Quote to note

"Sheik Ahmed was frustrated that more people were not interested in hearing his message that their own sinful behavior had prompted the sea to swell."

> — Hafun, Somalia The New York Times January 13, 2005

Inside

Ask the ethicist

Should this 96-year-old woman be	
allowed to die?	
By Xiuyun Yin, PhD	
Benfu Li, MD	
Yali Cong, PhD	

The legal column

Legal issues in the use of controlled substances in pain management By Sandra Johnson, JD, LLM

A medical ethics forum from Harvard Medical School

Stem Cell Research: Science, Ethics and Policy Dan W. Brock, PhD George Q. Daley, MD, PhD Michael J. Sandel, DPhil Jonathan D. Moreno, PhD

Ethics and the humanities

"Ward No. 6" By Anton Chekov Discussed by Jack Coulehan, MD, MPH *9*

Dialogue

Bioethics in space By Paul Root Wolpe, PhD Walter M. Robinson, MD, MPH

The opinions expressed in the journal, Lahey Clinic Medical Ethics, belong to the individual contributors and do not represent the institutional position of Lahey Clinic on any subject matters discussed.

This issue is dedicated to the memory of our esteemed colleague and managing editor Patricia Busacker.

Lahey

in collaboration with Dartmouth-Hitchcock Medical Center



Human Gene Banks

The past five years have seen a new wave of interest in the storage of human genetic materials. This interest partly reflects increased knowledge of genetics and partly the hope of further understanding and new applications.

On the one hand, states – and especially their police forces – have seen that quite basic existing genetic knowledge is of great use to them. The ability to identify individuals in terms of a near unique "genetic fingerprint" has already proven forensically very valuable. As the number of samples held in police databases increases, so too does the usefulness of these databases for linking samples found at crime scenes with individual identities.

On the other hand, medical and scientific interest in genetics begins with the fact that we have barely begun to decipher the meaning of this identifying data. We can identify some mutations of single genes that result in rare and extreme diseases - a good example is Huntington's disease. But in most cases the connections between human genetic variability and health remain hidden, and we have hardly any knowledge concerning the interaction of large numbers of genetic variations. Given our poor understanding of gene expression, the best weapon to study these is sheer statistical force – to compare health outcomes across large numbers of people with their genetic variations. To do this, new human gene banks orders of magnitude larger than the many well-established gene banks dedicated to the study of particular diseases are needed.

Not only is banking "genes" important – we also need information about the

Garrath Williams,PhD Lancaster University, Lancaster, UK

health or phenotype of the sample donor. In the large-scale research gene banks that have attracted much recent attention, this personal information is meant to be continually updated. This has the significant implication that samples cannot be made fully anonymous; otherwise, we could never link new data back to the original sample. Our ability to identify individuals on the basis of genetic samples means that gene banks pose significant privacy issues that will only increase as we become better able to decipher genetic information.

Bioethics has given the most attention to human gene banks for medical research. This is natural, in that bioethics is especially concerned with research and human health. Also much more publicity has surrounded these projects. But something is odd about this emphasis, because the biggest, best funded and most effective human gene banks are forensic ones. The UK National Police Database, for instance, includes samples from 2.75 million people (September 2004) – twice as many as it did two years ago – and is still growing.¹

By contrast, the gene banks that have attracted recent attention remain more promise than reality. The two best known examples are the Icelandic Health Sector Database² and UK Biobank,³ neither of which has yet gathered any genetic samples. In the US, an interesting third example is First Genetic Trust,⁴ a private company that essentially mediates between researchers and individual donors.

The Icelandic database has been controversial for several reasons. Meant to include the entire population of Iceland -270,000

Gene Banks continued on page 2

Gene Banks continued from page 1

people - it features medical data on an "opt-out" basis: that is, individuals are not asked for their consent, but may register their dissent and withdraw from the database. So far, only a small minority of the Icelandic population has opted out. Moreover, the database has been licensed, by act of Parliament, for a twelve-year period to the company deCode Genetics,⁵ closely linked with Hoffman La Roche. As many see it, the genetic heritage and health data of the Icelandic people have been sold to a private company at a low price and with scant regard for the principle of informed consent. However, although the license was granted in 1998, deCode has yet to gather any genetic samples.

By contrast UK Biobank is intended to include more samples – 500,000 – from only a subset of the British population – 45- to 69-year-olds (the age range when many common diseases of Western societies set in). Research subjects, who must specifically consent, will complete lifestyle and health questionnaires as well as grant access to their health care records. Funded by the UK government and its Medical Research Council as well as the Wellcome Trust (the world's largest medical research charity), UK Biobank will be open to both public and private researchers on terms yet to be announced.⁶

Two obvious issues for human genetic banking are posed by these cases: commercial exploitation and the consent of individual research subjects. Samples and information have often been spoken of as gifts by the donor (the reference is to Titmuss's work on blood donation in the context of a publicly funded health care system).7 "Gift" is ambiguous, though. Donation is a free and consensual act; the sample is donated supposedly with no thought of return or recompense. Yet while people may be happy to give to public health research, this may be because they receive ongoing benefits from that system - so that gifts are not quite so one-sided as may be thought. It is less clear that people are, or should be, so willing to "give" to profit-making entities.

Consent is problematic because these proposed gene banks promise a new form of health research, one that is essentially collective and peculiarly open-ended – aiming to learn more about the relations between genetic variation and health. This seems to render informed consent impossible: Researchers cannot tell donors in advance what their sample and data will be used to research. The sheer scale of the projects also makes asking donors about each individual study quite impractical – something one might anyhow think burdensome to individuals and problematic from a privacy point of view. Commentators and policy documents, therefore, tend to speak of "blanket" or "broad" consent.

Beyond this, it is not clear that these massive new biobanks represent a sensible priority for research. Gathering high-quality data for such a large number of people seems impractical. Perhaps the best that the large gene banks can do is to facilitate the identification of a much smaller pool suitable for intensive investigation of a particular drug or condition. In this case, how important the gene bank was in the first place is open to question; the many much smaller disease-specific banks would serve just as well. Likewise, the promise of technologies for population genetic screening is unlikely to be realized or to represent a sound public health investment: We already know that most chronic ill-health and premature death in Western societies owes to factors such as diet and exercise patterns, not to mention wealth inequalities. Testing individual genetic predispositions can only be the most minor supplement to addressing those factors.

Doubts of this sort may have slowed private investment in large scale, openended biobanks over the past couple of years - resulting in the failure of deCode to begin collecting genetic samples. Markets and private companies are unlikely to sink large sums into projects whose pay-offs are so uncertain. This leaves biobanking in the hands of public and charitable concerns where one may think ensuring that investments are directed to public health benefits is much more important. But because a project like UK Biobank is so enormous a £60 million budget (\$120 million), which many suspect is only the beginning - it has escaped the usual processes of scientific peer review. Yet if we are going to place less weight on informed consent than we do for standard medical research – as it seems we must if such projects are to be practicable – then clearly we must place much more weight on scientific and public

scrutiny. That is, we must be sure that the projects are both scientifically well conceived and reflect proper public priorities for research. My own view, in line with the doubts sketched in the preceding paragraphs, is that such a case has simply not been made.

Interesting parallels and illuminating differences exist between forensic and medical biobanks. Costly as forensic biobanks are, they are certainly much cheaper overall, because they do not require the same sort of detailed data collation as research biobanks. Their benefits, in terms of crime detection if not crime prevention, are much clearer and more immediate. Consent has not been thought an important principle in the case of forensic banks - it would be plainly absurd for police forces to have to require consent from someone they have good basis to suspect of a serious crime. At the same time, it is disturbing that forensic databases have attracted even less debate than research biobanks – despite the fact that they pose serious privacy issues and represent a huge potential growth in state power.

While few bioethicists are willing to endorse the Icelandic example and bypass consent entirely, it now seems clear that individual consent is not the most important issue posed by this new form of collective and prospective medical research. Much more central is whether research biobanks represent a well-conceived priority.⁸ This question may be even more difficult to debate than in the case of the forensic databases; yet it surely deserves to be debated more vigorously and more widely than it has so far.

¹Williams R, Johnson P, Martin P. Genetic Information & Crime Investigation. London: Wellcome Trust; 2004. Available at http://www.dur.ac. uk/p.j.johnson/

²http://brunnur.stjr.is/interpro/htr/htr.nsf/pages/ gagngrens.htm

3http://www.ukbiobank.ac.uk/

⁴http://www.firstgenetic.net/

⁵http://www.decode.com/

⁶See the excellent briefing papers on UK Biobank by Genewatch: http://www. genewatch.org/

⁷Titmuss, RM *The Gift Relationship*. Oakley A, Ashton J, eds. Rev ed. New York: The New Press; 1997.

⁸See also Ruth Chadwick "The Icelandic Database – Do Modern Times Need Modern Sagas?" *Br Med J* 1999;319:441–444.

Ask the ethicist: Should this 96-year-old woman be allowed to die?

uestion: A 96-year-old-woman is on a mechanical ventilator in the Intensive Care Unit (ICU) because of respiratory failure. She has multiple medical problems that include a severe cardiomyopathy and cerebrovascular disease. The patient had previously told her physician she did not want to be placed on a mechanical ventilator or resuscitated. However, her children have insisted that all life supports be continued and have specifically requested the placement of a feeding tube.

The health care team is distressed, because they believe continued treatment is almost surely futile, the patient is suffering needlessly and that by honoring the family's wishes they are violating the patient's wishes.

How would an ethicist in China advise the health care team?

esponse: Recently, a similar case involved one of our colleagues whose 84-year-old mother was hospitalized in the ICU with multiple organ failure. The health care team consulted with the colleague about whether to use a mechanical ventilator because of respiratory failure, since otherwise, her mother would die soon. Having taken care of her mother for many years, the colleague often heard her mother say that she did not want to be placed on a mechanical ventilator or resuscitated at the end of life. But other family members, especially the elder brother, didn't agree with her wish to act in accordance with her mother's will.

Her mother was placed on a mechanical ventilator and given full medical treatment. Several days later, no miracle happened, and all family members agreed unanimously to withdraw the breathing machine and stop treatment. The mother died soon afterward.

This may be the most common way such problems are resolved currently in China. First, the key element of clinical decision-making is not the will of either the patient or the health care team, but that of the patient's family members. The "patient" has a special role in Chinese society and is viewed as someone who deserves care and love and should be free of responsibilities, such as decision-making. Although usually a group decision, it may be expressed by the most authoritative family member, such as the patient's spouse or an adult child if the patient doesn't have a spouse. Sometimes it is the elder son; usually it is the one who contributes most to the family.

The health care team's advice is very important and usually accepted by the family. The ethical issues here are not only the advice itself, which may be the opinion of the physician in charge (and may be wrong), but also potential conflicts of interest. If there are spare beds in the hospital, the physicians may prefer to accept the patient and administer futile treatment in order to raise the income of the hospital. Conversely, if a patient doesn't pay the hospital, the doctor will be under pressure from his department and the hospital to discharge the patient.

In the case of the 96-year-old mother, in the US health care team's view, the treatment is almost surely futile. But a Chinese health care team would not inform the family member that it is "surely futile," except in the state of brain death,¹ when the mechanical ventilator cannot prolong life. We can say that the Chinese health care team usually views the situation from the standpoint of "quantity" (how long the patient will live), rather than "quality of life." The question the health care team usually asks family members is "Do we give up treatment or not?" and the answer of family members at first usually is don't give up, whether or not the patient has expressed his or her wish for continued treatment. But how long treatment lasts depends on the cost, whether the cost can be covered by patient's insurance and the economic condition of the family. If the economic condition is not good, the treatment will be stopped after a short period. The cost for one day on a mechanical ventilator is 500 yuan (\$60.39) or 15,000 yuan (\$1812) a month; the average monthly income in China is 1022.62 yuan (\$123.50).2 Therefore, these expenses can be a large amount for a family.

To properly analyze this question, we need to clarify several cultural differences:

1) In the United States, the ethical issue is whether to withdraw treatment. This is not the issue in China, where the decision to "give up" treatment is, in fact, commonly made for economic reasons.

2) There are differences in the role of family members. In Chinese tradition each member of the family is not an isolated person but part of the family; family members usually share a similar mindset with the patient, which reflects the family members' emotions and the effects of external pressure from other people who may judge them to be lacking in filial piety if they don't treat the patient. The treatment, even if futile, may last for a time during which the family can adjust psychologically. Otherwise, they will feel guilty.

3) Another significant difference is in the United States, the health care team is distressed by having to administer futile treatment and violate the patient's wishes. Whereas, in China, it is uncommon for the health care team to raise such questions, for they will not regard the interests between patient and family members as in conflict. Only if the whole family has made a decision will the health care team act according to the family's requirement. When the health care team is distressed, usually it is because they think the patient should be treated and believe there would be a good outcome, but the family members don't agree due to the lack of financial support or other reasons.

Theoretically speaking, the ethical issue in such a case is who can represent the best interest of the patient. The US health care team's distress relates to issues of autonomy, both their autonomy and the patient's. But in China, the health care team and whole family share similar values, that is, for the best interest of the patient. Here the "best interest of the patient" is not seen from the view of the patient, but of the health care team and all the family members.

The autonomy and voice of the patient in China has begun to emerge (but not strongly enough) with more attention paid to the patient; however, decisions are still usually made by the family. The patient is not regarded as a person who has the capacity to make decisions, so the health care team will not be troubled by the patient's wish for termination of treatment or by any violation of patient autonomy. Informed

Ask the Ethicist continued on page 12

The legal column: Legal Issues in the Use of Controlled Substances in Pain Management

This recently, legal risks for the medical neglect of pain have been nearly nonexistent, while the physician who treated patients for pain with medications that are controlled substances faced significant risks, including disciplinary action by the state medical board.

Research in the mid-1990's indicated that standards used by state medical boards to review the prescribing practices of physicians treating patients in pain did not conform to newer knowledge and practice patterns, especially for patients in chronic pain. Instead, boards appeared to rely solely on the amount and duration of the prescription of controlled substances and to reject evidence of patients' improved function and pain relief.¹ For example, in 1996, the Florida Court of Appeals rejected disciplinary action against a physician who prescribed controlled substances for pain management, noting that it was "surprising to see agency disciplinary action based upon such a paucity of evidence." In this case, the board's experts had relied solely on pharmacy prescription records and had not evaluated any patients or reviewed any patients' medical records.2

In response to this research, the Federation of State Medical Boards developed "Model Guidelines for the Use of Controlled Substances for the Treatment of Pain."³ The Model Guidelines made three significant policy statements. First, the guidelines stated that controlled substances "may be essential in the treatment of acute pain... and chronic pain." Second, the guidelines rejected "quantity and chronicity" alone as the basis of inappropriate prescribing. Third, the guidelines required certain practice management techniques including physical examination of patients, documentation and appropriate consultation.

In a 2004 revision, the Federation defines "inappropriate treatment of pain" to include "nontreatment, undertreatment, overtreatment and the continued use of ineffective treatments" and specifically recognizes that state medical boards should "consider inappropriate treatment of pain to be a departure from standards of practice..."⁴

At least 40 states have adopted policies, guidelines or regulations governing disciplinary actions related to prescribing for pain.⁵ In addition, at least 23 states now have statutes relating to prescribing for pain, and almost all of these statutes provide physicians with immunity from any disciplinary action if the physician complies with certain requirements.⁶ These immunity statutes typically require that the prescribing be for "therapeutic purposes" or meet accepted standards for medical practice. The statutes do not protect physicians who do not maintain documentation of examination and evaluation of the patient, or who self-prescribe or write false prescriptions. A survey completed in 2002 indicated that attitudes of state medical boards have improved creating a less hostile environment for the use of controlled substances for pain relief.7

Liability for Neglect of Pain

Some advocate increasing the risk of liability for neglect of pain. They believe this can counteract physicians' undertreatment of pain to the extent undertreatment is based on a fear of disproportionate legal risk for prescribing pain medication, outdated knowledge or carelessness.

Two landmark cases have imposed liability on physicians for neglecting pain. In Bergman v. Eden Medical Center and Tomlinson v. Bayberry Care Center, the surviving family members of two patients in California filed suit against the physicians, hospitals and the nursing homes that cared for the patients.⁸ In Bergman, the jury returned a verdict of \$1.5 million, which the court reduced to \$250,000. In Tomlinson, the defendants settled with the plaintiffs for undisclosed sums.

In each of these cases, the patient had terminal cancer and received patently inadequate medication for pain. There is a strong medical and legal consensus that the pain associated with terminal cancer should be treated aggressively without concern over addiction or diversion.

Saint Louis University School of Law and Center for Health Care Ethics

By Sandra Johnson, JD, LLM Tenet Endowed Chair in Health and Ethics

Lawsuits claiming neglected pain as the only basis for legal action face several obstacles. For example, many states cap the amount of damages that can be awarded for pain and suffering or bar such damages if the patient has died. Further, in Bergman and Tomlinson, neglect was readily apparent, but the treatment of pain in other cases may be more complex and difficult to litigate. It is quite unlikely that such litigation will reach beyond the most egregious cases of medical neglect or recklessness.⁹

Drug Enforcement Administration

After state medical boards established a more positive legal environment for physicians treating patients in pain, the focus shifted to the role of the DEA in monitoring physician prescribing under the federal Controlled Substances Act (CSA) through the DEA's registration requirements. In implementing this registration system, the DEA is authorized to monitor prescribing practices of physicians in relation to any of the medications scheduled under the CSA for the purpose of preventing abuse and diversion.10 As with any prosecutorial activity against particular physician practices, there is a challenge in providing needed oversight without discouraging physicians from taking care of their patients.

In 2001, the DEA issued a joint statement with more than 20 health organizations: "Promoting Pain Relief and Preventing Abuse of Pain Medications: A Critical Balancing Act."¹¹ In August, 2004, the DEA, again after much consultation, issued a Frequently Asked Questions (FAQ) document but subsequently retracted it, stating that it contained statements that were "erroneous" and that "further discussion of the subject is warranted" because "abuse of pharmaceutical narcotics and other prescription-controlled substances is increasing" and because

The legal column continued on page 12

Stem Cell Research: Science, Ethics and Policy

This is an edited and updated transcript of a forum presented by the Harvard Medical School Division of Medical Ethics in November 2004. It was moderated by Dan W. Brock, PhD, Director of the Division of Medical Ethics.

ew medical ethics issues have attained the public prominence of stem cell research. There are a number of reasons for this that we will explore today. One of course is the great scientific and medical promise that stem cell research holds both for understanding many diseases and then, further down the line, treating them. There's also great ethical concern because producing embryonic stem cell lines requires the destruction of human embryos. At least some persons view human embryos as full human persons. Many more view them as at least deserving of significant respect. There are also policy concerns about how to regulate stem cell research. Other countries such as Great Britain have a regulatory body to license research in this area, but at this point, the United States does not.

George Q. Daley, MD, PhD, is Associate Professor of Pediatrics in the Division of Hematology/Oncology at Children's Hospital and Associate Professor of Biological Chemistry and Molecular Pharmacology at Harvard Medical School.

I will start by defining the stem cell as a single cell that can both self-renew and generate progeny that continue to differentiate or specialize. In contrast to the rather restricted developmental possibilities for stem cells in the adult, the stem cells of the early embryo are fated to become all of the tissues of the body. One can isolate these embryonic stem cells from the five-day old human blastocyst, grow them extensively in culture and coax them to form specific cells and tissues that scientists hope will one day enable the treatment of a range of diseases by cell replacement therapy.

What are the diseases that might be treated by cell therapies? I offer three simple criteria: 1) diseases that represent the loss of a single cell type, 2) diseases for which evidence already exists that transplantation of whole organs or cells will ameliorate the condition and 3) diseases for which the current supply of organs or tissues are limited. By these criteria, insulindependent diabetes type 1, which results from autoimmune destruction of the insulin-producing beta cells of the pancreas, is an excellent target. Diabetes can be treated effectively by whole pancreas or islet cell transplant, but organ supply is severely limited. A second disease is Parkinson's, a movement disorder caused by loss of mid-brain dopaminergic neurons. Patients who receive transplants of midbrain tissue from aborted fetuses have shown motor improvement in some cases. Clearly, embryonic stem cells represent a preferred source for dopaminergic neurons. Finally, work in my own laboratory is aimed at treatment of a variety of genetic and malignant blood disorders. Bone marrow transplantation harnesses the regenerative power of hemopoietic stem cells to cure leukemia, but unfortunately most patients don't have suitable tissue-matched bone marrow donors. My laboratory has succeeded in generating a supply of adult hemopoietic stem cells from embryonic stem cells.

There are two significant challenges to using embryonic stem cells in therapy. First, undifferentiated embryonic stem cells have tumor-forming potential, and therefore we must go to great lengths to purify the specialized cell of interest away from the undifferentiated embryonic stem cells in order to minimize the risk of tumor formation in treated patients. Second, the tissue products of embryonic stem cells will face the same immune barrier that complicates organ transplantation. Until we can overcome this threat of rejection of transplanted cells, we must poison the recipient patient's immune system with immunosuppressive drugs, leaving the patient susceptible to life-threatening infection. One of the most theoretically appealing strategies for overcoming the immune barrier to cell transplantation is to combine somatic cell nuclear transfer (SCNT) with embryonic stem cell biology to create tissues that are genetically identical to the patient.

Let me take you through how SCNT might be applied to a patient with sickle cell anemia. This procedure would involve microsurgical extraction of the nucleus from one of this patient's cells, say a skin cell, and transfer of the nucleus into a human egg (from which the DNA has first been removed by a micro-needle). This reconstructed cell is then activated chemically or by an electric shock. With this process, the genes that are active in the skin cell nucleus are silenced, and the genes that are normally active during early embryonic development are reawakened. The skin cell begins to cleave, and the cluster of cells that develops begins to adopt the structure of a blastocyst, an early stage embryo. That embryo harbors pluripotent stem cells that can be extracted and placed in the petri dish, and grown as a continuous line of embryonic stem cells. Because these embryonic stem cells derive from the nucleus of our patient, they are a perfect genetic match and carry the genetic lesion typical of sickle cell anemia. The genetic lesion can be repaired directly in this line of cells. The repaired cells can then be differentiated into blood stem cells and transplanted into the patient without the need of immune suppression, because the blood cells are genetically identical to the patient. If successful, normal blood cells would grow in the patient, effectively reversing the sickle cell anemia.

While much of the promise of embryonic stem cells derives from our hopes for treating patients, I want to make a very important point. Even if embryonic stem cells are never successful as therapies, they

Stem Cell — continued on page 6

Stem Cell — continued from page 5

remain enormously valuable tools for scientists in basic research. These cells can teach us about aspects of human developmental biology and gene control. They're becoming increasingly employed in the pharmaceutical industry as a way of validating drug targets, for providing assays for drug development and as surrogates for certain forms of drug toxicity testing, thereby limiting the use of animals.

The science is progressing very, very quickly and is proceeding under the cloud of a vigorous ethical debate. The debate hinges on the source of embryonic stem cells, which are human blastocysts - the earliest stage of human embryonic development. Couples that undergo in vitro fertilization are often left with excess blastocysts and are, thereafter, faced with the decision to discard them as medical waste, or to donate them to medical research. Many in the general public don't appreciate that the human blastocyst is a miniscule speck of cells, a cluster smaller than the period at the end of this sentence. The blastocyst harbors no specialized tissues, no neurons and no bodily form. The fact that it is a primitive, unspecialized clump of cells doesn't negate the fact that the moral status of this entity is what is at issue. At conception, a new genome is formed, a fact that is frequently offered as a biological definition of the beginning of life. But from a biologist's perspective, the beginning of meaningful individual life is a bit fuzzier. Of course, one can quibble with the definition of individual, but twinning can occur up to 14 days after conception, and some normal individuals are actually the products of two distinct conception events and represent the coalescence of four gametes, a condition called tetragametic chimerism, which can be compatible with normal human development.

President Bush supports research on a small set of embryonic stem cell lines that were derived prior to August 9, 2001. The NIH Registry lists 22 such lines, a small minority of the cell lines that were promised when Bush announced his policy three years ago. Today, the numbers and variety of human embryonic stem cells is increasing daily. Many of these lines have advantageous features that make them valuable to scientists interested in studying particular diseases, including lines that carry disease-specific mutations, essentially modeling human disease in the petri dish. Unfortunately, none of these new, medically relevant lines can be studied with federal dollars. There is also no funding for the use of SCNT to treat disease.

Let me finish by reiterating that embryonic stem cells are important research tools. Scientists are already making important discoveries that advance understanding of human development and disease. One hopes that eventually our capacity to direct the differentiation of human embryonic stem cells will usher in a critical new modality of medicine: cellular therapy. My advocacy of human embryonic stem cell research is in no way meant to trivialize the value of somatic or adult stem

These cells can teach us about aspects of human developmental biology and gene control.

cells. I support research on both. I also believe that research into the process of somatic cell nuclear transfer is critical to realizing the ultimate and full potential of stem cells.

Michael J. Sandel, DPhil, is Anne T. and Robert M. Bass Professor of Government at Harvard University and also a member of The President's Council on Bioethics.

There are two main objections to embryonic stem cell research. One might be called the embryo objection. This has to do with the fact that extracting the stem cells kills the embryo. It destroys what some regard as a human life and what most people would agree is at least potential human life. The second objection is the slippery slope objection. It holds that, even if embryonic stem cell research isn't wrong in itself, it is likely to lead to morally objectionable practices. According to this objection, stem cell research today on embryos left over from fertility clinics will lead tomorrow to the desire to go further: to create embryos for stem cell research through cloning or somatic cell nuclear transfer. And if therapeutic cloning becomes a widespread practice, the argument continues, sooner or later it will lead

to human reproductive cloning. Let's first say something about the slippery slope objection.

Perhaps the most familiar and serious version of the slippery slope objection is the worry that it will lead to human reproductive cloning. Reproductive cloning is currently unsafe; I would argue that, even if it were safe, it would be morally objectionable. The desire to create a child through cloning is objectionable because it springs from the desire to create a child of a certain kind. This is the designer baby worry, which seems to me a reason to oppose human reproductive cloning even if the safety objections were overcome. But is the slippery slope worry decisive as an argument against embryonic stem cell research? I don't think so; there are ways to avert or at least to minimize that danger through sensible public policy and legislation, including a ban on human reproductive cloning as most European countries have adopted and limits on how long stem cells can be allowed to develop in vitro.

A second version of the slippery slope objection fears that permitting embryonic stem cell research on spare embryos from fertility clinics will lead to the desire to do therapeutic cloning or to create embryos for the sake of research. This argument goes as follows: It is one thing to carry out research on existing, spare embryos languishing in IVF clinics. According to one estimate, 400,000 embryos are in freezers in IVF clinics, most of which will ultimately be discarded. Some argue that it is morally permissible to use such embryos for life-saving research, but morally impermissible to create embryos for the sake of research. According to this argument, to create human embryos for the sake of experimentation and research is to cross a moral line.

What about this distinction? It seems sensible at first glance, but on reflection, it doesn't hold up. Imagine a clinic that accepted egg and sperm donations for two purposes, reproduction and stem cell research. Such a clinic would have two groups of embryos – one from gametes donated for the purpose of IVF and another from gametes donated by people who care about advancing the cause of stem cells research. Now which of these embryos may an ethical scientist use for stem cell research? If you believe that there is a morally important distinction between the

two, you would have to say that researchers may only use the embryos created for the sake of reproduction, not the ones that were created for the sake of research. But why draw the line there? If it is immoral to create and sacrifice embryos for the sake of curing or treating devastating diseases, why isn't it also objectionable to create and discard spare IVF embryos in the course of treating infertility? Or to look at the argument the other way around, if the creation and sacrifice of embryos in IVF is morally permissible, why isn't the creation and sacrifice of embryos for stem cell research also morally permissible? Both practices serve worthy ends. In fact, curing diseases such as Parkinson's and diabetes is at least as important as enabling infertile couples to have genetically related children.

If this argument is right, what it shows is that stem cell research on IVF "spares" and on embryos created for research, whether natural or cloned, are morally on a par. This argument only shows that all of these practices stand or fall together, morally speaking. It remains to ask whether they all stand or all fall. To answer that question, we have to return to the embryo objection.

It is important to recognize that, if the blastocyst is morally equivalent to a person, then embryonic stem cell research is wrong and should be rejected. So it is impossible to resolve the ethical status of embryonic stem cell research without resolving the question of the moral status of the embryo. Many of you may be tempted to think that the moral status of the embryo is a religious question, impossible to resolve. But the mere fact that a certain view about when personhood begins may be informed by certain religious convictions doesn't mean that it's not possible to assess and evaluate competing answers to that question. That is what I will try to do now.

What is the argument of those who regard the six-day blastocyst as morally equivalent to a person? It goes like this: Human beings are inviolable; they can't be treated as things or used as mere means. Human beings are worthy of respect. But when does this inviolability kick in? When does human life become worthy of respect? The answer can't depend on the age or the developmental stage of a particular human life. Even infants are inviolable, and few people would advocate yanking organs for transplant even from a fetus. Human development is a continuous process. There is no clear biological line that can tell us definitively when human life becomes worthy of respect. Therefore, the argument continues, while it's true that only some embryos develop into mature human beings, it's also true that every human being began life as an embryo. If we believe that our lives are inviolable and worthy of respect simply by virtue of our humanity, then it would be morally arbitrary to say that at some younger age or earlier stage in our development we weren't worthy of respect.

That's the argument. Is it persuasive? I think it is flawed for the following reasons. The fact that every person began life as an

The fact that every person began life as an embryo doesn't prove that embryos are persons.

embryo doesn't prove that embryos are persons. Consider an analogy: every oak tree was once an acorn, but it doesn't follow that acorns are oak trees. Those who view embryos as persons often assume that they must be persons, because the only alternative is to treat them with moral indifference, as mere things. But that assumption is mistaken. You don't have to regard the embryo as a full human being in order to accord it a certain respect. To regard an embryo as a mere thing, open to any use we desire or devise, seems to me to miss its significance as potential human life. Few people would favor the wanton destruction of embryos or the use of embryos for trivial purposes, like developing a new line of cosmetics, for example. What this suggests is that personhood is not the only warrant for respect. The moral test that embryo research has to pass is that it should be for a weighty purpose related to life or the sustenance of life. Given the diseases at which it aims, and given the prospects of success in developing cures, it seems to me to pass the test.

There are other ways of challenging the idea that an embryo in a petri dish has the same moral status as a person. One way is to play out the full implications of that idea. If harvesting stem cells from a blastocyst were truly on par with harvesting organs from a baby, then the morally responsible policy would be to ban it, not merely to deny it federal funding. If some doctors made a practice of killing children to get organs for transplantation, no one would say that the infanticide should be ineligible for federal funding but allowed to continue in the private sector. Current federal policy-which restricts federal funding but does not ban embryonic stem cell research-therefore, cannot rest on the premise that embryos are persons, but must presuppose some version of the slippery slope objection. But the best way to deal with the slippery slope objection is not to deprive promising biomedical research of federal funding, but to enact sensible regulations to prevent abuse, beginning with a simple ban on human reproductive cloning.

Jonathan D. Moreno, PhD, is Emily Davie and Joseph S. Kornfeld Professor of Biomedical Ethics and Director of the Center for Biomedical Ethics at the University of Virginia. He is also Co-Chair of the National Academy of Sciences Committee on Guidelines for Human Embryonic Stem Cell Research.

I'm going to talk about human embryo research policies both here and around the world. The first policy option, of course, is to ban all human embryo research. Some jurisdictions have done that. The second is to permit research only on existing lines. This is essentially the Bush Administration policy, which permits research on lines existing as of August 9, 2001. The third option is to permit research only on socalled "spare embryos" left over from patients' reproductive purposes in IVF clinics. This is probably the consensus favorite for those who would like to see embryo research go forward but don't want to see some of the other possible sources utilized. The fourth option is to permit research on spare embryos and embryos created for research via in vitro fertilization. The fifth option is to permit the use of embryos created by cloning or somatic cell nuclear transfer (SCNT). There is dispute about whether the cloned embryos

Stem Cell — continued on page 8

Stem Cell — continued from page 7

really are properly called embryos. Number six is to permit research on spare embryos and on embryos created for research via SCNT using non-human animal eggs. This is the way that the options have been characterized. I'm going to go around the world, region by region, indicating where various countries stand.

The UK and Belgium, and perhaps Sweden, permit embryonic stem cell research on IVF embryos and on embryos created by somatic cell nuclear transfer. A number of countries in the European Union (EU) are rather conservative and for internal political reasons have prohibited all embryo research. There is a very interesting problem for the EU now in trying to develop consensus guidelines within their system when member countries vary so much in their views. Germany permits research only on existing lines. They also import stem cell lines from Israel. Most European countries seem to be moving in the direction of at least permitting research on spare embryos. The Middle East is a very interesting situation, because both the Jewish and Islamic traditions agree that the embryo does not have the same status as the fetus has later on in gestation, and not the same status as an infant. So in Israel there's a lot of work being done on artificial reproduction, including human embryo stem cell work. Embryonic stem cell research is also permitted under Islamic law. In Asia and the Pacific Rim there's a very aggressive move toward creating a whole biotech platform around artificial reproduction. Closer to home the Canadians allow research only on spare embryos.

Here at home, of course, we have a lot of policies. In August 2001, President Bush established a policy that only human embryonic stem cell lines that had been created by August 9, 2001 were eligible for federal research support. About 68 or so lines were listed as available, but in reality, there are so far 22 lines. The state responses are quite varied. All human embryo research is banned in 11 states. Two states explicitly endorse research cloning – New Jersey and California. In the remaining 35 states, nothing is prohibited by law.

Right now we are in a very interesting period. The results of Proposition 71 in California, the Stem Cell Research and Cures Initiative, will provide \$3 billion over 10 years. We are also hearing that Massachusetts, Wisconsin, New Jersey and other states are now concerned. They want to keep up. The marketplace seems to be moving in a very interesting way and very rapidly.

So this is where we are now in the United States. Since August 9, 2001, about \$28 million in grants have been awarded by NIH for human embryonic stem cell research on the 22 available lines. It is estimated that 128 cell lines are available around the world. It's growing fast.

If you look at all the policies, if you look at the laws, if you look at the regulations in various countries, you see a number of themes that repeat themselves.

The moral test that embryo research has to pass is that it should be for a weighty purpose related to life or the sustenance of life.

Prohibited research includes reproductive cloning of a human. You also see that the standard tends to be that research on the embryo is permitted for a 14-day period, before the primitive streak appears. The guiding principles tend to be that the project must serve an important research aim, that there is no other way to do this work and that whatever review mechanism is imposed must recognize the special moral status of the human embryo. There is general agreement that there is something about the human embryo that must be respected and the process for approval of this work has to somehow incorporate that. You also tend to see pretty specific rules concerning the nature of embryo and egg donation to avoid exploitation of women. There is also agreement that there has to be separation between the pregnancy termination process - and embryo donation for research. Finally there are various statements around the world, in the UK and Canada especially, concerning what has to be in a consent form required for people who are interested in donating eggs. A very important point is that the egg donor

or the couple donating the fertilized embryo must realize that they will receive no financial reward if others make a lot of money out of this activity.

Clearly there needs to be some kind of oversight process. Although the institutional review board (IRB) seems to be the obvious place to send these protocols, it is not clear that the IRB, which is set up to review human subjects research, is appropriate in the case of a human embryo. Would that be bringing the human embryo under an ambit that some people will feel is inappropriate? It is also the case that very few IRBs have the expertise to review embryo research.

Let me conclude by saying a little bit about what the National Academy of Sciences is doing. The National Academy of Sciences has already taken the position that both human embryonic stem cell research and adult stem cell research should go forward. Our committee is not revisiting that foundational question. Rather, the question is, given that human embryonic stem cell research should go forward, what should the conditions be?

To show you what the topics at our public workshop were, just to get a sense of what some of the issues are that we are exploring, the first day was mostly devoted to getting up to speed on the science and where it is now as well as the legal and regulatory requirements here and abroad. The second day was mostly concerned with the ethical issues and oversight problems. For example, in a very interesting talk the vice president of BIO, the Biotechnology Industry Organization, said, "Please regulate us. Industry needs regulation so we know what we can do and what we can't do." This is a little different than the response from the sciences. I've never yet heard a scientist say, "Please regulate me," but capitalists like regulation, because it tells them what is feasible and what isn't. So The National Academy of Sciences Committee will file a report, probably by March that will then go through the usual external review process and modification prior to release. The Committee is very much in the middle of its work. Its conclusions, we hope, will be of some help to the scientific community in this country in developing a set of standards that are consistent and respect the special moral status of the human embryo.

Ethics and the humanities: End of the Line: Depression and Burnout in Ward No. 6

"Ward No. 6" in Chekhov's Doctors: A Collection of Chekhov's Medical Tales (Kent State University Press, 2003)

Jack Coulehan, MD, Editor

hen Anton Chekhov graduated from the University of Moscow Medical School in 1884, he had a decision to make. During the previous four years, the young man had supported himself and his family by writing humorous sketches and stories for Moscow weekly magazines. By that time Chekhov was so well regarded as a writer – at least 150 published pieces – his editors clamored for more. Why waste his time practicing medicine? Nevertheless, the newly minted Dr. Chekhov hung up his shingle and for the next five years or so practiced primary care medicine.

But he managed to avoid that either-or decision. At night and on weekends, he wrote as much as ever, publishing an additional 190 stories before 1890 and, along the way, winning the Pushkin Prize, the Russian equivalent of America's Pulitzer, by the age of 28. As Chekhov's fame grew, he closed his urban practice and moved to the country, where he continued to work as a district doctor and public health officer until incapacitated by tuberculosis in 1897. For example, in less than five months in 1891, Chekhov reported seeing 453 patients at a district clinic and making 576 house calls. He also busied himself with grassroots activism, building schools for peasants, raising money for famine victims and, most famously, exposing inhuman living conditions in the czarist prison colonies on Sakhalin Island.

Chekhov always maintained that medicine was his lawful wife and literature, his mistress: "When one gets on my nerves, I spend the night with the other." But in reality, he never kept them separate; his professions interacted and enhanced each other, especially the influence of medicine on Chekhov's plays and stories. Obviously, one such influence was the author's deep insight into the medical life, which he conveyed in his numerous stories about physicians. Chekhov's doctors range from callow medical students to obnoxious, insensitive practitioners and from courageous public health workers to beloved village physicians. However, some of his most fascinating creations are the physician characters who suffer from disappointment, ennui or burnout.

"Ward No. 6," a long story published in 1892, is a masterpiece of burnout. The protagonist is Dr. Ragin, the withdrawn and depressed director of a district hospital. He had arrived at the job 20 years earlier, as an energetic young doctor: "At first Dr. Ragin worked very hard. He received patients every day from morning to dinnertime, performed operations, and even did a certain amount of midwifery..." But over the years, his energy has dissipated. He now realizes how poorly equipped and out-of-date his hospital is. He professes the "palpable futility" of medical practice, because social and economic forces beyond medicine's control determine health and disease. Thus, Ragin has retreated into a shell, detached not only from his patients, but also from all human contact. While a junior doctor actually takes care of the hospital patients and runs the clinic, Ragin spends his days sitting in his study and drinking beer.

While heavy demands and poor working conditions contribute to Ragin's predicament, he faces a deeper problem as well. Is his sense of futility solely a consequence of medical practice? Or is something deeper missing? Ragin comes across to us as unreflective, apparently having suppressed his emotional life and replaced it with a set of abstract beliefs. Ragin's lack of self-knowledge has crystallized around a profound sense of emotional numbness. When he was younger, he evidently meant well and worked toward his professional ideals, but the commitment was superficial. In the long run, he never learned to look beyond the accumulation of day-today disappointments to find satisfaction in meaningful relationships with his patients and others.

Early in the story, Ragin visits the mental ward (Ward No. 6), where he meets Ivan Gromov, a brilliant paranoid who embraces life passionately. The passion attracts Ragin like a moth to a candle. Ragin yearns to *feel* something, anything, even to experience suffering, rather than to remain suspended

Jack Couleban, MD, MPH Department of Preventive Medicine State University of New York at Stony Brook

in his emotionless cocoon. He develops an obsession that only by making himself suffer will he be able to experience an emotional life and, therefore, be truly human. Predictably, this new obsession makes him even more dysfunctional, a situation that allows the junior doctor to have him fired as hospital director and, ultimately, committed to Ward No. 6 as mentally ill. Once Ragin becomes a "nobody," his isolating cocoon disappears. The ward orderly hits him when he tries to escape, thereby giving Ragin an opportunity to suffer. Shortly thereafter, he has a stroke and dies.

A dismal story, perhaps, but full of psychological insight. Many health care professionals become vulnerable to depression and burnout, because we lack the inner resources to cope, day in and day out, year after year, with our difficult work. We learn during professional school and postgraduate training to distance ourselves emotionally from the situation at hand, to be "objective" and exhibit "detached concern" (an oxymoron, if you think about it). Too often, we learn the "detached" part very well, by suppressing our feelings and avoiding self-reflection. But we often tend to intellectualize the "concern" part, so that caring becomes a series of concepts and procedures, rather than a compassionate presence for the patient.

In medical education you frequently hear repeated Dr. Francis Peabody's famous one-liner: "...for the secret of the care of the patient is in caring for the patient." While this is true as far as it goes, a further step is necessary as well: the secret of caring for the patient is to develop selfawareness; that is, caring first for oneself. Dr. Ragin's plight is extreme, but the dynamics that led him eventually to withdraw from practice may threaten any health care professional who works so hard at detachment from patients that he or she also becomes detached from his or her own emotional life. "Ward No. 6" serves as fair warning of what can happen if we totally ignore the dictum, "Physician, heal thyself!"

Dialogue: Bioethics in space

Uter space is inimical to human life, and constructing sub-environments that preserve life in a cold vacuum far from earth is no easy task. Along with other harsh environments – Antarctica, the Himalayas, the deep sea – the need to sustain and repair the body in hostile territory has led to the development of a specialty known as "Medicine in Extreme Environments"¹ and journals such as *Human Performance in Extreme Environment.*² As long as human beings insist on colonizing these inhospitable places, they will be faced with an ongoing set of medical and bioethical dilemmas.

Walter Robinson's thoughtful article, "Ethics for Astronauts," (Lahey Clinic Medical Ethics, Fall 2004, www.lahey.org/ ethics/) correctly identifies three of the thorniest current bioethical issues facing the space program: 1) astronauts' rights as research subjects versus our need for data on the physiological and psychological impacts of space flight; 2) astronauts' right to privacy versus the need to disseminate such data to the scientific community, and 3) the difficult decisions facing clinical care for astronauts on long duration space flights. All three evoke much debate and hand-wringing at the National Aeronautics and Space Administration (NASA), which is one of the reasons that NASA asked the Institute of Medicine (IOM) to create the Committee on Creating a Vision for Space Medicine During Travel Beyond Earth Orbit, on which Dr. Robinson served. The Committee produced a report, Safe Passage: Astronaut Care for Exploration Missions,³ which was a thoughtful and probing study of the medical needs of long-duration flight, and NASA is incorporating many of its insights into its planning for such missions. In such a new and difficult area, there will be differences and debates, and so I welcome an opportunity not only to respond to Dr. Robinson's article, but also to the broader set of recommendations made in the Safe Passage report.

Dr. Robinson is correct that the participation of astronauts in clinical research and the related issue of astronaut privacy are problematic. However, Dr. Robinson claims, "The fact that astronauts always consent to participate in all the offered protocols strongly suggests a problem: An Institutional Review Board (IRB) should question the effectiveness of a voluntary consent

process in which no one ever declines consent." But it is simply not so that astronauts never decline protocols. In the Life Sciences Spacelab Missions, for example, there was about 20 percent non-participation in planned protocols.4 (In a post-flight exercise test asked of astronauts in five separate missions, only 30 percent participated.) Of course, that very fact presents the exact opposite dilemma – if the data collected is crucial to understanding the health and treatment of astronauts in future flights, and the number of subjects in any space-based protocol is of necessity severely limited, how can we permit astronauts to refuse to participate in protocols at all?

Similarly, Dr. Robinson and Safe Passage both make the claim that astronaut privacy concerns have impeded the collection of important data; Dr. Robinsons suggests that issues of astronaut privacy were "repeatedly cited by NASA" as a barrier to collecting data, and Safe Passage similarly states, "The possibility that an astronaut could be identified is seen as an inescapable barrier to the collection and interpretation of astronaut health data." However, the incidence of refusing to release medical information is actually quite low; in Skylab, for example, all nine astronauts concurred, and six out of seven in Spacelab Life Sciences Mission 1.5

In other words, two problems are postulated by Dr. Robinson and IOM: the first has to do with astronaut consent (either Dr. Robinson's contention that it is coerced and so is never declined, or the opposite problem that astronauts refuse to participate and so important data is not gathered), and the second is data lost to astronaut insistence on the privacy of their medical information. Establishing the validity of these claims is important because they are the hook on which both Dr. Robinson and the IOM committee hang their policy recommendations. Yet in neither Dr. Robinson's article nor in the close to 300 pages of Safe Passage is any data brought forth to support either claim. They are simply asserted as true.

The truth of the claims would not be of much concern, except they are being used to justify a modification of the Common Rule,⁶ our single most important regulatory standard of subject protection.

For example, Safe Passage states it explicitly:

NASA should pursue...a long-term, focused health care research strategy to capture all necessary data on health risks and their amelioration... [which would require] a modification of the interpretation of the Common Rule (45 C.F.R., Part 46, Subpart A) for human research participants.

The reality is that the astronaut is, in most cases, the only individual from whom clinical information relevant to space travel can be collected. Therefore, reliance on the voluntary participation of astronauts in clinical research to the same extent as reliance on volunteer participants on the ground may not be appropriate. This is especially true when the information gained is potentially critical to the lives and well-beings of both the individual astronaut and the astronaut corps.

It is true that astronauts are in a unique position to gather certain kinds of information on human functioning in space, and that the data is important for the future of space flight. And here Dr. Robinson's suggestion, if not the reasons he gives, seems right to me: We should consider some kinds of data collection in an occupational health model (and, in fact, already do; but the kinds of data included should be expanded). I also agree with Dr. Robinson that other kinds of research, not related to the safety of flight but with terrestrial commercial or industrial uses, clearly falls within the Common Rule and should never be forced upon astronauts.

However, space research does not fall so neatly into those two categories. Spacebased medical research can be invasive or uncomfortable and yet still be directly related to future medical or life science needs. Drugs metabolize differently in microgravity, and we must understand that process to accurately prescribe in space, and so drug trials are necessary. Space research can involve blood draws, muscle biopsies, the wearing of harnesses (which can actually be hazardous during some space-based activities), sleep studies that require waking up periodically (sleeping in space is very difficult as it is, many astronauts are severely sleep deprived, and such studies can exacerbate the problem) and so on. In which of Dr. Robinson's categories do invasive or hazardous studies that are precisely for the health and well-being of future astronauts fall? Calling those "occupational health data gathering" is incorrect, and if

the astronauts decide to assert their right to refuse consent for these studies, I suspect the Office of Human Research Protections will agree with their right to do so.

It seems to me that NASA should pursue a different strategy, one it has begun but must fully implement. Much astronaut refusal to consent in the past was due to lack of astronaut buy-in, coupled with poor central planning. For example, astronauts might be asked to participate in multiple drug studies, which confounded each other, or they would be involved in a number of studies, each requiring a blood sample, and instead of a single stick and shared blood, there would be multiple, separate blood draws. More recently, these problems have been addressed. Astronauts are now involved in the science of NASA from the top down (Shannon Lucid, who has spent more hours in orbit than any other American, has served as Chief Scientist of NASA; the Associate Administrator and head of the space program at NASA is William Readdy, also an experienced astronaut). Astronauts work in the medical corps at NASA, act as principle investigators on studies and sit on the IRB. The solution is not to replace coercion with new or modified regulation (simply another form of coercion), but to include astronauts in every aspect of scientific research at NASA, to reinforce participation in the life sciences as an integral part of astronaut responsibility.

The issue of clinical care is of a different nature, and here I fully agree with Dr. Robinson. The ethical issues of clinical care in long duration spaceflight beyond earth orbit are tricky. In the shuttle and space station platforms, the assumption has been that we can get an injured or ill astronaut back to earth fairly quickly, and so the goal was maintenance until the person could get full care terrestrially. The strategy breaks down on a trip to Mars where the ship is a year away from any possible rendezvous with earth. Before the mission leaves, careful thought must be given to what kinds of medical training to give the crew and what kinds of equipment should and should not be included on the ship. On such long duration flights, every ounce of weight must be carefully considered; higher likelihood injuries and illnesses must be served before rare or unlikely ones. Even so, the inevitable may occur: an astronaut may have an injury or illness that the available resources are ill-suited to treat. All involved – astronauts, their families, the NASA medical personnel - must be ready for such an eventuality.

Which brings us, finally, to clinical bioethics in space. What is the right thing to do if an astronaut suffers from a traumatic head injury and gets violent in a small craft millions of miles from earth, or becomes clinically depressed? What do we tell or not tell an astronaut, isolated in a way no human has ever been before, if his or her spouse develops cancer, or their child dies tragically? As Dr. Robinson suggests, these issues cannot be left to chance. NASA is already gathering together committees to discuss the medical needs of long duration flight, to establish protocols and procedures, and to try and grapple with some of these seemingly intractable problems. Do we now need the Journal of Extreme Bioethics?

Paul Root Wolpe, PhD

Center for Bioethics Department of Psychiatry, Medical Ethics, and Sociology University of Pennsylvania Chief of Bioethics, National Aeronautics and Space Administration

Editor's note: This column, is written in Paul Root Wolpe's capacity as a faculty member at the University of Pennsylvania and should not be construed as reflecting NASA opinion or policy.

¹Palinkas LA, Gunderson EK, Holland AW, Miller C, Johnson JC. Predictors of behavior and performance in extreme environments: the Antarctic space analogue program. *Aviation Space & Environmental Medicine*. 2000;71(6): 619–625.

²http://www.hpee.org/aboutjournal.html

³Ball JR, Evans CH Jr. (eds). Committee on Creating a Vision for Space Medicine During Travel Beyond Earth Orbit. *Safe Passage: Astronaut Care for Exploration Missions*. Washington DC: National Academy Press, 2001

⁴Personal Communication: Charles Sawin, Director of Research Johnson Space Center and Chair, Committee for the Protection of Human Subjects (JSC's IRB), November, 2001.

⁵Personal Communication: Charles Sawin, November, 2001.

⁶The Common Rule is Title 45, the Code of Federal Regulations that provides protection of human research subjects. It can be accessed at http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm

et me be clear: The problem with medical protocols in spaceflight is that they are mistakenly classified as conventional research and so are monitored using the Common Rule. Instead, many of these protocols should be viewed using an occupational model that recognizes the unique aspects of spaceflight and astronauts. I continue to believe that astronauts consent to research protocols based on the possibility, as stated clearly in the NASA IRB handbook, that they may not be selected for a mission if they decline to participate. I was told by IRB members, astronauts and NASA researchers that consent is very rarely withheld. The problem here is not that there may be "coercion" but that using conventional consent and protocol review procedures mistakenly views a highly unusual activity – gathering information about the physical and psychological effects of space flight – through the lens of conventional medical research.

I was also told by astronauts, flight surgeons, researchers and those responsible for medical operations that the possibility of identifying the data from an individual astronaut was a major restriction to gathering data on the physiologic consequences of space flight. If this is a misperception, it is a common one, raised again and again by all concerned.

Dr. Volpe argues that protocols that involve risk cannot be considered "occupational data gathering" and should not be required of astronauts. Some of the monitoring may indeed be risky, but risk alone does not classify it as research. Almost all activities during spaceflight entail a high degree of both uncertainty and risk. Inflight activities that are now required, e.g., mitigation protocols that are not considered "research," would be legitimately considered research if they were to take place with different subjects in a different context. The point is that there is very little about being an astronaut that resembles being a conventional research subject.

Spaceflight is a unique activity undertaken by a unique population under unique social, cultural, economic, political and psychological constraints; application of a set of regulations and procedures developed for an altogether different set of circumstances is mistaken. The current system does not work. Thirty years of experience in human spaceflight has yet to yield sufficient clinical information to make long duration flights medically possible. Without serious and sustained efforts to rethink the study of humans during spaceflight, we unnecessarily risk the health and safety of astronauts on future long-term missions.

Walter M. Robinson, MD, MPH

Assistant Professor of Pediatrics and Medical Ethics Harvard Medical School, Boston, MA

The legal column continued from page 4_

"chronic pain is a serious problem for many Americans."¹² The reason for the apparent reversal is not clear. The DEA promises more detailed guidance in the future, and advocates are actively engaged in the issue.¹³

¹Johnson SH. Disciplinary actions and pain relief. *J Law Med Ethics* 1996; 24(4):319–327. Four symposium issues on legal matters in pain management are available at http://www.aslme.org/research/painjournals.php.

²Hoover v. Agency of Health Care Administration, 676 So. 2d 1380 (Fla. App. 1996).

³http://www.medsch.wisc.edu/painpolicy/domestic/model.htm.

⁴http://www.fsmb.org/.

⁵http://www.medsch.wisc.edu/painpolicy/matrix.htm.

⁶Johnson SH. Providing relief to those in pain. J Law Med Ethics 2003;31(1):15-20.

⁷Hoffman DE, Tarzian AJ. Achieving the right balance in oversight of physician opioid prescribing for pain: the role of the state medical boards. *J Law Med Ethics* 2003;31(1):21–54. Gilson AM, et al. Improving state medical board pain policies: influence of a model. *J Law Med Ethics* 2003;31(1): 119–129. Joranson DE, Gilson AM. Controlled substances and pain management: changes in knowledge and attitudes of state medical regulators, *J Pain Symptom Manage* 2001;21(3):227–237.

⁸Tucker KL. Medico-legal case report and commentary: inadequate pain management in the context of terminal cancer. The case of Lester Tomlinson. *Pain Med* 2004;5:214–217.

9Johnson SH. Commentary on medico-legal case report. Pain Med 2004;5:219-220.

¹⁰Noah L. Challenges in the federal regulation of pain management technologies. *J Law Med Ethics* 2003:31(1):55–74.

¹¹http://www.medsch.wisc.edu/painpolicy/Consensus2.pdf.

1269 Federal Register 67170 (November 16, 2004).

¹³See correspondence at http://www.medsch.wise.edu/painpolicy/DEA/IPSresponse.pdf

Ask the Ethicist continued from page 3_

consent is obtained mainly from the family, not the patient, and the family's decision is accepted even if the patient would have chosen differently. \Box

Xiuyun Yin, PhD Assistant Professor

Benfu Li, MD Professor, Chair of Chinese Medical Ethics Association

Yali Cong, PhD Professor, Associate Director of Medical Ethics Program Peking University Health Science Center — ethics@mail.bjmu.edu.cn

¹The concept of brain death as equivalent to death has not been widely accepted by the average Chinese person.

²Income is higher in cities like Beijing (1500 yuan or \$ 181.16/month) and Shanghai (2000 yuan or \$241.55/month).



41 Mall Road Burlington, MA 01805

Medical Ethics

Lahey Clinic Medical Ethics encourages reader participation. We welcome comments for our "Dialogue" column and invite submission of ethical dilemmas for "Ask the ethicist." Send correspondence and requests for complimentary subscriptions to David Steinberg, MD.

> David Steinberg, MD, Editor Lahey Clinic Medical Center 41 Mall Road, Burlington, MA 01805 david.steinberg@lahey.org

James L. Bernat, MD, Assoc. Editor Dartmouth-Hitchcock Medical Center One Medical Center Drive, Lebanon, NH 03756 bernat@dartmouth.edu

Editorial Board

Nancy Knoblock Hunton Managing Editor

David M. Gould, Esq.

Susan M. Donovan

Legal Editor

Daniel Callahan, PhD Allan M. Brandt, PhD Dan W. Brock, PhD Diane M. Palac, MD Thomas J. Prendergast, MD Paul Reitemeier, PhD James A. Russell, DO Andrew G. Villanueva, MD

Generous funding for Lahey Clinic Medical Ethics is made in memory of Harold Karp, by the Karp Family Foundation. This publication is partially funded by the Robert E. Wise, MD Research and Education Institute.

Lahey Clinic Medical Ethics can be found on the Lahey Clinic Medical Ethics website at www.lahey.org/ethics/.

Lahey

Nonprofit Organization U.S. Postage PAID Boston, MA Permit No. 9