is being made here in order to destroy.

DR. OUTKA: That is a very important point and thank you for mentioning it.

DR. MCHUGH: Sorry to interrupt.

DR. OUTKA: No, no, no, I'm glad you did. If I am wrong about this one, then a lot of things go by the board, and I could be wrong about this one. I actually had wrung my hands about it quite often.

It involves a description of what is done that does include my importing a kind of conclusion about what is in effect going on that researchers might not immediately consent to.

But it does seem to me that if you ask a researcher why are you creating this entity, and the answer is, well, I want to do something to it, which will certainly kill it, but I am doing it for the sake of third-parties.

Then that seems to me to be an instance of instrumentalizing it. So the in order to destroy, or in order to disaggregate, is internal to the description of the act I want to argue. Now, one might try to get at the position by challenging that, but it is hard for me —

DR. MCHUGH: You just used the word intention, that it was intention in order to destroy. I mean, you had several intentions.

Perhaps, and I might accept that, but there were several intentions involved here. But you put it all on the basis of in order to.

CHAIRMAN KASS: Could I lend a hand on this? I mean, had you not raised the question, I would have at some point.

DR. MCHUGH: I am sure that you would have.

CHAIRMAN KASS: But I think I can — if I am right, Gene, let me have a try. I think the proper way to state the intention is we create these embryos — and by the way, I don't think this paper is primarily — I don't think it is at all about somatic cell nuclear transfer.

I think the question really should be taken up universally, regardless of how the embryos come to be.
I think that Michael is right about that, and this paper was written without even a reference to it. But the researchers — and there have been people who have come forward to — well, people have come forward to donate their eggs and embryos for the sake of research. And the researchers who go to work on that wouldn’t say that we want these embryos in order to destroy them.

We want these embryos because we want to use their stem cells for understanding or for treatment. But it is the unavoidable and inescapable entailment of that intention that the embryo be destroyed in the process.

If there was some way in fact to get the stem cells without destroying the embryo, people would be delighted I assume. And it seems to me that you can make the same case as follows.

This is not to say that the embryo is the human being, but if you were to say that you too, out my heart in order to save my friend, Wilson, here who needed a transplant.

And that you weren't taking out my heart in order to destroy me. All you were really trying to do was to save him, but if there was no way to do that without destroying me, then that material fact of your intent becomes embraced in the overall act with great clarity.

So I think that I myself would not describe this as saying to create it in order to destroy it. I would create it in order to do something else, but the necessary and inescapable entailment of which is the destruction, and therefore you embrace that intrinsic aspect of the act.

I think that is a better way to do it and it doesn't try to gain mileage, if you don't mind, from a more lurid expression that implies that the people are in the destruction business because they like destruction. I don't think that is the flavor or the intent.

DR. OUTKA: No, I take that as — I will regard that as a friendly amendment, and certainly agree with it. I think the reason that I used that language was simply to underscore that it is unavoidable that we can't ignore this as part of a full characterization of the act.

CHAIRMAN KASS: Sorry to have intruded. I want —

DR. OUTKA: That was very helpful. Thank you.

CHAIRMAN KASS: I have Mary Ann.

PROF. GLENDON: Well, doctor, you were very kind when you started out to adopt an egalitarian approach, and suggest that we are all on a equal footing with respect to the moral dimensions of these very difficult problems.

I must say that I feel a little backward maybe because I am a lawyer, but I am still — from the very beginning, from my very first meeting, I have been struggling with a problem that maybe you can help me with.

I am having a hard time seeing the difference between what is done — forget about motive and intention, but what is done in in vitro fertilization, and what is done in creating an embryo for research purposes, and let me explain why.

I think that in both cases the procedure is done with full knowledge that embryos will be destroyed. Now, many people, and not just at this meeting, but at previous meetings, many people have said that the difference is that in vitro fertilization is done for a worthy end.

And I think you or Professor Sandel said to help couples with infertility. Well, we all know that that is not quite right. That very often it is not couples. I don't know whether couples are predominantly the ones, but certainly a large proportion.

But leaving that aside, there are a number of factors that I can think of that to my mind call into question a casual assumption that what we are dealing with here is such a worthy end that it would justify the destruction of embryos.

I will name some of them. One is — and I am naming these as a constellation, and not that each factor would be decisive in and of itself. But it is an extraordinarily expensive procedure.

It is highly uncertain in outcome. It has unknown long term health effects for women who are subjected to massive doses of hormone injections, and the evidence coming out now is suggesting that children born from this procedure may have an unusual proportion of defects and disabilities.
And then finally as I said, it involves creating an embryo with the certain knowledge — or creating embryos with the certain knowledge that some of them will be destroyed.

So I guess that my problem is that not only that I wonder how that can be easily said to be a worthy end, and then I guess more seriously, if we accept the creation of embryos with the certain knowledge that they will be destroyed for purposes of in vitro fertilization, doesn’t it become or haven’t we gone very far down the road indeed toward justifying the creation of embryos for research purposes?

**DR. OUTKA:** Well, I thank you very much for that question and I think it is forceful and important. And my perhaps only flagellations at the end of the paper suggest that I feel its force.

But for better or for worse, let me at least sketch the lines of a reply, even though I don’t think this addresses all the things that need to be addressed in your important set of objections. One is that I do think that there are two things in conflict here. One is infertility, and the other is excess embryos, and we welcome neither. I think that is where we have to begin.

But I indicate that the datum leaves me deeply disquieted, and I don’t easily assume that it is simply a good. I agree with you that it is expensive and uncertain.

It nonetheless is something, and I have talked to a few people who have been through it, and who have actually — it has resulted for them in children, or grandchildren, and they are nonetheless very thankful for it.

But I suppose the spirit again of my approach is to say, look, this is a practice about which there are many, many questions. But I am a little uneasy with the grand — now that a lot of people are beginning to realize this, and are quickly denouncing it, they often use the language of we. That we are responsible for this, and this isn’t like a contingent disaster. This is something that we have created by our own hands, and I would register a slight disquiet with that, too, because I don’t think that we did it.

I think that most folks who have the gift of fertility don’t worry very much about this. And so this was developed — and I agree that we didn’t object to it, or resist it, but it was developed by people with vested interest in it, both the infertile and those would were prepared to create these industries in order to address that problem.

And now it is time it seems to me to air whether or not the current arrangements can be justified, where you have 10,000 new spare embryos being created every month, et cetera. I mean, there are a lot of questions that have to be asked.

But I would also say that in the case of nothing is lost, I do observe that nothing is lost sometimes can be justified even in response to an evil practice.

I mean, there are some interesting cases. For instance, in Jewish rabbinic literature, about acquiescing to the demands of the tyrant under certain circumstances. So you can invoke that nothing is lost even when you don’t think that the situation that got you to here is admirable, or free from a certain amount of evil.

And I think that it is in that spirit that I will want to say that however we got here, and whatever we should do from now on, we do have this datum of a hundred-thousand embryos frozen in perpetuity, or slated for destruction, and we do have to reflect about that.

I am not sure that is a very satisfactory reply, but it is to evidence a good deal of sympathy with your reservations, without I think ignoring that one datum.

**CHAIRMAN KASS:** Gil Meilaender.

**PROF. MEILAENDER:** Gene, as you know, I think it is a very nice paper, and as you also know, that doesn’t mean that I have no questions about it.

And there are several things that I wanted to ask about, but I want to stick with the nothing more is lost, because it is central to your case, and which I take it to mean — I mean, if we were thinking about what other kind of language would we use to describe that, it means with respect to the particular human subject, human entity, that we are talking about, that there is nothing that we can do that would further diminish its life prospects. I mean, that is just by the nature of the case.

**DR. OUTKA:** And also nothing much we can do to help its life prospects.
PROF. MEILAENDER: Yes. And there are a number of analogies that we might think of. I want to come around to one of them in particular, but there are a whole number; the condemned person, whose last appeal has been lost; the irretrievably dying person, who has only days to live; the permanently unconscious person; the fetus in the process of abortion, or after a decision for abortion has been irrevocably made.

I mean, there are a whole number of such, but let's take the anencephalic infant. I take it that there is nothing that you can do to further diminish its life prospects.

I don't know whether you are prepared to think that under those circumstances that it may be instrumentalized for various research purposes, but I would like to sort of hear you reflect on it, since in a certain way it almost seems to me that the case might be stronger for that than for the spare embryo.

The spare embryo is sitting around waiting to be instrumentalized because we made some choices. The anencephalic infant is just there. I mean, it is not any choice of ours that got it there, and it almost seems to me that the argument would be stronger.

So I would just like to hear you reflect on that, and see how you would think about that in relation to the kind of argument that you make.

DR. OUTKA: I know that is a first-rate question, Gil, and since the anencephalic infant case came up in connection with that suggested in your correspondence to me, I should have been more careful probably in how I used it.

My unsatisfactory response to this is that I see the logic of saying that in some ways, since we didn't have a role in bringing this about, there might be greater warrant for using it.

But I guess the context of my discussion of that, of pairing them, was the context only of saying that we are unable to do anything for them. That there is a kind of cessation of the injunction to treat them as ends rather than means. We are limited in what we can do.

Our love can't affect very much, and I really only wanted to make the comparison in that connection. I didn't want to sort of suggest that in such cases that it would be quite all right to go ahead then and use anencephalic infants for research purposes.

But I think that you are right in suggesting that that would have to be a loophole that I would have to close. I mean, I am worried about this datum of the hundred-thousand spare embryos.

I mean, there is a kind of overwhelming fact to go back to the earlier question that I think we need to say something about. Is there anything that we are doing that is preferable morally by freezing them in perpetuity.

And my one place where I do not understand the conservative concern about them is that I don't know what people who don't want to destroy think they are saving that is significantly different —

PROF. MEILAENDER: Gene, can I just make one suggestion?

DR. OUTKA: Yes.

PROF. MEILAENDER: We are not embracing their death as our aim.

DR. OUTKA: Right.

PROF. MEILAENDER: I mean, just as a hypothesis, might that not be what someone would reply?

DR. OUTKA: They certainly could reply, but the result of that is this peculiar situation of perpetual potentiality, and so the witness looks very marginal to me. It almost looks like it doesn't have very much to do with them.

It simply has to do with a refusal to do something that would bear on them, but at that point — and I would agree that my application of nothing is lost, and it might have a slightly consequential sound to it there.

But I would be willing to risk speculating about consequential steps there if there was something to be done that might do some third-parties good.

But in any case, back to your excellent example. Yes, I would have to say that I would have to be
careful, and if the logic of the position involved my saying that there would be some even stronger case for doing something before the infant died, then I would have to address that and modify the position so that that consequence was not allowed.

How I would do that is a nice question, but I think I probably could devise a way to do it that would not be unlike these other ways that I have tried to devise of saying, look, this is a very special case, this class of perpetual potentiality types.

And it is not to be generalized from to allow nothing is lost to generally be invoked to harvest organs from the living, or from those whom the government has condemned as criminals, or whatever.

I do accept that there is a whole range of those cases that I don't want to allow in, in my use of the nothing is lost principle for the sake of talking about embryos discarded.

**DR. KRAUTHAMMER:** Could I interject?

**CHAIRMAN KASS:** On this point?

**DR. KRAUTHAMMER:** Yes, on this point, and a suggestion for an answer. And that would be that there is a fundamental moral difference in the status of an embryo and of an anencephalic child.

The child is a full human being, and anencephalic or not, a comatose person is a full human being, comatose or not, and we don't tear them apart for their parts.

They are inviolable, and so I don't think it is a terribly strong objection. An embryo has an intermediate, if you like, moral status, but certainly is not the moral equivalent of a child or an adult who is in a coma.

So I don't think that you open yourself up under your argument, professor, to tearing up people who are in comas or who are anencephalics.

**DR. OUTKA:** I will accept that as another friendly amendment. Thank you.

**CHAIRMAN KASS:** I have Alfonso next.

**DR. GÓMEZ-LOBO:** I'm afraid that I am going to disagree with Charles here, but he knows that. Going to Michael Sandel's point. I would put it in very simple terms.

Namely, if you go into a lab and you have an embryo in a dish there, and you would not be able to tell whether it was created for research or for reproductive purposes. There is nothing in the being itself.

And what I am trying to do is this, is turn the discussion back to what I think is the key point, namely what kind of being we are dealing with here. There were parts of the paper where you, Professor Outka, seemed to be treating embryos and fetuses as if they were different entities.

And I think at a given moment you would talk about these entities and these other entities. And it seems to me pretty common sensical that we are talking about stages. Every fetus was previously an embryo, and an embryo developing naturally will become a fetus.

These are names that have been coined for certain periods in the live of what, of a human being, if we are talking about human embryos. Just the fact that we can talk about ovine embryos shows that the world embryo doesn't tell us what sort of thing it is. We need the word human there.

Now, if that is the case, then of course the big problem is if we have one human being, and you agree that from conception onwards that we have a human being, then why this "diminution of value" in one stage, and then from then onwards — I don't know, is there an increasing value?

You seem to take implantation as the breaking point, and I have heard that before. Of course, you are familiar with the work of Tom Shannon, I assume, right? You quote him.

**DR. OUTKA:** I cite him in a footnote.

**DR. GÓMEZ-LOBO:** Sure. Sure. Now, the real critical question is this. Are Shannon's arguments convincing? Is it the case that there is such a decisive break there that we may — I think you would be more consistent totally to disregard the value of the embryo, or to say, well, it is part of a human being, and therefore it is equally valuable as that same human being at a different point.

Now, I don't know if we want to get into the discussion of potentiality in the individuation.
But those would be the key points it seems to me, because if a human being starts its conception, if we have there the basic genetic information that is going to carry this organism through the phase in which we find ourselves, then of course I see no reason to think that there might be less value at that point than at another point.

In a way, it seems to me that people like Robertson are a lot more consistent at times, and say, well, let's respect — or Mary Ann Warren for that matter, but let's respect them after they are three years old, after they are rationale, or something along those lines.

So the point that I am trying to focus in is why or on what grounds establish this magic break point at 14 days?

DR. OUTKA: Well, thank you for that question. I actually think your characterization of the position — well, I would want to offer the following amendments to it, but then let me talk about whether I think I have given anything like adequate arguments for the positions that I take.

But the great or the only bright light that I see in this range of possibilities is conception. So, conception is the point at which someone becomes a kind of primordial part of the human race, and an embryo has the genetic wherewithal to become a person just like the rest of us given the right opportunities.

So conception is the first and the brightest line for me. Implantation is none of the other subsequent discriminations that I also defend are anything more approximate, but they are approximate.

So I don't actually make as much of the 14 day period as Shannon does. I don't have this big commitment to individuation versus the other. I stay with conception.

But I do say that there is approximate discrimination at the point where implantation occurs, because now we can describe this entity as a power under way, a self-developing power under way. You can't say that about the embryo.

DR. GÓMEZ-LOBO: Why?

DR. OUTKA: Because it is not implanted. It isn't yet a self-developing —

DR. GÓMEZ-LOBO: That's a circular response.

DR. OUTKA: No, it's not. A self-developing power under way means that if left to its own devices will, and if not interfered with, come to term.

No embryo is going to do that prior to implantation. It won't. I mean, that is not circular. With respect, I don't think so.

DR. GÓMEZ-LOBO: A fetus left to its own devices won't survive either.

DR. OUTKA: In one way it will, in the sense that it certainly depends upon the woman, and I have tried to argue that the one person in all the world for at least the first 20 weeks, and that makes the circumstances of pregnancy sui generis in my view.

It is a satisfactory analogy that are entirely satisfactory elude us. But nonetheless, there is now a natural process where if the woman doesn’t do anything but live normally, that entity will come to term.

And that is not a generalization that you can make about the embryo. You can only make it about the fetus. So I do think that there is nonetheless a difference.

PROF. MEILAENDER: Leon, may I just ask one question of Gene with respect to his response to Alfonso. Given what you have said, why did you accept Charles Krauthammer’s comment as a friendly amendment since you have just — it seems to me — committed yourself to a very high estimate of the embryo, if not from conception, at least from the time of implantation?

DR. OUTKA: Well, then it is no longer an embryo. It is a fetus. There is a —

PROF. MEILAENDER: Well, his distinction was at birth, and that was the friendly amendment that you —

DR. OUTKA: Well, I know that it was, but the embryo, though it has irreducible value, I want to argue still — that until it becomes a fetus, it has moral standing, but not the same moral standing
CHAIRMAN KASS: By fetus, you mean simply implanted?

DR. OUTKA: I mean implanted. So there is a irreducible value, but not the same kind of moral standing that a fetus has. I try to lay this out. Whereas, equally protectable value, only occurs when it is viable.

CHAIRMAN KASS: Could I intrude myself in this just because I think that we spent most of the time here on the nothing is lost point, and the distinction between using the spare and creating for.

But it seems to me, and I am intuiting from the silence of some of our colleagues, whose manner of making a living I am aware of and you are not, but that we might like some help from you on something else in this paper, which actually has to do with the question of the evaluation of the status of the pre-implantation embryo, which is after all central to our business, whether we are talking about cloning for biomedical research, or down the road to embryonic stem cells.

So central to your — I mean, I think if I understood the paper, you make a lot out of — the reason that you do not regard either abortion or the destruction of embryos as murder, though you regard the embryonic life as having irreducible, but not necessarily, therefore, equal value if I am not misunderstanding.

And that turns on some notion of potentiality, which you develop richly, and there are people in this room from previous discussion who have used the term embracing it, and others use it dismissively.

You would, I think, make a contribution to our ongoing discussion if you could say a little bit more about that notion, and to do it in a way in which it might be persuasive, and not to the moral theologians in the room, but to those of us who studied some science.

Can you help? How does the notion of potentiality, how does it help us think about this thing that we have before us created in vitro if it is not a full person, which if I understand your paper, you don’t claim that it is?

That seems to be the core of your teaching to us about its value, and if we don’t understand that, I think we may miss this. So can you help?

DR. OUTKA: Well, I can try, but I’m afraid that I will probably reiterate what is already on the pages. But maybe to refresh our memories, I say that potentiality applies to embryos and fetuses.

And I take fetuses first, and I say that potentiality refers to what they are not yet, and also what they are. And I try to keep fairly low flying here, in terms of trying to offer a descriptively accurate characterization of them.

They are not yet an equally protectable life because by virtue of this dependence on one person in all the world, and I do make quite a bit of this, and that pregnancy does have this very special feature.

Only the woman can help in a certain way. She is strictly non-transferable. There is no one else in the world that can help if she doesn’t. Now, in a way that is a natural fact about us, but it is also a very peculiar natural fact, though it is very common.

It is kind of numerically common and yet it is striking in that there aren’t precise analogies to it. And I want to argue then that during this early period she is allowed special discretion by virtue of this absolute dependence that one entity in the universe has on her, and only her.

But potentiality also refers to what the fetus already is, and what the fetus already is, is this power under way, which I realize has not convinced all of you of its accuracy.

But nonetheless the fetus is very connected to the woman, and still totally dependent upon it, but nonetheless again if she lives a normal life, there is a self-developing quality to the fetus, which if simply left alone will result finally in an entity just like the rest of us.

That is also a natural fact about it, and it is this peculiar combination of what the fetus is not yet, and yet is, that represents its peculiar status in the world.

And so I want to say that to kill it causes it incomprehensible harm, and that is what makes abortion and infanticide so serious, because there is nothing that we can ever do to compensate, or make amends for that action to the entity.
But I also then want to argue that embryos are like fetuses with respect to having this reducible value. They have the genetic wherewithal, but they are not yet a power under way.

Now, I take it that given the overall assignment that you all have as a council, you want to see whether or not, and especially your scientific colleagues, or members of the council have any reactions to that with respect to its scientific adequacy, because that is part of your assignment, is to get clearer on that.

So I would ask any of you who care to, to comment on whether you think that is a useful description, or wildly inaccurate, or somewhere in between.

CHAIRMAN KASS: Does someone want to join on that? I mean, there are people still on the queue, and I jumped slightly. The question of potentiality came up here, and I know that it would be a shame if you left without our having a chance to address that, because it seems to be part of the case for the moral work that we had here. Paul.

DR. MCHUGH: Well, just a moment on your question of potentiality. I want again to underline something that the professor said. He said that this has the potential if left alone.

Well, that of course doesn't apply to, for example, the human development from somatic cell nuclear transplant. You have to do even more to it than just produce it to get it to be human.

And I just wanted to make the point that sometimes potentials depend upon further human actions. And the council knows why I am fussing about this, but I want to be sure that I heard you correctly when you said the potential here is if left alone, this entity will follow a course with —

DR. OUTKA: Well, you are perfectly right, but that applies to fetuses.

DR. MCHUGH: Yes.

DR. OUTKA: It does not apply to embryos. I mean, that is the difference between the two as far as I can see. If you don’t do something in addition to an embryo, i.e., implant it, it will never be a power under way.

CHAIRMAN KASS: Bill Hurlbut, and then — well, are you going to speak to this particular point about the science?

DR. HURLBUT: Yes. The first thing is that I think we need to come to the point of using the same terms. Scientifically speaking, at least in current literature, the term embryo is used for the first eight weeks of development.

But I sense that you are using it pre-implantation and then —

DR. OUTKA: Yes, I am. But I think that has almost become in a way a de facto use. Do you have a sense of that as well?

DR. HURLBUT: They are not using a term — people are using a term, and Elizabeth suggested that we use this in various contexts, pre-implantation embryo, or pre-embryo, but that actually has its historical derivation from the term pre-implantation embryo.

And scientifically speaking, an embryo is from conception until 8 weeks. There has been a little fuzzing over the history of it. But basically the distinction that is trying to be put in place there scientifically is that approximately 8 to 10 weeks the organization is set, and it is not just getting bigger after that, but it is much more like that.

The early development of form and organization are taking place. One little scientific comment and then I want to ask you a question. I personally don’t understand why you feel that in a natural setting at least the pre-implantation embryo has a different moral status than the implanted embryo.

The fact is that the pre-implantation embryo is drawing nourishment from its mother, and as is evident from the varied result that you get from putting it into a different medium for a while — larger offspring, for example, and more twinning, or example.

And so I can’t quite see why that really makes a difference. But that might be the wrong point to address. What I would really like to know — and this is a very vexing question to me. I have sat in this council now for — this is the third meeting, and every meeting the issue of potential versus actual, and accrued, or accumulated status keeps coming up.
And I feel the good intentions of those who bring it up, and I got in a little discussion with Mike Gazzaniga about this the first week. I felt the weight of it when Janet Rowley said it several times.

I keep wanting to know, and wanting to ask of other people why they assign a particular characteristic of accrual as being the moment of implicit dignity; and why the various sides of this equation can’t find some meeting point.

So I would really like — I would personally very much value an exchange between you and somebody at least on this panel, or on this council, who is taking a position of accumulated or accrued personhood, or something of that nature. Do you understand what I am getting at?

DR. OUTKA: Well, I think so, but let’s be sure I do. I mean, my position is — well, I hope nuanced, but it is hard to pin down, because I both want to attribute irreducible value to any entity after conception, and still make as you say some distinction between the embryo and the fetus.

And I accept by the way your pervasion that by embryo I mean pre-implantation entity, and that’s what I mean. And if there is an acceptable way to refer to that and that makes for clarity, I would happily accept it.

And you may be right that the embryo is dependent upon the woman, too, in a way that I ma not fully doing justice to. It is perhaps significant that I am thinking of embryos as potentially in a state of limbo by virtue of in vitro fertilization clinics.

I mean, that has made me more aware of implantation as a kind of stage that is discrete in some ways. So I may be overdoing that. You are certainly right that unless we are talking about embryos created that way, or conceived that way rather, we are not talking about an entity that is not also dependent like a fetus is on the woman.

But now let’s go to your basic concern, and maybe you had better repeat that for me, because I am not sure that I do have it clearly, and it is clearly an important point to you and to some others, and I want to promote whatever I can by way of clarity about your ongoing discussions.

DR. HURLBUT: Well, I would really, really like personally to hear a good deep discussion on the issue of the moral significance of potential.

And I don’t know if it is too much to ask for specifically from one of my colleagues. For example, if Mike Gazzaniga would actually jump in here and engage this, because a lot hinges on this subject.

And a few of us are deeply enough trained philosophically to know the real or the deep thoughts on what this term so factual and potential actually mean.

DR. OUTKA: Well, I don’t think that even the philosophers, however deeply trained they are, have come to any agreement. This is why in a way I felt more emboldened just to say, look, whatever position you take on this status of the embryo and the fetus are going to have major implications for a position that you take on stem cell research.

But there is so much disagreement all the way down the line, and yet those disagreements matter so much, I am going to tell you what my own views are.

Now, I don’t defend them altogether, and that goes back to something that came up earlier. There is a booklet in which I talk about abortion, where I defend them a bit more.

But some of that defense is still to come, but nonetheless I think I am clear now on the general lines of the argument, even though I haven’t fully justified all the parts of it.

CHAIRMAN KASS: Let me say — and because there are people in the queue, and we are moving toward the end of this session, I want to let the people who have asked to speak, to give them a chance.

Could I simply say that this question of either absolute or prima facie, were tied to something actual or potential, it is not going to go away. And that we had better put it on the agenda for ourselves.

Lots of people had a stake in this discussion, and I think Professor Outka has in fact, if we revisited those 3 or 4 pages of the paper. He has given us something to chew on, but I suggest that we perhaps bracket it for now.

I just wanted to highlight it as important, and unless someone really wants to join in on and solve this one, let me suggest that we take the people who are waiting.
And let's try to do this in about 10 minutes, and then break. I have Robby, Frank, Janet, Michael, and Rebecca. That is rather long for the time that we have, but let me ask for a certain concision if I might. Who was the first? Robby? Please.

PROF. GEORGE: Thanks, Leon. Well, I will then lay aside the discussion and I was going to go right into the questions that Bill and Alfonso raised, but let me lay those aside right now, because I have another set of questions that will take us back to Michael's original comment and the exchange with Gene.

And perhaps I will write to Gene with my own two cents about this question about the status of the embryo. But back to the set of distinctions that Michael was calling into question, Michael Sandel.

I take it that our position is that once there exists an embryo, who will not be implanted, and whose life will soon end one way or another, then it is either — and you can tell me which, and I don't know whether it matters.

It is either not instrumentalization to disaggregate the embryo for good reasons, or if it is an instrumentalization, it is not a wrongful instrumentalization.

I don't think you have declared yourself on that, and I don't think that much turns on it, but do you want to say which way you will look at it?

DR. OUTKA: it is probably closer to it. I think that is a fine question, and I haven't really thought about it, but I think it is probably closer to not a problematical instrumentalization. I think that is probably what I would say.

PROF. GEORGE: Okay. I take it then, if I were going to try to defend a position given that point against my point, I wonder if you would accept this way of defending it.

I have to confess in the end that I don't think it can be defended, but I am just trying to see how far it can be defended against Michael's particular critique.

Then I think you would have to say that the morally bad thing is in — and I am sorry to use this language, but I think it is in the spirit of what you have been saying. I am not going to talk about motivation.

But the morally bad thing is in the intention to create the embryo as an object. That is to say, to create the embryo as a means only. Is that right?

DR. OUTKA: Yes.

PROF. GEORGE: So that in way you have distinguished creation by whatever means, and Michael has to be right that the means don’t matter, but the creation of the embryo for reproductive purposes from the creation of the embryo again by whatever means for research that would involve its destruction. Yes? Okay.

PROF. GEORGE: Then I think what has to be defended to make that out would be the idea that embryos created for purposes of reproduction are not created as means or objects, but are created as ends in themselves, even if we know that some of the embryos that are created will in fact not be implanted, and therefore will be subject to licit disaggregation. Right?

DR. OUTKA: Yes. That is okay. Licit disaggregation is probably all right, but note the somber quality of this, of accepting all of this. This is mournful stuff. I mean, I mean I am not happy about it.

PROF. GEORGE: No, I understand.

DR. OUTKA: It is not licit in a kind of pure moral sense at all. It is like we have this aftermath, and what do we do with it.

PROF. GEORGE: That it is permissible and that is the key. We may be unhappy about the whole thing, and regret how it came about. Okay. Then the question becomes can we distinguish the treatment of the spares created, again by whatever method, in such a way as to make sense of the idea that despite the fact that they are going to be discarded, and therefore subjected licitly to disaggregation as ins in themselves.

And how does that argument go? Does that argument have something to do with the idea that each has a chance of being the one implanted? Does it have to be an equal chance, and that gets us into Jim Wilson’s problem about embryo screening?
DR. OUTKA: I don't think I have fully worked out what I want to say about that. In part, it is because I see the moral calculations that I am trying to defend as working in response to decisions made by others, which I don’t necessarily either rejoice over, or even approve, but where I am nonetheless forced to now deal with them.

And what it is maybe licit to do to them. I mean, there the status of fetal cadavers would be a sort of — well, the use of fetuses terminated in abortion decisions would have a similar kind of status for me, where I am deliberating about things where I am not wholly happy about this data, but I am going to have to now confront it and make some determinations with respect to it.

And I am trying to offer a moral case for doing that. But I think that sometimes the force of some of these questions implies that one is more of an actor with respect to what is being decided about than one is.

And I would want to be wary about that, and I think the way that you put that almost hints at that, and I would want to resist it.

PROF. GEORGE: Oh, I am willing to grant you that, but it seems to me that then on the other side, by the same terms, we have got Michael's scientist.

You know, he was not involved in any of this, and he is just facing a batch, or at least one embryo that is now in the condition that objectively from your vantage point renders it legitimate for disaggregation.

And he is willing to do it and doesn’t see any moral reason not to, because it seems to pass the test that you set out.

DR. OUTKA: I said that there were gray areas.

CHAIRMAN KASS: Let me just remind you of the — I mean, I would still like to get other people on the queue, and so if you could —

PROF. GEORGE: I'm sorry, I will —

CHAIRMAN KASS: Well, I mean, could we ask the following? This sounds like a nice dialectic. Would you be willing to put in writing, and Gene, would you be willing to respond, and we share this exchange?

PROF. GEORGE: I would be intending to write to Gene about the status of the embryo issue anyway, and we can —

DR. OUTKA: That’s excellent, but these are very important questions.

PROF. GEORGE: Just a final point on where we would go and why I think it is relevant. I mean, I am just wondering if at the end of the day what you have got left to say to Michael as a scientist is really a practical or prudential matter; that simply if you go ahead and experiment or use it to disaggregate these embryos, you will be encouraging other people to do.

DR. OUTKA: I am not sure — I am going to try to assimilate Michael's scientist's case into the general case that I want to make about the appropriate use of discarded embryos. That is what I am going to do with it.

I am not going to allow it some kind of independent status that derails the basic distinction that I want to make.

CHAIRMAN KASS: Frank.

PROF. FUKUYAMA: Well, I apologize, but I am going to have to leave as soon as you respond to my question, as I have one last class to teach this afternoon.

DR. OUTKA: I won't misinterpret your departure then.

PROF. FUKUYAMA: This is in a way a devil's advocate kind of question. But I am struck in these discussions of bioethics often that you begin with a moral rule or principle, and then as we have done, have a very subtle discussion about the application of it.

But there is no prior agreement on that principle, and the one here is the Kantian distinction between a means and ends, which we have all been — I mean, nobody has questioned that basic
framework.

Now, I personally would much prefer that you be a Kantian than a utilitarian, and so I am not hostile
to Kantianism, but it has got a lot of problems.

I mean, for one thing, pure Kantianism presupposes a dualistic ontology that I think no natural
scientist sitting around this table would be willing to accept.

I mean, noumena do not obey the laws of physics. You know, laws of natural causation. But I think
also Kantian ethics is a big mess, because if is ethics of intentionality.

I mean, I don't really see under Kantian ethics how you can fight a "just" war. I mean, when Douglas
MacArthur was a division commander in France, he once said I will give a thousand men to take that
hill.

I mean, if that is not pure instrumentalization, and every military commander that has ever lived has
had to make a decision like that, and if that is not instrumentalization, I don't know what is.

And this came up — I think Mike Gazzaniga brought this question up in kind of our e-mail
discussion prior to this meeting, that making the distinction between treating human beings as
means and ends just begs a lot of questions as to where you make that distinction.

I have heard, for example, people argue that since Kant believed that the noumenal quality had to do
with our ability to reason that it is actually only fully adult human beings that deserve that kind of
protection.

Which means actually that you could experiment on infants, and a lot of other people by those rules.

So I just would like to hear you defend why we should start from a Kantian premise rather than some
other kind of premise.

**DR. OUTKA:** Well, I mean, my reasons are actually much lower flying than you might fear. For one,
it did come up in the literature that I was reviewing.

Doerflinger mentioned it. In his case, and in mine, too, there is a kind of Christian — but I think you
could have some more generally religious. I think you could have some specifically Jewish or other
kinds of formulations, too.

So it is set in a larger framework, and that is point one. It was handy because it had already been
cited, and I was desperate to try to find some ways to tie into what I had already presented for
reasons of space.

But I don't think that it commits. I don't want to be committed to Kantianism, per se. I want to be
committed to the second formulation of the categorical imperative is one potentially felicitous way to
identify some things we should continue to care about.

But I will sort of reserve the right to interpret it in my own ways, and also stress its importance for
our purposes only with reference to illuminating this, the problematical character of doing
something to X in order to, or with Leon's friendly amendment, and as part of our plan to create in
order to destroy, or some variant of that.

That seems to me to be objectionable, and this was one way to try to make that point. So low flying
acceptance, your cautions are very well taken.

**CHAIRMAN KASS:** Very briefly, Janet, and then Rebecca.

**DR. ROWLEY:** Actually, one of these is a response to Jim Wilson, who unfortunately has stepped
out. But I think it is not correct to say that the mother to be walks in and looks at a petri dish and
says that I want that egg, and that one, and not the others.

My impression is that is not how it happens, and there is no way at the present time for us to suggest
or to screen for hair color or intelligence, or any other features.

We can screen for sex, and we can screen for known genetic abnormalities that might actually be
relevant based on family history. The other issue that keeps coming up again is we are preserving
these eggs in perpetuity.

And for me perpetuity is hundreds and thousands of years, and I think that is not what the IVF
embryos — their fate and future is. One question that I personally am sorry that I didn't get a chance
to talk to, or ask to John Gearhart, is how long can you really keep frozen embryos and expect them to be viable when you thaw them out.

Now, I suspect it is some number of years, but I don’t know precisely if these embryos are kept in liquid nitrogen, which is very expensive, and you have to keep replenishing it in the tanks at major costs to someone or some institution.

It is also clear that he said that at least in his experience that one does look at the embryos that are developing as a result of a particular in vitro fertilization for a family, and selects those that appear to be the best.

And he didn't define exactly best, but presumably either are growing somewhat larger, or have more cells, or whatever features are used.

And the leftover ones are not as good, and that they have a much lower efficiency or viability than do the ones that are selected for implantation.

So I think for us to say that every single embryo left over from IVF has the potential to go on and develop into a robust embryo fetus and child is probably totally incorrect.

And I think that we ought to be a little more careful in how we frame some of these things, because I think we are not taking into account some of the other issues.

DR. OUTKA: If you all ever find out that question about perpetuity, and how long that actually is, I would be very pleased to know.

DR. ROWLEY: Well, what do you think, Liz?

DR. BLACKBURN: Well, enzyme solutions, which are much, much more biologically simple than — not only cells, but blastocysts, or stages around them, and enzyme solutions will go "off" as you store then for a couple of years, even with care and liquid nitrogen.

So there must be some sort of half-life, and so it is maybe a few years. I honestly don't know from IVF clients how that is going to be an assist, but just based on the precedent of even less biologically delicate material, I would be surprised if it was more than a few years.

DR. OUTKA: That is a very important question. The United Kingdom, I think, discards them more decisively doesn't it?

DR. BLACKBURN: My accent is Australian.

DR. OUTKA: Sorry.

CHAIRMAN KASS: It is no longer that united.

DR. BLACKBURN: I am jumping ahead to your inference. I don’t know. I don’t know what the policy is. So I am just speaking from my very direct laboratory experience of delicate biological material, which is much less delicate than these.

CHAIRMAN KASS: Look, we need to break. I want to give Rebecca the last word if I might.

PROF. DRESSER: I didn't try very hard, but I was trying to find out the answer to this question, and I did see last year that there was a report of a healthy live birth from an embryo that was stored — I believe it was 9 years, and they presented it as if this was the longest duration that they were aware of.

But obviously it is difficult on how you do the research to find out the answer. I was interested in the fourth point that you mentioned at the beginning, where you were going to focus on four points, and the fourth point was this issue of political and legal context.

And you mentioned this issue of whether there should be a different policy for private funding and public funding. And I know that is not really your specialty, but I wondered if you had any thoughts for us on that fourth point?

DR. OUTKA: Well, nothing really interestingly beyond what is on those pages. I mean, I am distressed at the amount of liberality out there in the private sector, where it really is just taken as a matter of course that a thousand research flowers may properly bloom out there.

And I think that really is making too many decisions by default, but that doesn't help us very much.
And I did remark though that I think that a number of people have come to the conclusion that if you try to impose some overall governmental criteria, you are going to get conclusions that certain people regard as too conservative and constraining.

And so it is better to leave it alone, and I am not myself prepared to just accept that without further adieu. But much more work would need to be done on that.

PROF. DRESSER: But you wouldn’t take the step that, well, that your position should be the position that should be our public policy?

DR. OUTKA: No, I would not necessarily presume to that, but I am a great admirer actually of Canadian ways of managing their health care. I just have to confess that.

And I do note in the last version of this paper that the position I take is actually closer to the recently announced Canadian one than it is either to the more restrictive policies that the United States has, or the more liberal permissive policies that the U.K. has.

So on this, or on Canada’s attitude towards reproductive technology, and all of that, it seems to me that they have been more responsible than we have.

CHAIRMAN KASS: I want to thank Professor Outka for an excellent paper, and for a very forthcoming and lively discussion, and for all of you for actually sitting patiently through what is a long and for many of us an intellectually challenging and stretching session.

Thank you very much for being with us, and we will take a break for 15 minutes, and then have our last session.

(Applause.)

(Whereupon, the meeting went off the record for a break at 3:15 p.m.)

SESSION 4: HUMAN CLONING 10:
ETHICS OF CLONING FOR BIOMEDICAL RESEARCH

CHAIRMAN KASS: Could we come to order? Why don't we begin? I think a few of our members have had to leave either for class or had a conflict for this last session. I think we’re just missing Dan Foster at the moment and maybe he — ah, perfect. Good, thank you.

This is a session in which we return to the topic of our last meeting and revisit our project on cloning. The specific questions are the ethical issues of cloning for biomedical research and I would simply remind us of the approach that we have adopted in full recognition that not that we have failed to reach agreement, but we never expected to reach agreement because this is a vexed, moral question where reasonable people put the moral weight in different places, and that our effort is to explore these differences with no expectations that they're going to be overcome, but rather that they can be clarified.

The aspiration in this discussion and, if you will, on this part of what we eventually produce, a common document owned by us all in the sense that we agree that this is, in fact, a good representation of the state of the question, while preserving and even sharpening our differences so that no position held by any member of council or by some person not in council that deserves to be represented in council isn’t given its fullest and fairest expression.

We have been proceeding as colleagues, as fallible human beings with a certain, I don't like the term, but it's been used, with a certain kind of epistemic modesty about our own claims, I mean, to encounter thoughtful people who ought to know better than not to agree with us, ought to give us somehow pause and make us a little more humble about where we stand and that we are interested, maybe when we leave this room, we’re interested in victory, but at least for the sake of our meetings, we are adopting the pretense we are interested in clarity and wisdom and not simply beating the other side down.

I would suggest and so far, I think with some perhaps exceptions, we have tried to recognize that the people with whom we disagree have something vital to defend and if I might be so bold, vital to defend even for us whether we know it or not, and therefore it behooves us to make sure that we don’t shortchange ourselves. And one formulation would be to say that it would be — nobody would want to see us callous to the needs of suffering humanity. Nobody would want to see us cavalier
regarding the treatment of nascent life at some stage or other and no one ought to be indifferent to the effects on a society of doing A rather than B, or B rather than A, or C or none of the above.

So I want to tell you where I think we stand in this discussion to see whether I’m right in where we stand and then continue to have — to advance the discussion. The question of the vexed status of this entity, the cloned embryo, we’re now back to the cloning topic. It’s related, but not identical, with the status of the embryo created by IVF, which will be, I think, central to the question.

I want to remind us of something that we’ve gotten from Stephen Carter in a message to us about the importance of upholding the distinction between what’s legal and what’s moral, between the realm of what is permissible legally and what is either good or bad, better or worse, noble or base, right or wrong.

All too often and perhaps for understandable reasons, the question of permission or ban hovers over the moral conversation, but it’s certainly possible that someone might conclude that this activity is morally dubious, but ought to be permitted and there are all other kinds of possibilities. So I would like us, as best we can, to have this conversation still on the moral plane which is where we’ve had it before.

I would also make an observation and this has come also in some of the conversations, that some of us have been adopting the language of competing goods to describe the present situation before us. And I would at least like to put before us that that might be a way of putting the question that is congenial to some, but that there is another way of formulating what’s here and might help us understand why this is so intractable.

In moral philosophy there is a distinction made between the right and the good in which the good is an object of desire. There are multiple goods. They don’t have any kind of absolute standing for us and you can compromise them to get more of one for the sake of less of the other, whereas claims of right or of justice are things which lay down a kind of marker and at least there’s a prima facie claim that they should not be violated, that the burden of proof is on someone to show why they should — why they can’t be violated. And I have the sense, at least in some of the previous discussions, that for those people who regard the embryo as either one amongst us or enough like us to be entitled to some kind of irreducible respect, that is not being treated as a category of a good to be preserved, but as a matter of right. And therefore, arguments of that sort are less likely to — people who hold that view are less likely to want to put that into a pan balance of competing goods, but who want to insist that this is one of those markers like "thou shalt not" because there's something inviolable here.

I don’t want to shape the discussion, but I at least want to introduce that distinction as possibly being helpful to us and seeing what might seem to be simply a matter if we talk long enough, we can find the right balance, when in fact, for some people this is not a balancing operation at all, but two different kinds of moral discourse.

I think that's — there are other things to be said, but I want to really open the discussion with the following observation. We have tried in staff conversations and in conversations with you all to stake out several moral positions with respect to cloning for biomedical research and while two of them seem to have come to the fore and have commanded at least some support, I suspect that the two might indeed be enlarged to four. And let me state them and see where we are.

It seems to me there are two possible grounds for approving or finding morally acceptable cloning for biomedical research and two possible grounds for disapproving. One would be to approve and to let’s say approve with eagerness and without qualification because one does not believe that any harm is being done. This would be a view that held that the embryo in question was beneath the status of having any moral worth and I don’t want to get into the language of person and things. I’m not sure that’s helpful, but it is not the sort of thing that ought to restrain us from use when good might come of it. Let’s call it the position of “approve with zeal” or “approve without qualification.”

The second would be to recognize that there is something in the embryonic life here that one is at least agnostic about it or one thinks it has some kind of standing, but that one engages in a balancing operation and it approves with humility and is willing to accept some kind of restrictions or restraint on what can be done, recognizes that there is a harm being done to the embryo, but does not regard that as a moral wrong, that is to say, a violation of some stricture of right. This has been put into a balancing operation.

A parallel on the side of the disapprove, it seems to me I’m going upwards in scale. You’d have a position that one could call disapprove with regret or has been said, with tears. I’m sorry, the tears belong on the other side. Approve with tears and here, disapprove but with regret, recognizing that
there might be certain kinds of benefits had, but making calculations on prudential grounds or on certain kinds of moral considerations about where this might lead, that one decides, on balance, that the goods to be had are not worth the cost of the balancing operation. And there could be the position that would disapprove as a matter of principle and without qualification because it is immoral to treat even the earliest of human embryos as anything but one amongst us, no matter how much good might come from it.

I take it those are four positions that have been heard around the table, not necessarily articulated in those ways. In the intermediate conversations between the last meeting and this one, we've been mostly working in the middle, that is to say, we have — I'm not exactly sure about that, but we've had expressions of views that look like disapprove with regret and positions that argue for approve, but with humility and the willingness to accept some kind of restraint.

I think from some of the correspondence that there are at least some amongst us who believe that their view of this matter is not adequately represented and I think it turns on the question of whether we haven't made all too much fuss about these little 7-day old embryos.

Let me see if I have correctly stated analytically where we are and if so, then the question is where we can go to make sure that these viewpoints are properly developed before we actually either try to persuade one another to move from where we now are to some other place or we finally have to choose and come down with what we really think about this.

I think I've said both too much and too little, but let that be — to prime the state of our own discussion. I remind you, cloning for biomedical research, the arguments of course overlap with the question of the embryos used for research, but we're back on our more narrow topic and the larger one is still in the offing though perhaps informed by some of the things we've just been talking about.

Comments, questions, arguments, corrections?

Gil, please.

PROF. MEILAENDER: Just very briefly, I just want to note that it's not necessarily a question of whether someone thinks his or her position has been kind of adequately represented in that focus on the middle. For instance, as I recall, one of Frank Fukuyama's comments that he sent in was really questioning whether the approve with humility position was the right representation of the going argument in a way and I, myself, had questioned whether it was really the strongest form of the argument. So it's not — I think it's not just a question of whether one thinks one's own position is represented, but just where the balance of the argument should lie.

CHAIRMAN KASS: Mike, do you want to get in on this, please?

DR. GAZZANIGA: I'll take the bait. I think we should do everything we do with great humility. You realize how often in life you're wrong, it's a good model. But someone with I guess my particular view would not see the need for the preceding two hours of torturous debate of trying to shoehorn into this problem all of the issues that are trying to be shoehorned into us. So I view the embryo by which we mean the blastocyst, either formed by IVF or through somatic nuclear cell transfer as a thing that deserves human respect like all human tissue, but provides me with absolutely no moral dilemma to proceed into biomedical research on it.

CHAIRMAN KASS: Does someone join on that? This is, in fact, I suspect, a not uncommon position. It might even be more common in this body than simply Michael, so could we have some discussion?

DR. GAZZANIGA: I guess what I was — I don't know what other people think and it's up to them to say. But I do like what you've done here which is to broaden the spectrum of response to the question at hand.

CHAIRMAN KASS: Right.

DR. GAZZANIGA: And I think that was an important gesture.

CHAIRMAN KASS: Right. Rebecca, please?

PROF. DRESSER: This isn't exactly in response to what you were saying, but in thinking and reading about this, it seems to me that people in both 1 and 2 categories, the approval categories are affected by some notion of duty to rescue or duty to be a good Samaritan and that it's not just some
judgment about the value of the embryo or the viability of the embryo, but it’s a moral — a strong moral feeling that this is what we ought to do to help people who are very ill. And I just wondered if that is a concept worthy of exploring with these two positions, that is, you know the moral philosophy on duty to rescue and when do we have one and what are the considerations that ought to go into determining whether people have a duty not just to refrain from harming, but to actually act to rescue people who are in dire circumstances. So I’ll just throw that in.

CHAIRMAN KASS: Let me add one further thing. As you know from the start we have been trying to place our limited moral arguments in the larger context. In the case of cloning for producing children, we tried to put it in the context of human procreation and with the help of some comments from Michael Sandel and others, it’s clear that human procreation also means relations between parents and children. It’s not just the procreative act. We’re trying to put these things — the right context for this is not just what’s the status of the embryo, but the right context for this is what is the vocation of healing and what is, in fact, the mission of biomedical research and these are not simply technical activities. These are activities informed by deep moral commitment and principles and the question is whether these duties are absolute or relative and so on is, of course, for discussion. But I think it’s absolutely welcome. We can’t simply hash this out over the status of these 100 cells. We also have to think really about the moral principles that guide us here. So that’s, I think, very welcome.

Elizabeth, please.

DR. BLACKBURN: I’ve been grappling with this and I think that I’m in position 2, as you’ve outlined it, approval, but thinking seriously about it and for me a helpful metaphor was thinking about, well, if one were, let’s say, there with a blastocyst and you had to do something to keep it alive and then you saw a child drowning, who would you save, if it was a matter of you being in one or the other place and you knew that if you went and helped the child drowning, and I’m using a dramatic example, but if you helped the child drowning, you would have to let the blastocyst die because you couldn’t carry out whatever next thing you had to do to keep it alive. So to me, then the choice — it very much comes down to choosing between two things and making a choice as to what is the more morally imperative, so equating research with its goal of therapy isn’t therapeutic benefit and other medical advantages to the idea of saving an existing life in some way that is a fully formed life. So to me, it sort of came down to an either/or. Which one does one weight. So I think your category 2 seems to be fitted by that metaphor.

CHAIRMAN KASS: Please, Alfonso?

DR. GÓMEZ-LOBO: I think that was a very nice illustration, actually, and very helpful, although since both are duties of care, I don’t think that there is any really serious and deep moral conflict. I think that it’s perfectly legitimate to care more for one than the other, if you can’t save both. In fact, I would like to take up the — perhaps the challenge sketched by Rebecca and I think it’s a general way of clarifying things or trying to clarify things. I think we do have duties of care, moral duties of care, duties to take action to preserve the goods or to promote them and doubtless, our duties involved in health care are usually of that nature. I mean we make all sorts of effort to say bring our child to the emergency room when the child is sick, etcetera. And of course, that’s a very, very important aspect of our moral life.

On the other hand, we have duties of respect and we have duties not to harm. Physicians of the older generation perhaps were quite familiar with this, the “first, do no harm” principle. And now these duties have to do with the impermissibility of taking action intentionally that will deprive someone of a good. So in a way it’s symmetrical with the other one and the first case we have a duty to promote, protect a good, otherwise would go unprotected and that would make it a moral obligation.

Now what happens when there’s a conflict between the two because that’s what we’re talking about. If there were no conflict we wouldn’t have much of a problem. Now I don’t — I do agree that some things we have duties of care, but duties of care are usually not that dramatic because if something goes wrong with one of the options, we’re really not 100 percent responsible for it as in the case of letting the blastocyst die.

Now what happens when we have, I’m sorry, did you want to interrupt? Okay. What happens when we have a conflict of care and we have a conflict between care and respect? If I understand it correctly, the tradition of moral philosophy tends to say well, if the duty of respect is such that if you act intentionally, you would be producing an important harm to human good, then that should take precedence over the care.

Let me give you an example, perhaps a trivial one, but one which appears in ethics books very often.
You have a bandit who has kidnapped 20 hostages, an American college woman goes by and this man says look, if you kill one, I'll let the other 19 go and of course, that is perceived as a conflict because of course this woman has a duty of care, apparently, to save 19 people. But in order to achieve that goal she has to harm, that is, intentionally kill one person. Since that is the primary action in which she is engaging, it follows that the agent in this case should morally refuse to do it.

Now I'm sketching this argument because for me —

PROF. SANDEL: Excuse me, would you say that even assuming that you know for sure that the villain will kill the 19 of the 20 if you don't?

DR. GÓMEZ-LOBO: Yes. Well, first of all, you never know for sure because there's another agent making another decision there. I mean we're not as predictable. Bandits are particularly unpredictable and in most ethics books the bandit is called "Pedro."

(Laughter.)

That says something.

PROF. SANDEL: The reason I asked is if that condition did apply, then we would have the nothing is lost principle to argue for killing the one.

DR. GÓMEZ-LOBO: Sure. Well, I don't subscribe to the nothing is lost principle by all means.

PROF. SANDEL: Nor do I.

DR. GÓMEZ-LOBO: Don't sign me on on that one. Plus, I don't think there was a good application of the principle of double effect in our previous discussion. So I'm torn. I'm definitely in group 3 here because from the marvelous exposition this morning, I see that, well, we had heard that from Dr. Weissman already. I see how promising all of this is and I see that there are these duties of care, but if — I know many of you will not concede the "if" clauses of the following sentences, but if embryos are human beings at an early stage of the development, and if we should not intentionally kill innocent human beings, it follows for me that I should not violate the harm principle in this case and that's why I'm on level 3. I do think that this is a morally impermissible action, but I regret it and that's why my question is going to be whether the scientist can't figure out a way of harvesting the stem cells without doing harm and the reply, unfortunately, was no.

CHAIRMAN KASS: Gil Meilaender and then Paul.

PROF. MEILAENDER: Well, you're in charge.

CHAIRMAN KASS: No, go ahead. My rudeness and his gentlemanliness give you the floor.

PROF. MEILAENDER: Well, s. I just want to note with respect to the example that Elizabeth gives, I mean I agree with what Alfonso says in the sense that it really brings us back to your comments kicking off this session. Elizabeth's original way of formulating it was a way of thinking about several goods, clearly in competition since you could only save one. Alfonso's way of reformulating it has to do with how he changed it into the question of respect and care, but it's really — that's a form of the right and the good, in a way. And it's worth noting that there might be other factors that would enter in. I don't know what you'd say to this, but even thinking of it just in terms of the competing goods model, suppose the blastocyst is mine and the drowning child or whatever it was, is somebody else's? Does that count? I mean there are all sorts of factors that enter in here, in fact.

So the notion that we've only got one kind of thing, namely stages of development that makes a difference, when we weigh competing goods is not the case, in fact. It's considerably more complicated.

We have obligations to try to do good as much as we can, but that means within certain kinds of limits and it means taking account of a whole range of factors, and so it's just worth noting that it's there.

Then the other thing I wanted to comment on was just to come back to Michael's comment that basically what he was saying was he falls into category 1, as you outlined, that there's not really a moral problem here, but that doesn't get us very far to say that because we want to know then what will give us a moral problem. If the early embryo doesn't, at what point would we have a moral problem and why? In order to think about how persuaded we are by that, we need some kind of characteristics or criteria or something that will help us think about it. Otherwise, we only have a position and we don't yet have a kind of a piece of reasoning that we can go to work on. We just need
CHAIRMAN KASS: Michael has in previous meetings, in fact, in the very first meeting if I’m not misremembering, articulated what might be the criteria for moral standing and they were pretty much neurological, but I wouldn’t speak for him. Could we draw you out on this because it would be welcome.

DR. GAZZANIGA: Sure. One hates to try to answer impossible questions, but you can certainly take approximations. And the approximation that is safe for all concerned who are concerned about your question is that by 14 days the British line in the sand, we're dealing with a system that is brainless and has no capacity for sentience. The brain cells aren't even born and that's pretty raw, elementary biology to — for me to draw the line at the 14th day and then people come back and give you the potentiality argument and I also said something about that which — so yes, I'm willing to draw for — where are we, 2002, that a 14-day line in the sand is a pretty comfortable, keeps you free from thornier issues and I'm going to let someone else draw the next line.

CHAIRMAN KASS: I'm sorry?

DR. GAZZANIGA: I'm going to let someone else draw the next line.

PROF. MEILAENDER: Can we have 20 days maybe?

DR. KRAUTHAMMER: Michael, could I pursue that? Michael, I just want to ask you, forget about the legal issue here. At what point, clearly, you're not at all morally disturbed by working on a blastocyst. At what point in the development of this entity are you personally morally disturbed?

DR. GAZZANIGA: Well, you know, let's see how she goes. One step at a time. What's before us in terms of what the scientists are saying we can provide untold remedies, hopefully they can be provided. For the time being, they would be happy and everybody would be happy with the line that I've drawn. The line that I've drawn — a line. So in 10, 15, 20 years, if they come back to the meeting and say look, we need to move that line, how much — how good their argument is, what people think about it is for another time to be considered. I don't think we have to think that far into the future. I think can we make a comfortable decision in 2002 and I think we can.

DR. KRAUTHAMMER: But clearly, what you think about when this organism deserves some respect has to have some influence on your thinking on this, I would assume that you believe a newborn child deserves protection.

DR. GAZZANIGA: Of course.

DR. KRAUTHAMMER: And I understand that what you're saying of the 7-day-old blastocyst is just a piece of tissue, clearly there's a point at which if you were asked to do the research on this organism, you would say no, and I'm just curious to know what that — you certainly have thought about this.

DR. GAZZANIGA: Well, I don't know if I have.

DR. KRAUTHAMMER: Perhaps you could give it a try.

DR. GAZZANIGA: I mean the obvious, from the neurologic base, the obvious fact on the ground is that the organ that is responsible for everything going on in this room is the brain. And the discussions of the issues of human dignity, of human concern, piety, sympathies, those are all constructs of the human mind and so that means you need a brain around to enable those concepts to be used. So one could say that you at least needed the presence of a nervous system and a nervous system doesn't start forming for 4 or 5 weeks and that nervous system, as you know, is impoverished, it's not ready to do the kinds of things we're doing now. And then you start getting into all these unanswerable questions and I just would rather set those aside because I don't have those problems at 14 days.

CHAIRMAN KASS: Do you want to continue?

First of all, Michael is very good natured and he's not shy, if I may speak for him. And I think that this, if we're here, let's pursue this a little bit further and see if we can get some clarity on this, if people don't mind. I'm taking advantage of your good nature.

DR. GAZZANIGA: We'll see how good natured I remain.

DR. ROWLEY: Have you checked with his wife?
(Laughter.)

**DR. GAZZANIGA:** Sure, go ahead, push me, push me.

**CHAIRMAN KASS:** Did you want to go further?

**DR. KRAUTHAMMER:** Well, I don’t, as a former psychiatrist, I’m guessing here, but I don’t think I’m going to succeed. The position I’ve taken which cut down a lot of trees to publish in *The New Republic* this week, is based on basically a slippery slope argument. It begins by trying to not assume any intrinsic worth to the 7-day blastocyst, but asking were we to pursue this research, particularly in cloning where you create for the purpose of using the blastocyst and destroying it, what will we become? So I think it is relevant. If you think that it becomes wrong to do the research at a fairly near point after that, and as I understand what you’re saying, Michael, it would be at the point where there’s beginning of neural development. But you seem to also be saying that you want to draw the line at two weeks, so the slope here, I don’t know how slippery it is, but it isn’t a big slope between 1 week and 2 weeks.

**DR. GAZZANIGA:** This is where I am in over my head. I like to call up philosophers I know and say can you help me with this slippery slope thing.

(Laughter.)

And they say oh, that’s been written about and there’s a pro side and a con side. And I say okay.

(Laughter.)

I’ll take the con side and we hang up. You can get a driver’s license when you’re 16, right? Now someone said well, what about 15 years, 11 months, 30 days, is that really different than 16? Nah, it’s not really different. Well, about 15 years, 11 months, and 29 days. Pretty soon with the slippery slope argument you can get down to where babies could be getting driver’s license. And of course, that’s nonsensical. So what we develop as a species is a capacity for form categories, categories of action, what is generally acceptable. And all I’m suggesting is that we have a category here that we can make a clear decision about and in that way get around the slippery slope analogy which I think can find you in some pretty slippery situations.

**CHAIRMAN KASS:** Bill?

**DR. HURLBUT:** Here’s what it seems to me to come down to. Some people would say that what you’re talking about here is not a license to drive, but a license to kill. Now I’m not a lawyer and unfortunately, as I look around the room, it seems to me there aren’t any left.

Oh, good, right, okay. Rebecca, you’re here. But my understanding of the law concerning abortion is that it was not fundamentally a right to take a life. That was a circumstantial secondary effect. The woman had a right of privacy to evacuate her womb of this alien presence that was not, she did not have an obligation to have. Okay? Maybe you can correct me in a second, but let me keep going. So now we have — you say we have this capacity to form categories. And I want to say parenthetically, I have a lot of trouble figuring this out too, so I’m not trying to attack in saying this, but I’d like clarification on it. You say we have this capacity for categories. Well, one of our major categories is this distinction between a life present or in process and its right to continue or whatever you want to call it. I don’t even want to use the language of rights, but this is a major category, this position that you should never take an innocent life in process.

Now here’s what troubles me about all this from the slippery slope side of the argument. I’m also troubled by the potential argument, but let’s put that one aside for the moment and here, Mike, I want to ask you a specific question.

So if you really go down and you talk to people about stem cell technology as I’ve tried to do and by amazing circumstances I know quite a few of the major figures in this field, my assessment of it is, yes, we might be able to find the reagents and bathe the culture in them and get the proper cells we want, but that in fact, we’re more likely to get what we want if we were to gestate it for a while, either in utero or artificially of some kind of ectogenesis could be generated.

So now what I want to ask you —

**DR. WILSON:** Mike, what was that? What could be generated? I didn’t hear you.

**CHAIRMAN KASS:** Growth outside, ectogenesis. It grows outside the womb.
DR. HURLBUT: It turns out that a lot of what happens in the development process is highly circumstantial. So people working with stem cells are beginning to appreciate how there are these other little micro environments, that if surrounded in a semicircle by one kind of cell which are sending a diffusible agent in in a particular way, then another agent coming from the other side will cause the differentiation, but you can’t just bathe it in the reagents.

The point is that it seems more logical to me that you reasonably could produce more useful therapeutic tissues by allowing gestation or some kind of artificial gestation to go for a while.

So I want to take the opposition position for a moment and say why not go beyond 14 days and why restrict ourselves to 14 days now if brain criteria — I think even now my assessment is we could learn a lot and progress faster with the science if we didn’t draw that boundary. So I really feel as though that boundary is really just shifting the question of not taking an innocent life to 14 days instead of point of origin.

DR. GAZZANIGA: Are you in a position 1, we’re haggling price here?

DR. HURLBUT: No, because I said I’m prescinding from the question of potential for the moment. So just on your principles, I want to know why we would draw the line at 14 days. And why now?

DR. GAZZANIGA: I just told you. It is a line that is comfortable for me to draw. It is a line that would allow the research to go forward. I won’t keep repeating myself.

DR. HURLBUT: But you said a minute ago that you are comfortable with the fact that until there’s a neurologic system which you said was 4 to 5 weeks, that you didn’t think there was any increased moral standing, so why would you not set that boundary for the moment at 4 to 5 weeks which would make science progress much faster.

DR. GAZZANIGA: I don’t know enough to know whether you’re right or wrong. I leave it to the adjudicating regulatory panels might inform us on that. I don’t see this as a crucial point whether it’s 14 days or whatever. I’m comfortable with 14 days and I’m simply stating my position of 14 days.

DR. HURLBUT: I’d also like to comment on — I’m sorry Mary Ann is not here. Her summation of the last which is relevant here that she seems to be moving towards a conservative position on this issue because of the failure of — to see any demonstrable products or line of research that are coming out of various stem cell efforts.

DR. GAZZANIGA: There’s a wonderful article in Science a couple of weeks ago entitled “Some History Should be Repeated.” And they review the claims and concerns of people about the recombinant DNA research in 1976 where there was a group of people from Cambridge, Massachusetts where a lot of this was going to go on at MIT that felt funny little organisms were going to ooze out of the MIT labs and envelop Cambridge and people were going to die of these horrible things, yadda, yadda, yadda.

And in a similar meeting held in 1970, the late 1970s, they set up this regulatory agency and as a result of now going ahead with recombinant DNA research, none of which was immediately envisioned at the time, we now have, according to this article, 11 major drugs that are used in diabetes, hepatitis, acute myocardial infarction, rheumatoid arthritis, stroke serving and saving the lives of millions and millions of people.

So the notion that I think some people not scientifically trained don’t quite understand is that let the scientists roll. They’ll figure it out. They’ll figure it out and they’re the most conservative people in this room.

DR. GAZZANIGA: They beat each other up on a daily basis as to whether what they’re saying is correct or wrong. But you can’t project into the future what they’ll find out. You have to just understand the competencies that they’re currently arguing for and then let them go to work.

CHAIRMAN KASS: Dan.

DR. FOSTER: I just want to interrupt for one second.

CHAIRMAN KASS: Please.

DR. FOSTER: I want to say something a little bit later, but I want to respond to Bill in one sense. We, ourselves, as a council, tend to have different views. We can sort of sense what, as Leon said, and he’s come a long way to try to get us into thinking about these things. I think it’s critically
important in terms of, as Charles would say, building a fence, that we not try to expand what has already been done already when — outside. I think it's critically important. I myself would be perfectly happy to draw the line at the blastocyst level because I think all the initial basic science can be worked out there and to start moving beyond to the 20 days and so forth. Maybe that would speed up the science. I don't know about that at all. We may find something from the blastocyst in terms of mutation rates and all sorts of things, going to pass away.

My own view is I'm starting to get — but I think it would just be crazy from a practical standpoint to try to say the council wants to come up and extend what we can't even agree on here ourselves. So that's not a moral — the only reason I'm hesitating to say this, it's not a moral issue, but sooner or later, we have to get off of the high standards of moral things and talk about practical things as well. I think we're starting to talk about very practical things this afternoon. I maybe want to come back to that a little bit, my comments about that a little bit later, but I sure would — Gil, I always learn things from what you say and write and send me, but I think this time, you're wrong. I think it's wrong to try to extend this thing out, both practically and in terms of trying to get a consensus on some views, our views here in the council.

CHAIRMAN KASS: Let me say I think I understand. I don't want to pretend to have mind reading capacities. But I've been in a number of these discussions and I begin to get to know who's talking. I think what's at issue in this conversation, let me see if I've got it right. Mike Gazzaniga sees no moral difficulty with using blastocysts because he does not regard them as being things of moral worth. He was asked by several people to say well, all right, and he also enunciates a powerful moral principle for going forward, namely, we're going to learn good things and important things and people will benefit from it.

So no harm, and great good. What's the problem?

Then people want to know well, is there a place where you would have a problem so that if we want to join you we want to know where this train is going and where the limits are which is partly why I think it's not a moral — the only reason I'm hesitating to say this, it's not a moral issue, but sooner or later, we have to get off of the high standards of moral things and talk about practical things as well. I think that's what, in effect, Michael was saying. But there are people who are nervous and who want to hear the principled defense because what they hear here is something like the duty to care and cure being treated as an unqualified imperative beneath which everything else has to submit. And so part of the question for those of us who would care about something, about not doing harm or not violating that which should not be violated, they want to know is there a place.

Now other people have used the 14-day marker not as a merely time saving place for the time being, but who really think that 14 days is a transitional point, whether it be implantation — I don't mean by that just transfer into the woman, but actual physical implantation into the wall of the uterus where you actually have the beginning of a pregnancy, until that time, you don't — or who want to talk about the primitive streak or who want to talk about the absence of twinning and who try to provide some kind of biological foundation for saying ah, there's something here now not fully one of us, but that's a biologically-based boundary, not in a nervous system, but something else that might count for the discussion.

So for some of the people in the conversation who want to know, is there something in the nature of things that would give us a guide if the blastocyst is not it yet? I think that's part of the conversation. And the other part of the conversation seems to be to test out what actually is the limit of the moral imperative on the side of going forward or are we simply going to say there are sick people out there who need these things and until you come to newborn infants, which I think was the implication of Charles' question, it's ultimately fair game because we can't really, I think, and this is not my — this was an attempt to summarize what I thought was going on in the conversation. I would add a position of my own. Yes, we are faced with a certain practical decision here and now, but we have to think about the meaning of the kinds of decisions we take here and now for what it legitimates in the future. Yeah, and therefore, we should try and find a good moral foundation as well as being prudent and practically sensible here in trying to reach this and to see whether we can find a place to rest our head, if we can. If not, I think we're in danger of reaching an unprincipled kind of compromise which offers no guidance to those who are going to come after and who might look to this body which was invited to think about this with a view to where this is going, admittedly with uncertain knowledge, but with some power to predict some of the things that might be coming ahead.
DR. FOSTER: Leon, I always seem to start these long speeches that I was not speaking to the issue that you posed before us about the moral things. I was talking about a very practical thing and I didn’t want to divert off into some other thing. I want to get back to this. I was not making any moral argument at all. I think it’s perfectly legitimate to do that. So if you were lecturing me, I was not attempting to make a moral argument.

CHAIRMAN KASS: Excuse me, it wasn’t a lecture to you.

DR. FOSTER: Well, it sounded like it.

CHAIRMAN KASS: No, sorry, Dan. It was heading off what I thought were going to be people pouncing on you.

DR. FOSTER: I’m so delighted that you’re going to take care of me just like the fetus, you have to take care of me, right? Okay, I’m just kidding.

DR. HURLBUT: Can I respond, Leon, just to that because I have a very salient point to respond to that.

CHAIRMAN KASS: Okay.

DR. HURLBUT: And it ties to what you’re saying.

CHAIRMAN KASS: Okay.

DR. HURLBUT: Dan, we were told this morning that fetal primordial neural cells may be useful in Parkinson’s disease, right? Okay.

DR. FOSTER: Some people believe that.

DR. HURLBUT: But let’s assume it’s right for the moment. Now it’s not abstract and it’s not way off in the future. It’s here and now. So why then would we say, on what principle will we say that a person should not clone himself, gestate or hire somebody or gestate for themselves the embryo up to the age to harvest out those particular very useful cells? This is right here, right now. And yet, the question — and look, let me make two other points. I am a physician. I really want to see the science go forward very, very, very much. I feel the weight of this. I dream it actually, but I think if we define our principles, we will allow the science to go forward because then we will, for example, if we say, full, generative potential is not acceptable to violate, then we’ve got the possibility of creating partial generative potential, perhaps, and going around it, the moral problem in a moral way.

If we define our larger principles well, it will allow the science to go forward. Otherwise, it’s going to get stuck in this morass of conflict. So what I see myself as saying here is something positive to try and set the future in an open way.

Moral reality is a fragile reality in any given society and it’s something we have to contend with. We can’t just ignore it. I think it’s harder to set a moral tone of cooperation in a society than it is to make scientific progress. But hopefully, they can go forward together.

CHAIRMAN KASS: Paul McHugh. Thanks for your patience, Paul.

DR. MCHUGH: Well, I’m going to distract us, I think, from that kind of conversation, but only to reiterate what has been and to emphasize what has been the subject of the conversation between you and me in our epistolary debate in the e-mails.

I feel that we will totally submerge into arguments of opinion over actions if we don’t agree or come to hear that the somatic cell nuclear transfer clonote is different than the zygote. With Michael, I can partially agree that the clonote should have — be the subject of study because I think of it as an artifact and I think it different from a zygote. Where I disagree with Michael is that dealing with a zygotic natural program is equally okay. In fact, I wanted to make a point about Mary Ann Glendon. I think she would say her argument was not conservative, but liberal in the sense of wanting to encompass more people under the umbrella of our protection, but the issue of the science here in what we’re talking about is an effort to bring science forward in the best way.

I want to emphasize what I said in those notes, that is, that the lived experience of scientists making somatic cell nuclear transplants is not that they are creating a new individual, that they are then going to destroy. They are thinking that they are producing tissue that has a particular program and that they’re going to use that tissue at some time for the benefit of everyone and I’m approving of
that and I want to support that. In fact, I do support it. I believe that the artifact can then be misused if brought on into reproductive cloning, but the fact of it as a different kind of thing permits different kinds of actions towards it.

CHAIRMAN KASS: Do you want to answer publicly one question on this?

DR. MCHUGH: Yes.

CHAIRMAN KASS: You believe that the clonote is an artifact different in kind because it’s different in origin from a zygote, correct?

DR. MCHUGH: Different in its origins and in its constitution.

CHAIRMAN KASS: And in its constitution. And should that cloned — should that become cloned at the blastocyst stage and should it be implanted for reproductive purposes and should a child emerge, would that be a human child or would that be an artifact?

DR. MCHUGH: Well, first of all, those actions should not be done.

CHAIRMAN KASS: But —

DR. MCHUGH: That human person would be a different person, although you would extend to him because he was tragically created, natural rights to him, but you would see him as a person mistreated and never to have been created.

CHAIRMAN KASS: But not a member of our species?

DR. MCHUGH: Not quite a member of our species in the same way, yeah.

CHAIRMAN KASS: Even if capable of reproducing with another member of our species to produce more members of our species?

DR. MCHUGH: He would be different.

DR. KRAUTHAMMER: Is Dolly not a sheep?

DR. MCHUGH: Dolly is a sick sheep.

DR. KRAUTHAMMER: But Dolly is —

DR. MCHUGH: But this would be a sick person and we would have to take care of him.

DR. KRAUTHAMMER: But Dolly is a sheep, sick or not, she’s a sheep. I think she’s a sheep, right?

CHAIRMAN KASS: The question has been joined. I don’t know if we can sort it out.

DR. MCHUGH: The point of saying that the clonote has these potentials, that if they are illegally and I would believe that this would be as illegal as slavery or as genocide, that because it has those potentials, that therefore it should be treated as though only those potentials characterize it or that it should be conceived of as only characterized by potential would be an error, an error of logic and an error that would hold back the advancement of science.

CHAIRMAN KASS: Instead of arguing, let me see if I can put you on the map of positions, the moral positions on this question so we know what homework we have to do.

If I now understand you, you do not regard cloning for biomedical research to be a moral problem because the thing that is produced isn’t on the human moral scale and therefore —

DR. MCHUGH: I found it problematic to take your spectrum because I was looking at where I would place myself.

CHAIRMAN KASS: You’re in a fifth position.

DR. MCHUGH: To some extent I hold myself in the place where — between 1 and 2, okay? I don’t think any harm is being done by creating a clonote. I think something good is being done by creating a clonote. But because it is a special kind of new, a kind of biology, I would therefore not permit it to be implanted in a uterus, so maybe therefore I’m treating — approving with humility in some way because I’m putting limits around what I would do with it.
CHAIRMAN KASS: Okay.

DR. MCHUGH: You see, if you take the point that the clonote is something different, it’s something manufactured rather than begotten, then you would want to study, use its best potentials for human kind and not let its potentials for error and slavery appear, okay?

CHAIRMAN KASS: I owe you a 5-page e-mail.

DR. MCHUGH: Yes.

CHAIRMAN KASS: You’ll get it. Dan, please?

DR. FOSTER: I don’t want any e-mail. I never write e-mails in these things and the one that I sent I said don’t circulate. I’d rather talk personally, but that’s okay.

Let me make a preliminary remark. Leon said a moment ago in passing, he used a phrase that I think Adam Seligman popularized called epistemological modesty that in the philosophy of studying knowledge that you looked at limits and so forth. I think epistemological modesty means that you believe certain things, but you’re modest about these claims and you can be a believer and yet say I’m not really sure. And that’s sort of a fundamental fault line here in the discussion.

I take seriously and I’ve been influenced by the people who occupy position 3 here and I’m not willing to agree with Paul that this is just an artifact. I think there’s serious issues here that make me nervous.

But if you live in what Alfred Shutz called paramount reality, that is being wide awake in the every day world, that’s what paramount reality is, it seems to me that common sense shows that a 100-cell human embryo with a potential to ultimately, if everything goes right, becomes a human, has to be taken as serious, as being serious. But it seems to me from this wide awake view that it’s different and it doesn’t have the same demands for protection and respect as let’s say something a little bit later. But I don’t know that for sure. And that’s why I think one has to occupy what I think I and what I know I occupy which will be position 2.

It seems — I don’t — I’m not comfortable with Rebecca’s view that there’s some messianic demand to rescue people. I think there are great virtues in suffering and death that come to humanity. I think none of the things that are great in humanity would occur without threat and suffering in the world. If there were not pain, there wouldn’t be any need for mercy. If there were not fearful things, there would be no room for courage. One could go through the whole litany of what makes humans different and great or the consequences of risk and suffering in the world. That does not mean that when we’re given these brains that we should not try to make the world better. I’m distressed enormously by the fact that the slope of evolution in science appears to be steadily upward and that the slope of evolution for human kindness and beneficence and morality seems almost not to have moved at all.

And therefore, I think there’s an obligation for those of us who live in this world and want it to be better to try to make wherever we can the world better and if you take — I may be the only one in the room that really actively takes care of patients and —

DR. MCHUGH: Hold on.

DR. FOSTER: I’m sorry, Paul. He’s retired, but he still takes care of them. Okay, forgive me for that.

But it is a daunting thing to deal with death. I just lost my long-term colleague. We did 30 years of science together. We did good science together and from a glioblastoma multi-form and there are papers, somebody read the PNAS paper last year where you can mark, you can put human glioblastomas in and then just infuse adult neural stem cells in the peripheral blood targets, the glioblastoma, you can take the mass out, but they infiltrate, you can just see pictures. There are two new articles in Nature and Medicine just showing them infiltrating. But these adult cells clamp on to them and you modified them so that you can give a small drug and convert it into a chemotherapeutic agent across the blood-brain barrier. I mean we tried to see if we could do anything for humans like that.

So myself, for myself, it’s perfectly clear that we ought to try to do better in terms of medicine and the relief of suffering and I don’t think the worry, although I’m very worried about it is sufficient to stop that.

Here’s another point that I think I made —
DR. MCHUGH: Can I ask you a question then about that, Dan?

DR. FOSTER: yes.

DR. MCHUGH: Can I ask you would you take a blastocyst that was naturally formed, taking it out of a uterus, a natural blastocyst and use it in the way you want to use the clonote?

DR. FOSTER: No.

DR. MCHUGH: Why wouldn't you?

DR. FOSTER: Because then I would clearly be interrupting a progression, unless nature took it away.

DR. MCHUGH: Well —

DR. FOSTER: Let me answer it another way. Everybody talks about if you use this, you're going to destroy it. Well, I don't know what the figure is, but 30 to 70 percent of the embryos that form normally are deleted by nature. So what do we say that God is destroying these —

DR. MCHUGH: Would you put a filter in a uterus and pick up those and then use them the way you want?

DR. FOSTER: I would not.

DR. MCHUGH: I'm coming back to my artifact which you wish to use as an artifact, but deny. That's what I'm saying here.

DR. FOSTER: Well, I guess —

DR. MCHUGH: You are saying that things which occur naturally you wouldn't use, but things which come out by cloning you would use and I believe that that's because you see an artificial nature to the clonote.

DR. FOSTER: Well, I don't think that's what I believe —

DR. MCHUGH: Well, would you use a naturally occurring blastocyst formed —

DR. FOSTER: You mean while it's in the uterus?

DR. MCHUGH: Yes, when it falls out of the uterus.

DR. FOSTER: You mean if you take it out of the uterus?

DR. MCHUGH: yes.

DR. FOSTER: No, I wouldn't. I don't want to get into —

PROF. SANDEL: that's not the only possibility.

DR. MCHUGH: No, that's not the only possibility.

DR. FOSTER: I don't want to get into one of these long e-mail exchanges that you and Leon try to do. I'm just trying to make a simple, succinct point and then I'm going to stop right here in just a second, but I do think that we — that I feel a strong obligation not to stop this and the only thing I was going to say and I argued this with Charles a moment ago, I think if we allowed this to go forward, that is biomedical research, if it turns out that it doesn't work, I agree with Mike, the scientists would be the first to quit and so will biotechnology companies because if it doesn't work, if it's got mutations in it we'll end it. Or, if there are better ways to do this as I think there may well be, it will be abandoned quickly. We've seen that all over in medicine that we abandon things when they go through. So my view is, let's try to learn from this and keep it very limited and I'll pay the price of tears, if that's what it is, if it turns out that in some sense that the universe thinks I've killed a child, which I hope we get rid of that murdering and killing things. I mean there's some sort of an implication that scientists are unethical or immoral or less ethical or less moral than people who are not scientists and I want to try to get away from that. But if that's wrong, then I'll try to tell the universe sometime, I'm sorry, I made a bad mistake. But on the other hand, in the meantime I want to try to see if we can't help a whole lot of humanity with what to me seems to be a different sort of moral problem than the idea of beyond ending a life that's not neurons and other organs and things of that sort.
I didn't mean to talk so long. I just was really trying to say that I'm in the position of with a lot of concern as to whether I'm right or not about that.

CHAIRMAN KASS: Charles?

DR. KRAUTHAMMER: I'm a 3 and I'm there for prudential reasons. Mike says and I think if I have the quote correctly, those not trained in science don't understand that what we need to do is let science roll.

Well, we let science roll in the 20th century. We got eugenics. We got the Tuskegee experiment. We had such horrors in mid-century that we needed the Nuremburg Code. Humanity hadn't had to write it before, but it had to write it after. So I'm a little skeptical about letting science roll. Scientists are one of the great resources in any society. They do the science, but they don't own the science. And the reason that we're here is because we don't have a guild system in this society, we have a democracy. We don't say to auto makers you know how to make cars, therefore you will determine what safety standards will be in cars. No, it's the nonexperts, it's the lawyers and the Congress who decide what are going to be the safety requirements in cars and that is imposed on the experts who make the cars and that's how we do it in a democracy and that's why we have this council to advise the President and the country on what restrictions might or might not be applied on what is undoubtedly a wonderful enterprise.

But we don't have a guild system in which all the rules are made internally, not in a democracy.

The reason I'm against research cloning is not because of the reasons underlying position 4 which is somehow attributing a worth to the blastocyst equal or at least comparable to that of a human, but out of a prudential consideration as to what happens if we don't.

The first slippery slope and I think an argument that in and of itself would be enough for a person to oppose research of cloning is that I think there can't be any doubt that if we sanction an industry — and it will become an industry — for the creation of cloned embryos, it is absolutely inevitable that we will begin to see those embryos implanted and we will have the moral horror of having a cloned embryo in gestation which under penalty of law would have to be destroyed and that is a moral certainty that I think is intolerable. But as I wrote in my piece in The New Republic, that is a little bit too easy. I think it would be reason enough to prudentially oppose research cloning, but let's assume, put it aside. I think there are other reasons and the reasons are that once you start on this, once you start rolling along this road, it will lead us to places where I think that we don't want to go. I may be wrong, obviously nobody knows exactly how we will end up or where this will take us, but I think a prudent society needs to make choices based on past history and some understanding of human nature.

The problem, Daniel, is not that the research might fail. The danger is that it might succeed wonderfully and we will then have scientists say as we just heard, give me three more weeks with this embryo. Why not have a fetus where the organs are developed and use them for transplantation rather than have a Rube Goldberg system of growing it into a blastocyst, teasing out stem cells, tweaking them into developing into cell lines. Why not let nature produce with that wonderful machine a fetus and let's strip it apart for its parts? Most of us would say today that is unconscionable. Well, I suspect that if we live in a society where we do this kind of stuff at an earlier level, for a decade or two or three, it will be less unconscionable.

In the end, I think the major issue here is that we are crossing a new barrier with research cloning and that is the creation of embryos solely for their use and I'm afraid that once you do that and we create an industry in which this will be the business of that industry, embryo creation, that we will so desensitize ourselves to the use or misuse of this entity that we will end up doing things that we don't want to do and don't want a society to do.

I think that prudential argument is one on which we can argue about well, what are the likelihoods of these things happening, but I think we ought to be realistic, that once you start on that road, we will be, as a society, far less able to resist the temptations that today seem obvious that we ought to resist, but tomorrow, probably won't.

CHAIRMAN KASS: Jim Wilson?

DR. WILSON: I've listened for years to Charles and read Charles for years without, I think, disagreeing with a single word he's uttered until today. And my problem is with the slippery slope argument. The slippery slope argument which we hear much of in the literature although it's rarely defined, is kind of a warning sign that's put up on a highway, don't go any further or unknown bad
things will happen to you. But rarely is it carried out to show that if you walk past that sign, these
unknown, soon-to-be-named bad things will, in fact, happen to you. The slippery slope argument
here does have a name as what's going to happen to us if we permit the use of somatic cell transfer
for the purposes of creating clones for biomedical research. It is inevitable that we will soon have
cloning to make babies and perhaps cloning to produce from fetal organs parts to be used by human
beings and after that God knows, perhaps organs taken from babies.

That's an argument that can be used against every advance in medical science that has been made
that I can think of. We must not invent surgery because the use of the scalpel to take out an appendix
will inevitably, on the slippery slope, lead to organ harvesting and the selling of kidneys and livers on
the public market. We must not allow neurosurgery, even to cure a terrible tumor because it will lead
invariably to lobotomy. Now, in fact, lobotomies have occurred. And in fact, some instances of organ
harvesting have occurred, but the public's horror and the government's horror at these things has
quickly shut down those enterprises and penalized, often severely, the people who did it. Or perhaps
we shouldn't have automobiles because we will have fatalities. Well, we do have fatalities, but then
we balance the value of the automobiles with the value of the fatalities. Or we shouldn't — you can
make an argument about any human innovation and say we must not adopt it because we'll be on
the slippery slope and it is, in fact, a Luddite argument, unless you're able to show that sliding down
that slope is inevitable.

Now you might be able to say that sliding down that slope is inevitable oning because there will be su
ch a huge financial demand for the benefits of cloning that any form of cloning, however benign in
original intention, will lead to the worse forms of cloning to satisfy that demand. But from all the
scientific testimony I've heard so far, there isn't this huge financial demand and there isn't because
nobody has found yet the exact techniques that competent, but ordinary physicians can use to cure
these diseases, so that I want us to back away from the prudential or this particular prudential
argument because I don't think it's correct unless Charles is in a position to show that the slope is so
slippery, so covered with banana oil, that one step past the warning line we have now drawn on the
pavement will bring us down into chaos.

DR. KRAUTHAMMER: Well, let me give you a recent and empirical example of that slope. The
country had a debate on stem cells about a year ago and the major argument by the proponents of
stem cell research — and I was one of them — was that we are using discarded embryos, everybody
understood that, and we were going to bring a benefit from something that would otherwise bring no
good. The understanding was, in fact, Senator Frist made the presentation on the floor of the Senate
and he established conditions under which he would support stem cell research, the regulations that
we ought to institute in support of that research and among them he listed very emphatically that the
research would not be done with embryos created for the purpose of using for stem cells. That was
what he said.

Now and here we are a year later and we're arguing over a technique of cloning which can only be
done in a manner in which an embryo is created in order to destroy. So within a year, what we have
is the ground shifting on this debate on precisely a point that a year ago we had been assured would
be excluded by regulation and by law.

DR. WILSON: The Senator Frist example is a good one, a particularly good illustration of the
proposition that Congress doesn't often mean what it says. You could use an even better example
with the 1964 Civil Rights Act and Senator Humphrey's assertion to the Senate at large that it would
never be used to establish quotas or goals. These things do happen. But the fact that a year later, a
year ago or two years ago, whenever Senator Frist spoke, we now find ourselves discussing this
subject. It's very different from saying that the subject, once having been discussed and some
authorization once having been past, we have now slipped down the slope to the point where we are
creating clones for the making of babies and harvesting organs from fetuses.

CHAIRMAN KASS: Janet, did you want to comment? Please.

DR. ROWLEY: Well, let me first just respond to Charles because I think though Senator First may
have made some comments, I'm sure that anyone in the field of cloning and embryonic stem cells
would not have supported his point of view. So it isn't as though we started and we're downslope. I
believe that individuals in embryonic stem cell research had already envisioned that, so we haven't —
that position has not been changed of the people who are involved in it.

I would like to respond to the discussion that Leon framed as we began this session and my points of
view are certainly influenced substantially by my view that we are really, we have the potential of
being on the threshold of some major biological discoveries that will be of enormous importance, but
I qualify that with the same statement I made when we began this discussion in January, that this is
a hope and at the present time we have no idea as to how much that hope will actually be successful
and that was reiterated and confirmed again by both speakers this morning, that these are very, very,
very early days and the promise that many of us see in this kind of research may — I think it's not
fair to say that the promise will not be realized, but I think that it is fair to say that the promise may
take a very long time. And I just want to point out that we began the war on cancer in 1970 with the
notion that it was all going to be over in 10 or 20 years and we're far from it. We're far from it
because we're dealing with very complex systems in cells about which we are woefully ignorant, but I
think the part of the research that will be permitted by going ahead with cloning and some of the
aspects of experiments with somatic nuclear cell transfer will enlighten us so much that we'll be able
to see better how to expand on these in the future. And I would only echo our morning speakers by
saying that I think that to ban this kind of research which has the potential for therapy would be a
great tragedy.

CHAIRMAN KASS: Michael Sandel?

PROF. SANDEL: I just wanted to pick up on the last small uncharacteristic slip of Charles where he
slipped back into the polemical action description to use Professor Outka's phrase of what cloning
for biomedical research is. I thought following Paul's and Leon's corrective which Outka accepted,
we agreed that there are two possible action descriptions for both of these practices. By both, I mean
creation of embryos for reproductive purposes and creation of embryos for purposes of medical
research, a charitable description and an uncharitable one. The charitable description in each case
describes the action in terms of the end it's aimed at. So in the case of embryos created for
reproduction we point by the description to the end. Likewise, in the case of cloning for biomedical
research, the end there is the creation of an embryo for the sake of promoting the curing of disease.
There is an uncharitable description available equally to both and if we want to compare them,
compare the moral status of these practices, we should use either the charitable descriptions of each
or the uncharitable descriptions of each. The uncharitable descriptions in each case doesn't refer to
the end being aimed at, but instead to the foreseeable, though undesirable effect.

So it would be fair to say that with Charles and with Outka's paper that in the case of creating an
embryo for the sake of biomedical research to describe that as creating an embryo in order to destroy
it, but only in the same sense that we should describe creation of embryos for reproduction purposes
as the creation of embryos in order to discard the inevitable extras that will accompany the practice
of IVF. So both activities admit of charitable and uncharitable descriptions and if we're going to
compare their moral status, we should compare them either under one description, the things they
aim at or under the other description, the foreseeable, but undesirable side effects that accompany
both.

DR. KRAUTHAMMER: Michael, I'm surprised that you also made an uncharacteristic slip when
you said the inevitable destruction of the embryos in IVF because you know, as I know, we could, in
principle, establish an IVF clinic tomorrow in which you assign only a single embryo to a woman. So
you would thereby have a process of IVF where you have no inevitable, indeed, indeed no discarded
embryos.

On the other hand, in cloning, it is absolutely inevitable that that embryo, because it will be
disassembled, will be destroyed.

PROF. SANDEL: Well, if the practice of creating embryos for reproductive purposes involved no
spares, no extras, then it would have a different moral status and character from the practice we
currently have.

CHAIRMAN KASS: Elizabeth?

DR. BLACKBURN: It would be different from natural which, in fact, if anything the majority of
embryos naturally are lost and destroyed —

DR. KRAUTHAMMER: We'd be improving on God.

DR. BLACKBURN: That's good.

PROF. SANDEL: What the natural case Elizabeth raises is the — there's also an uncharitable
description of natural procreation which would be very odd, which is you're engaging in the
inevitable creation of spare embryos that will be sacrificed for the sake of having one that works.

DR. BLACKBURN: Well —

PROF. SANDEL: And there's no more warrant for that description than for the contentious version
of the description in the cloning for medical research case.

**DR. BLACKBURN:** Well, I think it might be helpful to return to somewhat more the homely and something Gil said that he said to me, well, would you say the blastocyst, if it were yours versus the child and I think I wouldn’t be able to look the parents of the child in the face if I hadn’t made an attempt to save the child. And I think that also addresses the issue of should we be trying to do cures, even though we know that they’re not inevitably going to work tomorrow, next year, 10 years or 20 years. I think we have to try and so I think this question of the fact that we don’t have successful answers right now for whether embryonic stem cells or somatic cell nuclear cloning is going to work, I don’t think that absolves us from the necessity to try when we see real human disease and suffering that we should try to act on, even though we know we may not be necessarily successful in every attempt.

**CHAIRMAN KASS:** Gil, and I then I think I would like to put my oar in and I’ll give rebuttals, but we should probably wind up. We need a nap before we drink, right?

**PROF. MEILAENDER:** Well, just a couple of things quickly. To pick up Elizabeth’s point again. The hypothesis was and I think it’s worth thinking about, the hypothesis was that you could only save one of the two entities, so that I don’t know how we set up this case the way the philosophers do it, but there’s a fire and you can go up one stair to save the newborn in the crib who’s not yours or you can go up the other stairs to save the blastocyst in vitro that is yours. Okay?

**CHAIRMAN KASS:** That’s a copy of your dead child, if you want to make it —

**PROF. MEILAENDER:** Whatever. It’s not — it’s not immediately apparent, kind of, that one choice must be made and that suggests that there are other considerations and it’s not just stage of development. The other thing I just wanted to say in response to what Michael — just — I mean Gene Outka can sort of take care of himself, but as a matter of interpretation, I think he didn’t quite grant what you described him as granting. I think he granted that creating in order to destroy was a tendentious description. He did not grant that the two situations were the same where he had recourse or double effect line which because he did still think that in the description of the one act, the killing was inextricably involved and I take that’s really what Charles was getting at. So it isn’t in terms of what he was granting, I want to be clear.

**CHAIRMAN KASS:** Okay, I’m winding up to — I want to say a couple of substantive things, but come to a procedural suggestion for what we should do next. First, since Jim Wilson began by being surprised that he could disagree with Charles, I’m surprised that I have to disagree with Jim Wilson with whom I’ve disagreed only once before and he since told me that I’ve persuaded him, but I’m not going to do it again.

**DR. WILSON:** Not this time.

**CHAIRMAN KASS:** The slippery slope, to call something a slippery slope argument is already to put it in a category where you can abstract it and then say you like those arguments or you don’t. Rather, it seems to me, it’s worth thinking about, not in general in the light of other examples, but to think about it in the context of the particular thing we are talking about.

I think I might have said once before that the reason that arguments about continuity of action are so appropriate in the area that we are here talking about is because development is itself a continuum and the value of the thing being developed, never mind morally, but biologically, increases with development and if it should turn out that tissues down the road are really more valuable for the treatment of the same patients we now want, the argument that’s now being made for doing it will be very hard to resist.

The real essence of the slippery slope argument is not a prediction, an empirical prediction. It is a question of the logic of justification and it’s very important how you somehow justify what you’re doing here because if, as in this area, the continuity of development and the continuity of research offers such great promise, you might, without even knowing it, be countenancing the next sort of stages and in the end you will wind up as Bertrand Russell said about pragmatism. It’s like a warm bath. It warms up so imperceptibly you don’t know when to scream. Eventually, we will get to some place that none of us would want to be and we therefore have to be very careful. It’s not a prediction of a certain kind of certainty, although we have seen, I mean five years ago The Washington Post editorialized on this question. No creation of embryos, especially for research — use these others. The newspapers are no better than the Senators on this and times change and there were no stem cells five years ago. The benefits to be had were less.
I think it's very important that we, instead of calling this a slippery slope argument, talk about the question of prudence and if we put it in those terms, then the question is: Is it really prudent to head down this road and I don't think you have to believe that the embryo is a full human person, at least to be worried, not just about what's — the destruction question. It may be a terrible thing to say in public, but I worry much less about the destruction of the embryos as I worry about the exploitive mentality on the part of not just the scientists, scientists are trying to do good, but of a community that comes to accept as routine, the instrumentalization of nascent life and in which we become sort of desensitized to this. This is not a question about the ontological status of the embryo, but about how we come to regard those earlier stages of our own being. I don't know what they are, but that they're somehow part of a continuity with what we are. Of that, as a biologist and not as a religious figure, I mean I see the continuity.

Two other things, just for your thought. I don't want to harangue much longer. The IVF case has been around a number of times, but let me suggest one thing. The fact that there are a lot of embryos lost in normal sexual procreation doesn't settle anything. It doesn't really settle anything. And it seems to me one could say something like this with respect to that in the IVF clinics. When a couple now undertakes to procreate by ordinary sexual means, if they've learned the facts about this, they know that they are saying yes to the sad fact that there will be a lot of loss.

That's just the way things are and without going Charles' route about improving God's way, when a couple now goes to the IVF clinic even with the extra embryos, they are saying yes in advance to the sad necessity that some of these embryos are going to be frozen in perpetuity or put to some kind of use. They're simply compressing into one month or into one visible time what in ordinary biology might take months. Well, situations are fairly comparable. I think it is a matter, somewhat different when you undertake to produce the embryos for the purpose of exploiting them for use in which the destruction is — I won't say a minor thing, but it is the deliberate exploitive disposition is what bothers me.

Lastly, to Elizabeth, if I might, the lurid cases are wonderful for focusing the mind and the examples, both of the business about the child and the exchange we had last time between Michael Sandel and Robby George about dismembering one's 2-year-old child for the organs and dismembering a blastocyst for the cells spoke, it seems to me, volumes. It seems like for my own sake a knockout case.

On the other hand, I'll give you another knockout case and we can wander away and ponder it. Let's imagine that you've got the last couple on earth and a couple of embryos and he has Alzheimer's disease. And the question is, do you sacrifice the embryos for the sake of the cure of the living or do you allow them to be what they in fact are, biologically speaking, the seed of the next generation? We can force ourselves not to look at that because there are so many extra seeds, but if you somehow focus the question and ask, then the merely instrumental use of this seed, even though it doesn't have a nervous system somehow begins to look rather different.

There's a lot there to be quarreled with and I probably abuse the privilege of the chair, but there were a number of things floating around here that only make the subject for me more complicated.

What we'll sort out finally is we have to move forward on this. I think if I understand the discussion here and Paul, you and I will have to work out a way to find room for your so far eccentric, that doesn't mean wrong, but unique position in this conversation, whether you want to have a separate —

DR. MCHUGH: I'm glad you say it doesn't mean wrong. One could be —

CHAIRMAN KASS: On this point we agreed last time that we don't want to simply decide on the basis of the wisdom of the vote of the majority to silence any arguments sincerely held and properly defended. It might very well be that an argument made and held by one person is the best argument and we would deprive our readers of the benefit of having to weigh that.

I'm serious about that.

DR. MCHUGH: I appreciate that.

CHAIRMAN KASS: And it goes across the board. I think we have to tidy up our work on the ethics of this and move on to the policy questions by the next time we gather.

I would like to ask everybody here, if they haven't already, if things that haven't been passed before you don't already speak for you and there are some people who we haven't properly, I think, taken
care of. If you would write from 3 to 5 pages and if it turns out that the argument is shorter, less, a statement of your view not on the question of ban or no ban, the policy question, but on the question of the morality of cloning for biomedical research and let’s have it in two weeks and then we can put this particular part of our discussion in a form that can be circulated for everyone’s approval. I hope that’s not too onerous. If there’s anybody who’s writing another paper for another course, I’ll give you an extension, but tomorrow morning we meet at 8:30 to take up the enhancement discussion and then the regulatory discussion. Thank you for your endurance, your patience, your good will and we’re adjourned.

(Whereupon, at 5:33 p.m., the meeting was adjourned.)
Leon R. Kass, M.D., Ph.D.

COUNCIL MEMBER

Leon R. Kass, M.D., Ph.D., is the Addie Clark Harding Professor in the Committee on Social Thought and the College at the University of Chicago and Hertog Fellow in Social Thought at the American Enterprise Institute. He was chairman of the President’s Council on Bioethics from 2001 to 2005.

A native of Chicago, Dr. Kass was educated at the University of Chicago where he earned his B.S. and M.D. degrees (1958; 1962) and at Harvard where he took a Ph.D. in biochemistry (1967). Afterwards, he did research in molecular biology at the National Institutes of Health, while serving in the United States Public Health Service.

Shifting directions from doing science to thinking about its human meaning, he has been engaged for more than 30 years with ethical and philosophical issues raised by biomedical advance, and, more recently, with broader moral and cultural issues. From 1970-72, Dr. Kass served as Executive Secretary of the Committee on the Life Sciences and Social Policy of the National Research Council/National Academy of Sciences, whose report, *Assessing Biomedical Technologies*, provided one of the first overviews of the emerging moral and social questions posed by biomedical advance.

He taught at St. John’s College, Annapolis, MD, and served as Joseph P. Kennedy, Sr., Research Professor in Bioethics at the Kennedy Institute of Ethics at Georgetown University, before returning in 1976 to the University of Chicago, where he has been an award-winning teacher deeply involved in undergraduate education and committed to the study of classic texts.


His widely reprinted essays in biomedical ethics have dealt with issues raised by in vitro fertilization, cloning, genetic screening and genetic technology, organ transplantation, aging research, euthanasia and assisted suicide, and the moral nature of the medical profession.

Dr. Kass is married to Amy Apfel Kass, Senior Lecturer in the Humanities at the University of Chicago and Senior Fellow at the Hudson Institute. The Kasses have two married daughters and four young granddaughters.

Return to Council Member List :: next >>
**REBECCA DRESSER, J.D., M.S.**

**COUNCIL MEMBER**

ELIZABETH BLACKBURN, PH.D.

COUNCIL MEMBER

January 16, 2002, to March 10, 2004

Elizabeth Blackburn, Ph.D., Professor, Department of Biochemistry and Biophysics, University California San Francisco.

Professor Blackburn, a distinguished cell biologist whose research is on telomerase and chromosome telomere structure, holds a number of awards and prizes, including the California Scientist of the Year Award (1999); American Association for Cancer Research-Pezcoller Foundation International Award for Cancer Research (2001); the General Motors Cancer Research Foundation Alfred P. Sloan Award (2001); and the 26th Annual Bristol-Myers Squibb Award for Distinguished Achievement in Cancer Research (2003). She is an elected Foreign Associate of the National Academy of Sciences (1993), and was elected as a Member of the Institute of Medicine (2000). Dr. Blackburn is an elected Fellow of the American Academy of Arts and Sciences (1991); the Royal Society of London (1992); the American Academy of Microbiology (1993); and the American Association for the Advancement of Science (2000). She has also served as President of the American Society for Cell Biology (1998).
Daniel Foster, M.D. John Denis McGarry, Ph.D. Distinguished Chair in Diabetes and Metabolic Research, University of Texas Southwestern Medical School. Dr. Foster, whose research is in intermediary metabolism, has received the Banting Medal, the Joslin Medal, the Tinsley R. Harrison Medal and the Robert H. Williams Distinguished Chair of Medicine Award for his work. He is a member of the Institute of Medicine of the National Academy of Sciences and is a Fellow of the American Academy of Arts and Sciences. He was chairman of the Department of Internal Medicine at UT Southwestern for 16 years.
FRANCIS FUKUYAMA, PH.D.

COUNCIL MEMBER

Francis Fukuyama is Bernard L. Schwartz Professor of International Political Economy at the Paul H. Nitze School of Advanced International Studies of Johns Hopkins University.

Dr. Fukuyama’s book, *The End of History and the Last Man*, was published by Free Press in 1992 and has appeared in more than twenty foreign editions. It made the bestseller lists in the United States, France, Japan, and Chile, and has been awarded the *Los Angeles Times*’ Book Critics Award in the Current Interest category, as well as the Premio Capri for the Italian edition. He is also the author of *Trust: The Social Virtues and the Creation of Prosperity* (1995); *The Great Disruption: Human Nature and the Reconstitution of Social Order* (1999); and *Our Posthuman Future: Consequences of the Biotechnology Revolution* (2002). His most recent book, *State-Building: Governance and World Order in the 21st Century*, was published by Cornell University Press in the spring of 2004.

Dr. Fukuyama has written widely on issues relating to questions concerning democratization and international political economy. He has, in recent years, focused on the role of culture and social capital in modern economic life, and on the social consequences of technological change.

Francis Fukuyama was born in Chicago on October 27, 1952. He received his B.A. from Cornell University in classics, and his Ph.D. in political science from Harvard. He was a member of the Political Science Department of the RAND Corporation from 1979-1980, then again from 1983-89, and from 1995-96. In 1981-82 and in 1989, he was a member of the Policy Planning Staff of the US Department of State, the first time as a regular member specializing in Middle East affairs, and then as Deputy Director for European political-military affairs. In 1981-82 he was also a member of the US delegation to the Egyptian-Israeli talks on Palestinian autonomy. From 1996-2000 he was Omer L. and Nancy Hirst Professor of Public Policy at the School of Public Policy at George Mason University.

Dr. Fukuyama is a member of the President’s Council on Bioethics. He holds an honorary doctorate from Connecticut College and Doane College, and is a member of advisory boards for the National Endowment for Democracy (NED), *The National Interest*, the *Journal of Democracy*, and The New America Foundation. As an NED board member, he is responsible for oversight of the Endowment’s Middle East programs. He is a member of the American Political Science Association, the Council on Foreign Relations, the Pacific Council on International Policy, and the Global Business Network. He is married to Laura Holmgren and has three children.
MICHAEL S. GAZZANIGA, PH.D.

COUNCIL MEMBER

Michael Gazzaniga, Ph.D., is the outgoing David T. McLaughlin Distinguished University Professor in Cognitive Neuroscience and Director of the Center for Cognitive Neuroscience at Dartmouth College and the incoming Director of Sage Center for the Study of Mind at the University of California, Santa Barbara. Dr. Gazzaniga conducts research on how the brain enables the mind. He is a fellow of the American Neurological Association, as well as the president of the American Psychological Society and a member of the American Academy of Arts and Sciences and the Institute of Medicine. His publications include *Cognitive Neurosciences III* (2004), *The New Cognitive Neurosciences* (2000) and *The Mind's Past* (1998). His new book, *The Ethical Brain*, was published in 2005.
ROBERT P. GEORGE, J.D, D.PHIL.

COUNCIL MEMBER

Robert P. George is McCormick Professor of Jurisprudence and Director of the James Madison Program in American Ideals and Institutions at Princeton University.


In 2008, Professor George received the Presidential Citizens Medal at a ceremony in the Oval Office of the White House. He is a winner of the Bradley Prize for Intellectual and Civic Achievement; the Sidney Hook Memorial Award of the National Association of Scholars; and the Philip Merrill Award for Outstanding Contributions to the Liberal Arts of the American Council of Trustees and Alumni.

A graduate of Swarthmore College and Harvard Law School, Professor George earned a doctorate in philosophy of law from Oxford University. He was elected to Phi Beta Kappa at Swarthmore, and received a Knox Fellowship from Harvard for graduate study in law and philosophy at Oxford. He holds honorary doctorates of law, letters, science, ethics, civil law, humane letters, and juridical science.

Professor George is a member of UNESCO’s World Commission on the Ethics of Scientific Knowledge and Technology. From 1993-98, he served as a presidential appointee to the United States Commission on Civil Rights. He is also a former Judicial Fellow at the Supreme Court of the United States, where he received the 1990 Justice Tom C. Clark Award. He is the recipient of a Silver Gavel Award of the American Bar Association, the Paul Bator Award of the Federalist Society for Law and Public Policy. In 2007 he gave the John Dewey Lecture in Philosophy of Law at Harvard. In 2008 he gave the Judge Guido Calabresi Lecture at Yale and the Sir Malcolm Knox Lecture at the University of St. Andrews in Scotland.

Professor George is a member of the Council on Foreign Relations, and serves as Of Counsel to the law firm of Robinson & McElwee.

<< previous :: Return to Council Member List :: next >>

The President’s Council on Bioethics

Home Site Map Disclaimers Privacy Notice Accessibility NBAC HHS
MARY ANN GLENDON, J.D., M.COM.P.L.

COUNCIL MEMBER

Mary Ann Glendon, J.D., L.L.M. Learned Hand Professor of Law, Harvard University. Professor Glendon teaches and writes on international human rights, comparative law, and constitutional law issues. The National Law Journal named her one of the "Fifty Most Influential Women Lawyers in America" in 1998. She is the author of Rights Talk; A Nation Under Lawyers; and A World Made New: Eleanor Roosevelt and the Universal Declaration of Human Rights.
ALFONSO GÓMEZ-LOBO, DR. PHIL.

COUNCIL MEMBER

Alfonso Gómez-Lobo, Dr. phil. Ryan Family Professor of Metaphysics and Moral Philosophy, Georgetown University. Professor Gómez-Lobo specializes in Greek philosophy, Greek historiography, the history of ethics, and contemporary natural law theory. He is the recipient of several awards, including a research fellowship from the Guggenheim Foundation. His latest book, *Morality and the Human Goods*, was published by Georgetown University Press in 2002.

<< previous :: Return to Council Member List :: next >>

The President’s Council on Bioethics
Home Site Map Disclaimers Privacy Notice Accessibility NBAC HHS
WILLIAM B. HURLBUT, M.D.

COUNCIL MEMBER

William B. Hurlbut, M.D. Consulting Professor, Department of Neurology and Neurological Sciences, Stanford Medical Center, Stanford University. Dr. Hurlbut's main areas of interest involve the ethical issues associated with advancing biotechnology and neuroscience, the evolutionary origins of spiritual and moral awareness, and the integration of philosophy of biology with theology. He has worked with the Center for International Security and Cooperation on a project formulating policy on Chemical and Biological Warfare and with NASA on projects in astrobiology. He is the author of "Altered Nuclear Transfer," a technological proposal to our nation's impasse over stem cell research.
CHARLES KRAUTHAMMER, M.D.

COUNCIL MEMBER

Charles Krauthammer, M.D., Syndicated columnist. Dr. Krauthammer, a board-certified psychiatrist who received his medical degree from Harvard Medical School and practiced psychiatry at Massachusetts General Hospital for several years, writes a nationally syndicated editorial page column for The Washington Post Writers Group. He won the 1987 Pulitzer Prize for distinguished commentary. For 20 years, he has written articles on several bioethical topics, including human experimentation, stem cell research, cloning, euthanasia, and assisted suicide.

Dr. Krauthammer was a recipient of the Inaugural (2003) Bradley Prize, awarded by the Lynde and Harry Bradley Foundation, as well as the recipient of the 2004 Irving Kristol Award, given by the American Enterprise Institute.
PAUL McHUGH, M.D.  

COUNCIL MEMBER

Paul R. McHugh, M.D. is the University Distinguished Service Professor of Psychiatry at the Johns Hopkins University School of Medicine. He was the Henry Phipps Professor of Psychiatry, Director of the Department of Psychiatry and Behavioral Sciences at the Johns Hopkins University School of Medicine, and psychiatrist-in-chief at the Johns Hopkins Hospital from 1975-2001. He is the author of 4 books and more than 150 papers.
Gilbert Meilaender, Ph.D.

Council Member

Gilbert Meilaender, Ph.D. Richard & Phyllis Duesenberg Professor of Christian Ethics at Valparaiso University. Professor Meilaender is an associate editor for the Journal of Religious Ethics. He has taken a special interest in bioethics and is a Fellow of the Hastings Center. His books include Bioethics: A Primer for Christians (1996, 2005), Body, Soul, and Bioethics (1995). He has recently edited (together with William Werpehowski) The Oxford Handbook of Theological Ethics.

<< previous :: Return to Council Member List :: next >>
Janet D. Rowley, M.D., D.Sc., Blum-Riese Distinguished Service Professor of Medicine, Molecular Genetics and Cell Biology, and Human Genetics, Pritzker School of Medicine, University of Chicago. Dr. Rowley is internationally renowned for her studies of chromosome abnormalities in human leukemia and lymphoma. She is the recipient of the National Medal of Science (1999) and the Albert Lasker Clinical Medicine Research Prize (1998), the most distinguished American honor for clinical medical research.
MICHAEL J. SANDEL, D.PHIL.

COUNCIL MEMBER

Michael J. Sandel, D.Phil., Professor of Government, Harvard University. Professor Sandel, who was a Rhodes Scholar, teaches contemporary political philosophy and the history of political thought. Sandel's books include *Democracy's Discontent: America In Search of a Public Philosophy* (1996) and *Liberalism and the Limits of Justice* (1982). He has received fellowships from the Ford Foundation, the American Council of Learned Societies, and the National Endowment for the Humanities.

<< previous :: Return to Council Member List :: next >>
JAMES Q. WILSON, PH.D.

COUNCIL MEMBER

James Q. Wilson, Ph.D. The James A. Collins Professor of Management and Public Policy Emeritus at the University of California Los Angeles and a lecturer at Pepperdine University. Professor Wilson, one of the nation's most respected political scientists, has written extensively on human nature and ethics. His publications include The Moral Sense (1997) and Moral Judgment: Does the Abuse Excuse Threaten Our Legal System? (1998). He has received numerous awards and honors, including the Presidential Medal of Freedom.

<< previous :: Return to Council Member List >>

The President's Council on Bioethics

Home Site Map Disclaimers Privacy Notice Accessibility NBAC HHS