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IN THIS ISSUE

Donors kept in the dark about stem cell research

The ethical and moral obligation of healthcare workers to provide informed consent to donors is usually vast, and somewhat cut and dried. According to research[1] recently released in the journal *Fertility and Sterility* and based on a government survey, many healthcare providers working within in vitro fertility (IVF) clinics in the United States are going against this ethical and moral obligation. The survey uncovered that IVF clinics across the United States don't find it necessary to inform egg donors that possible embryos made from their eggs might end up being used in stem cell research.

The survey indicates that this practice of not providing informed consent to donors is occurring even with common and widespread opposition to stem cell research. The researchers say that this practice is considered morally offensive by one-third of Americans, yet the practice still continues.

"The survey has nicely uncovered an extant ethical dilemma or better, an ethical miscue: namely, the lack of informing prospective donors that their eggs might be used in embryonic stem cell research," says **John Banja**, PhD, associate professor, Department of Rehabilitation Medicine, Emory University, Atlanta, says. "Presumably, some donors might be very disturbed to learn that because they believe their eggs will only be used for

EXECUTIVE SUMMARY

A government survey found that in vitro fertilization (IVF) clinics across the United States are not informing egg donors that embryos made from their eggs might end up being used in stem cell research.

- The survey indicates that this practice of not providing informed consent to donors is occurring even with widespread opposition to stem cell research.
- Although most egg donor consent forms inform donors that they will not have control over embryos resulting from their eggs, only 30% inform them that some embryos might be used for research, and even fewer mention stem cell research.
- Most egg donors in the United States, including some who might have a moral objection to research and stem cell research, are not being informed that embryos created with their donated eggs might be used for these purposes.

reproductive purposes."

The results of the survey indicate that of 222 U.S. IVF clinics that responded to the query, 100 clinics accepted donor eggs and provided some excess embryos for research.

The researchers received 66 consent forms from those 100 clinics, which showed that although most egg donor consent forms do inform donors that they will not have control over embryos resulting from their eggs, only 30% inform them that some embryos might be used for research. Even fewer mention stem cell research.

Paul Hofmann, DrPH, president, Hofmann Healthcare Group, consultants of ethical issues, in Moraga, CA, says, "The survey simply confirms an ongoing serious problem with some forms of clinical research, namely inconsistent and incomplete disclosure to individuals who must be informed if they are or may be involved in research activities, either directly or indirectly. Such information is essential to permit informed consent or refusal."

Banja adds, "Informed consent requirements would ethically compel clinics to include disclosure of how donor eggs might be used. I also believe that once having done so, women should be free to donate or refuse to donate their eggs."

Study co-author **Gerald Owen Schaefer**, BA, researcher, department of bioethics, National Institutes of Health (NIH) clinical center, Bethesda, MD, says in the paper that since possible research use of embryos, especially for stem cell research, may be material information affecting some women's decision about donation, egg donors should be so informed. Hofmann agrees and adds, "Regardless of how her eggs might be used, she must have the right to make an informed decision."

The research concluded that egg donors in the United States, including some who might have a moral objection to research and stem cell research, are not being informed that embryos created with their donated eggs might be used for these purposes. This issue can be corrected with the inclusion of succinct, nontechnical language in egg donor consent forms. *(For a sample informed consent form for egg donors, see resource, below.)*

This incident also raises the question as to whether ethics committees need to be put in place for such facilities. Banja says, "The committee would advise accordingly that egg donation is a medical procedure not without risks and, hence, demands informed consent; that given the contentiousness of embryonic stem cell research, many women might want to know how their eggs might or would be used as that could be a material factor in their deciding to donate or not."

REFERENCE

1. Schaefer G, Sinaii N, Grady C. Informing egg donors of the potential for embryonic research: A survey of consent forms from U.S. in vitro fertilization clinics. *Fertility Sterility* Dec. 22, 2011; epub ahead of print.

SOURCES/RESOURCE

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- **Paul Hofmann**, DrPH, President, Hofman Healthcare Group, Morage, CA. E-mail: hofmann@hofmannhealth.com.
- **Sample informed consent form:** http://bit.ly/wBHGTJ. ■

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EDITORIAL QUESTIONS

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Regions determine palliative care spending

Medicare patients with advance directives specifying limits in treatment who lived in regions with higher levels of end-of-life spending were less likely to have an in-hospital death, averaged significantly lower end-of-life Medicare spending, and had significantly greater odds of hospice use than decedents without advance directives in these regions, according to a study[1] in a recent issue of *The Journal of the American Medical Association* (JAMA).

Patients can use advance directives to document their preferences for the use or avoidance of life-sustaining treatments (living wills). Although advance directives have become more common in the past few decades, evidence is mixed on whether they change the course of treatment provided near the end-of-life, according to background information in the article. The article also indicates that the wide variation in end-of-life Medicare expenditures across geographic regions suggests that default treatment levels also vary regionally. Advance directives specifying limits at the end-of-life may have their greatest impact in regions where the norms are to provide very high-intensity end-of-life treatment.

Lauren Hersch Nicholas, PhD, MPP, research fellow, University of Michigan, Ann Arbor, and colleagues analyzed the relationship of advance directives for Medicare patients with the cost and aggressiveness of end-of-life treatment in geographic regions across the United States. The researchers collected survey data from the Health and Retirement Study for 3,302 Medicare beneficiaries who died between 1998 and 2007 linked to Medicare claims and the National Death Index. Various models examined associations between advance directives, end-of-life Medicare expenditures, and treatments by level of Medicare spending in the decedent's hospital referral region.

The average age of the beneficiaries at death was 83 years; 56% were women. Regions were characterized by quartiles of end-of-life spending averaged across a seven-year period. Decedent's region intensity was determined by zip code of residence.

Among the findings of the researchers, decedents residing in low-spending regions were more likely to have a treatment-limiting advance directive than decedents in high-spending regions (42% vs. 36%). In high-spending regions, adjusted spending on patients with a treatment-limiting advance directive was $33,933, whereas adjusted spending for patients without an advance directive was $39,518 (difference, -$5,585). Having a treatment-limiting advance directive was not associated with differences in aggregate end-of-life spending for decedents in low- and medium-spending regions.

In high-spending regions, patients without an advance directive had a 47% adjusted probability of in-hospital death, whereas those with an advance directive had a 38% probability of in-hospital death. "The equivalent results for in-hospital death for those in medium-spending regions were 42% without an advance directive, and 37% with an advance directive. In high-spending regions, patients without a limiting advance directive had a 24% adjusted probability of hospice use, whereas those with a directive had an adjusted probability of hospice use of 41%," the authors write.

Advance directives were associated with higher adjusted probabilities of hospice use in high- and medium-spending regions, but not in low-spending regions.

"Advance directives are associated with important differences in treatment during the last six months of life for patients who live in areas of high medical expenditures but not in other regions," the researchers say. "This suggests that the clinical effect of advance directives is critically dependent on the context in which a patient receives care. Advance directives may be especially important for ensuring treatment consistent with patients' preferences for those who prefer less aggressive treatment at the end of life but are patients in systems characterized by high intensity of treatment."

REFERENCE

1. Hersch-Nicholas L, Langa K, Iwashyna, T, et al. Regional variation in the association between advance directives and end-of-life medicare expenditures. *JAMA* 2011; 306:1,447-1,453. ■

Pediatric vaccine trial receives ethics review

An advisory board to the Department of Health and Human Services (HHS) has recommended that a proposal to hold pediatric trials of the anthrax vaccine be reviewed by an ethics board before proceeding.

The National Biodefense Science Board (NBSB) was formed by HHS in 2006 to consider ways to prevent and respond to potential public health emergencies that might arise from biological, chemical, or nuclear incidents. The board was asked to consider whether trials of the vaccine, which has been used

with adults for years, should be conducted with children. The concern of trial proponents is that in the event of a domestic anthrax attack, doctors would have little guidance as to the appropriate doses for children exposed to the pathogen.

"Our job as public health emergency experts and people who deal with preparedness response — disasters, bioterrorism, you name it — is to anticipate the unexpected," said **Daniel Fagbuyi**, MD, FAAP, medical director of disaster preparedness and emergency management at Children's National Medical Center in Washington, DC, who serves on the NBSB. "While people may be complacent and say that everything is fine, when something happens, the people who criticized planning ahead will be the same ones saying, 'Isn't this your job? You should be anticipating all these kind of things.'"

Opponents of the anthrax trials proposal argue that the likelihood of a domestic anthrax attack that affects children is so small that a child participating in a trial has almost no possibility of benefitting from it.

Paul Offit, MD, chief of the infectious diseases division and director of the Vaccine Education Center at The Children's Hospital of Philadelphia, PA, said, "I don't think you can do a trial on children from which they can't possibly derive benefit." Offit testified before the NBSB on the issue last summer. *(For more information on different pediatric vaccine trials, see related story, at right.)*

Assembling a review board

The NBSB did not specify what board should carry out the review, or if one should be assembled specifically to answer this question. Fagbuyi said a board comprised of ethicists, public health experts, and others representing the interests of children could be gathered to handle the issue.

Fagbuyi said the ethics review also should consider the review board process for any potential pediatric anthrax vaccine trials. "Who's going to be the [institutional review board] IRB of record? Who's going to be responsible?" he said. "There needs to be good dialogue about who's going to take that on. Is it going to be local IRBs, or a national IRB? That's one of the things they're going to have to deal with."

Mark Schreiner, MD, chairman of the Committee for the Protection of Human Subjects at The Children's Hospital of Philadelphia, sees no current medical need for a pediatric anthrax trial. "There is no current threat; it's very much a hypothetical threat," he said. "In order to approve research in children, it has to either be minimal risk, or there has to be only a minor increase above minimal risk, or there has to be the prospect of direct benefit."

In addition to suggesting the ethics review, **Ruth Berkelman**, MD, director of the Center for Public Health Preparedness and Research at Emory University in Atlanta, GA, also suggested a feasibility study to determine whether any parents would be willing to volunteer their children for anthrax vaccine trials. Fagbuyi said he believes that some populations who might consider themselves uniquely vulnerable in the event of an attack — military personnel, EMS workers, firefighters, etc. — might be more willing to enroll their children in trials.

"It is common knowledge that some military personnel have wondered whether they are in harm's way, with the thought that they don't want to expose their family if they're going to be on the front lines," he said. "There are other populations: those who work in biosafety labs, those who do studies with anthrax, those who work with wool and animal hides. Those are the ones who may be interested in those types of studies."

RESOURCE

• Minutes of the NBSB meeting are available at http://bit.ly/yZsMho. ■

Pediatric vaccines — a comparison of two

Association between anthrax and smallpox vaccines

Paul Offit, MD, chief of the infectious diseases division and director of the Vaccine Education Center at The Children's Hospital of Philadelphia, PA, generally argues in favor of pediatric vaccine programs, but he opposed a plan in 2002 to test smallpox vaccines in children when he was a member of the Centers for Disease Control and Prevention's Advisory Committee for Immunization Practices.

He discussed his opinions recently in light of the controversial proposal to test an anthrax vaccine on children. "I felt the same thing there — that the chances that a child would be exposed to smallpox were essentially zero, and therefore, it didn't make sense to do that trial."

The smallpox trials proposal drew criticism and eventually was scrapped. Offit notes that the anthrax vaccine is much safer than the smallpox vaccine. "The

way this [anthrax] vaccine is made is much more similar to the diphtheria and tetanus vaccines," he says. "You take protein that is made by the bacteria and inactivate it. It's going to be a very safe vaccine. So I don't think the children are at any risk, I just don't think those children are likely to have any benefit."

Proponents argue that the only alternative to trials is to wait for an attack to occur and then give any children exposed a combination of antibiotics and vaccine. Vaccine dosages would have to be guessed at. **Daniel Fagbuyi**, MD, FAAP, medical director of disaster preparedness and emergency management at Children's National Medical Center in Washington, DC, says, "We can say to parents, well, we have used it in adults, and that's as much as we have information on, and it's an emergency now. You can either take it or not take it, understanding the risks of mortality with an infection, especially a pulmonary, inhalational kind of infection."

At the recent National Biodefense Science Board (NBSB) meeting, the recommendation to seek an ethics review before proceeding with a trial was suggested by **Ruth Berkelman**, MD, director of the Center for Public Health Preparedness and Research at Emory University in Atlanta. Berkelman says that proponents made their case that vaccine trials would be useful. "We were asked, 'Is there a need for this, did people think it would be helpful to have this information in case there was a wide-scale anthrax event?' And the answer was yes, it would be helpful to have a pre-event trial. At the same time, the ethical considerations in children on this particular issue are quite large," she says. "We don't have ethicists on our board. And I thought this had such a large ethical component to it that it was important that ethicists review this issue." ■

Surgeons don't discuss end-of-life care

According to a recent survey[1], published in the *Annals of Surgery*, many U.S. surgeons fail to discuss their patients' wishes in case a risky operation goes awry, and even more say that they would not operate if patients limited what could be done to keep them alive. The survey indicates that the restrictions are being debated among doctors.

Margaret Schwarze, MD, an assistant professor at the University of Wisconsin School of Medicine and Public Health, Madison, WI, who was one of the survey's authors, said that reportedly, "[surgeons] feel the advance directive basically ties their hands behind their back, and they're not given the tools to get them through the surgery."

The survey's authors asked 912 surgeons who regularly perform risky operations 14 questions on how they discuss a patient's advance directives and whether the directives influence their decision to operate. More than four out of every five surgeons discussed which forms of life support the patients would like to limit. But only about half asked specifically about the patient's advance directive, which can include restricting the use of feeding tubes and ventilators to keep a person alive.

"I think some surgeons just don't discuss advance directives because they think it's so irrelevant," Schwarze added.

More than half the surgeons said they would not operate if an advance directive limited what could be done to keep a patient alive after surgery.

The researchers said such instructions also can cause tension between the surgeon and the patient because it shows the patient might be unwilling to accept the therapies that come with high-risk operations. The study also found that heart surgeons appeared to be much more likely than brain surgeons to decline an operation.

REFERENCE

1. Redmann A, Brasel K, Alexander C, et al. Use of advance directives for high-risk operations: A national survey of surgeons. *An Surg* 2011; pub ahead of print Dec. 1, 2011. Doi: 10.1097/SLA.0b013e31823b6782. ■

Survey demonstrates effectiveness of POLST

Treatment preferences honored 94% of time

According to published research, a program created to communicate the treatment preferences of those with advanced illness or frailty ensures those preferences are honored 94% of the time. The Program, called Physicians Orders for Life Sustaining Treatment (POLST), was launched in Oregon almost 20 years ago.

POLST enables patients to document preferences to have or decline treatments in the form of medical orders. Since that time, the program has expanded to several states. The latest research on the POLST program is printed online in the *Journal of the American Geriatrics Society*.[1]

The study was designed to assess whether the treatments provided were consistent with what was documented on the POLST form. A review of medical records and POLST forms for 870 living and deceased patients found that POLST orders about resuscitation were honored 98% of the time, and orders to limit medical interventions were honored 91.1% of the time.

"The research builds upon our previous findings that suggest the POLST program offers significant advantages over traditional methods like advance directives and Do Not Resuscitate orders to communicate patients' preferences about life-sustaining treatments," said lead author, **Susan Hickman**, PhD, an associate professor at the Indiana University in Bloomington, IN, and Oregon Health & Science University schools of nursing, Portland, OR.

When patients identify treatments they do not want, the POLST form directs clinicians to use more extensive interventions to enhance comfort if needed. A majority, 74%, of the medical interventions provided to patients with POLST orders for "comfort care only" were focused on enhancing comfort, such as sending a patient to the hospital after a fall. Near the end of life, 24% of POLST orders were re-written to reflect a change of preferences, primarily for more comfort-focused care.

Naomi Karp, senior strategic policy advisor at the AARP (formerly the American Association of Retired Persons) Public Policy Institute in Washington, DC, says, "This study renews AARP's conviction that POLST is a useful strategy for ensuring that people's treatment preferences are honored in their setting of care." Karp says the striking results bolster the growing body of evidence that POLST does two important things for people with advanced illness or frailty: It helps elicit and document their treatment goals and choices, and it enhances the odds that they will get the care they want. AARP's own research on state POLST efforts provides a road map for the many states looking to start POLST programs, and this new clinical research provides evidence that those states are on the right track toward improving care for frail older citizens.

POLST also helps people avoid unwanted hospitalizations. **Margaret Murphy Carley**, chair of the Oregon POLST Task Force and executive director of the National POLST Paradigm Task Force says, "This study shows that the patient's comfort remains a high priority. Sometimes that means moving a patient who preferred to stay at the nursing home to the hospital for a short time to treat an accidental injury or uncontrolled symptoms."

The next steps are to study the process of completing a POLST form to learn how to best support patients and families in making difficult decisions about treatment in the face of serious illness.

REFERENCE

1. Hickman SE, Nelson CA, Moss AH, et al. The consistency between treatments provided to nursing facility residents and orders on the Physician Orders for Life-Sustaining Treatment form. *J Am Geriatr Soc* 2011; 59(11):2091-2099. Doi: 10.1111/j.1532-5415.2011.03656.x.

RESOURCE

For more information about the POLST Program, visit:

• POLST, Physicians Orders for Life-Sustaining Treatment Paradigm. Visit: Web: http://bit.ly/z9qYEx.To review the POLST forms developed by various states, click on the "Programs" tab, then select "POLST Paradigm Forms." ■

Ethicalness of surgical care at end-of-life

Although the extent of hospital and intensive-care use at the end of life is well known, patterns of surgical care during this period are poorly understood. A study[1] that appears in a recent issue of *The Lancet* examines national patterns of surgical care in the United States among elderly fee-for-service Medicare beneficiaries in their last year of life.

Participants of the retrospective cohort study consisted of elderly beneficiaries of fee-for-service Medicare in the United States, aged 65 years or older, who died in 2008. Researchers identified the claims for inpatient surgical procedures in the year before death and examined the relationship between receipt of an inpatient procedure and age and geographical region. The authors of the study then calculated an end-of-life surgical intensity (EOLSI) score for each hospital referral region defined as proportion of decedents who underwent a surgical procedure during the year before their death, adjusted for age, sex, race, and income.

The study revealed that of the elderly beneficiaries of fee-for-service Medicare who died in 2008, about 32% underwent an inpatient surgical procedure during the year before death, 18% underwent a procedure in their last month of life, and 8% underwent

a procedure during their last week of life. The study also showed that many elderly people in the United States undergo surgery in the year before their death. The rate at which they undergo surgery varies substantially with age and region and might suggest discretion in the healthcare providers' decisions to intervene surgically at the end of life.

REFERENCE

1. Kwok A, Semel M, Lipsitz S, et al. The intensity and variation of surgical care at the end of life: A retrospective cohort study. *Lancet* 2011; 378:1,408-1,413. ■

Finding common ground on Common Rule

Consensus seen in several areas

In the waning days of the comment period for the advance notice of proposed rule-making (ANPRM) for human subjects protection regulation, some of the institutional review board (IRB) community's heavy hitters have weighed in.

In addition to a submission by the Association for the Accreditation of Human Research Protection Programs (AAHRPP), detailed comments also were filed by the Secretary's Advisory Committee on Human Research Protections (SACHRP), the Association of American Medical Colleges (AAMC), and Public Responsibility in Medicine and Research (PRIM&R).

While each organization has its own specific take on the proposed revision of the Common Rule, there were many areas of agreement in their comments:

• Minimal risk definition.

AAHRPP, SACHRP, and the AAMC all propose that the Department of Health and Human Services (HHS) should develop a better definition of "minimal risk" as it applies to research oversight.

SACHRP states that the definition should compare potential harms and discomforts in a study to those that an average person in the general population would ordinarily encounter. As an example, AAMC offers the case of a study of cancer patients. In that case, the risks and discomforts of the study intervention should be compared to those a healthy individual would encounter in a routine medical examination.

• Researcher/sponsor responsibilities.

SACHRP and AAHRPP call for the regulations to more clearly spell out the responsibilities of researchers and sponsors in protecting subjects.

Those responsibilities would include knowing when to seek IRB oversight, disclosing financial interests, employing sound study design that minimizes risks, ensuring there are necessary resources to protect subjects, recruiting subjects in a fair manner, using appropriate informed consent, and ensuring that subjects understand it.

"The Common Rule is written such that it applies to the institutions and the [institutional review boards] IRBs," says **Marjorie Speers**, AAHRPP's president and chief executive officer. "It is silent on the role of the researcher, who deals with the research subject every single day."

Other than requiring the investigator to obtain consent, the rule "does not spell out the responsibilities," she says. "They're just inferred. All of these regulations should address the roles and responsibilities of the major players."

• Informed consent.

All of the organizations believe that the revisions to the Common Rule focus too much on documentation of informed consent and not enough on the process of obtaining consent.

Ann Bonham, PhD, chief scientific officer for the AAMC, writes in that organization's comments, "This focus may have the effect over time of preventing IRBs from allowing the implementation of novel, effective methods of communicating critical study information to research subjects."

The groups did not support the ANPRM's proposal to set length limits on various parts of consent documents, but they supported the idea of moving some topics to appendices rather than the main document.

Proposed new consent templates could be useful, if they demonstrate to researchers how to craft a shorter document with an addendum that gives more detail, SACHRP proposes.

• Researchers self-exempting.

AAHRPP, SACHRP, and the AAMC raise concerns about the proposal to allow researchers to determine for themselves that their studies qualify for the new "excused" (currently exempt) determination.

Speers writes in AAHRPP's comments, "Anecdotal evidence from some accredited organizations suggests that between one-quarter and one-third of researchers misclassify research as exempt when it is not exempt."

She says that while the process of exempting or excusing research could be much simpler,

someone needs to review it, whether it's an IRB member or staffer or even a departmental board.

• **Central IRB for multisite research.**

While the organizations agree that the regulations should encourage more use of a single IRB for multi-site studies, some balk at making that mandatory.

SACHRP calls such a requirement "premature," recommending instead a more deliberative process of encouraging single-IRB use.

In situations in which one IRB is designated, organizations say that the IRB must be chosen carefully and must have the necessary expertise to handle the study and to communicate and interact with local sites. They note that the costs incurred by IRBs handling different levels of oversight need to be compensated fairly.

• **Training requirements.**

All of the organizations ask that HHS make education of review boards and researchers a requirement in the regulations.

"This system that we have now, and any system we have in the future, is based on people being knowledgeable and competent to conduct research," Speers says. "And if you don't have any education requirement, if you don't have any way to measure competency, then we're going to continue to have incompetent IRBs and researchers involved."

In all, more than 1,000 comments were filed with HHS during the extended comment period. ■

Protecting participants in human research

The Presidential Commission for the Study of Bioethical Issues has issued its report concerning federally sponsored research involving human volunteers and concluded that current rules and regulations provide adequate safeguards to mitigate risk.

In its report, "Moral Science: Protecting Participants in Human Subjects Research," the commission also recommended 14 changes to current practices to better protect research subjects and called on the federal government to improve its tracking of research programs supported with taxpayer dollars.

President Obama requested that the commission undertake an assessment of research standards following the October 2010 revelation that the U.S. Public Health Service supported unethical research in Guatemala from 1946 to 1948 that involved intentionally exposing thousands of Guatemalans to sexually transmitted infections without their consent. The president gave the bioethics commission two assignments: to oversee a thorough fact-finding investigation into the specifics of the studies (released Sept. 13, 2011); and to ensure that current rules for research participants protect people from harm or unethical treatment, domestically as well as internationally.

RESOURCE

• For more information about the report, see http://bioethics.gov/cms/node/559. ■

Lower reading levels benefit informed consent

A study[1] published in the *Journal of Cataract and Refractive Surgery*, says that informed consent sheets that are concise and written at lower reading comprehension levels, as well as videotaped presentations, work well in helping patients understand the risks, benefits, and treatment alternatives to cataract surgery. The study is the result of a randomized, prospective study.

Authors of the study, **Anita N. Shukla**, MD, **Mary K. Daly**, MD, and **Paul Legutko**, PhD, who conducted the research at the Veterans Affairs Boston Healthcare System, said that using these tools to increased patient understanding could decrease the risk for indemnity payments awarded because of informed consent perceived to be inadequate.

The researchers chose patients who were eligible for cataract surgery, then were randomly assigned to one of four groups. Each members of all groups received conventional verbal information about informed consent. In addition, members of the second group received a brochure written on a second-grade reading level, the third group received a brochure written on an eighth-grade reading level, and the final group received an American Academy of Ophthalmology-produced patient education DVD titled "Understanding Cataract Surgery," which includes an aid to informed consent.

After the informed consent process, patients in each group were asked to answer 12 questions about cataract surgery, its benefits, its risks, and the alternatives. Patients in the groups who received materials written on the second grade reading level and who received the DVD received scores that were a great deal higher than those of patients in the other two groups. The researchers found that previous cataract

surgery and education level did not significantly influence patient recall of the informed-consent process.

REFERENCE

1. Shukla A, Daly M, Legutko P. Informed consent for cataract surgery: Patient understanding of verbal, written, and videotaped information. *J Cataract Refract Surg* 2012; 38:80-84. ■

Safeguards needed to stop discrimination

Despite the emergence of new tools that can diagnose Alzheimer's earlier, no effective interventions have been identified to stop the progression of the disease. A new report from the Perelman School of Medicine at the University of Pennsylvania, Philadelphia, tackles the ethical and logistical challenges of safely and effectively communicating a diagnosis of pre-clinical Alzheimer's disease in light of the gulf between diagnosis and treatment.

The study appears in the journal *Neurology*[1] and was sponsored by the Marian S. Ware Alzheimer Program and a Robert Wood Johnson Investigator Award in Health Policy Research.

Alzheimer's disease is among the most feared diseases of aging. The disease has been known for its role in memory loss and other clinical symptoms. But increasingly, patients learn they have the disease before symptoms start impacting their ability to function in daily life.

"We need to develop systems now, to navigate the challenges of a pre-clinical Alzheimer's diagnosis," said **Jason Karlawish**, MD, professor of medicine and medical ethics and author of the paper. "It's only a matter of time before we are able identify Alzheimer's before the patient is ill, like we've done with cholesterol and heart disease. Given the unique nature of this disease, which strips people of their independence as the disease progresses, safeguards are needed to protect those at high risk or with a pre-clinical diagnosis."

On the individual level, people strongly differ in their desire to know their risk and will react differently to a high Alzheimer's risk score or diagnosis in the early stages of the disease. In some cases, biomarker test results can be harmful; patients might develop anxiety or serious depression. To safely and effectively communicate a diagnosis of pre-clinical Alzheimer's disease, Karlawish recommends that researchers and clinicians track the emotional and physical impact of a pre-clinical diagnosis, then develop and disseminate best practices. *(For information on a controversial genetic test for Alzheimer's, see related story, below.)*

When an effective Alzheimer's therapy or intervention is found, a process will be necessary to ensure the patients who stand to benefit most are prioritized accordingly. Prognostic and predictive evidence should be gauged against not only an individual's risk but the entire population at risk, especially if failure to intervene could cause large numbers of people to be impacted by any disease progression. A "National Alzheimer's Education Program" is proposed, to address how to translate research results into clinical practice for those with pre-clinical disease.

"The Alzheimer's disease label does not equate to disability," said Karlawish. Tto ensure that patients' daily lives, i.e. driving, financial planning, work status, aren't negatively or prematurely limited, laws and policies need to be revised to prevent stigma, discrimination and, when patients do suffer disability, exploitation, he says.

"The discovery of pre-clinical Alzheimer's disease may be how we prevent the tsunami of Alzheimer's disease dementia, but we must not drown in the challenges created by our own discovery," warned Karlawish.

REFERENCE

1. Karlawish J. Addressing the ethical, policy, and social challenges of preclinical Alzheimer disease. *Neurology* 2011; 77:1,487-1,493. ■

Controversial test may predict Alzheimer

There is a new, controversial genetic test of a gene called Apolipoprotein E (APOE) on the horizon. APOE is a susceptibility gene where certain variants have been found to significantly increase a person's risk of developing Alzheimer's disease. That gene, along with a family history of Alzheimer's, greatly increases the risk of developing the disease.

The genetic test was conducted as part of the Risk Evaluation and Education for Alzheimer's disease Study (REVEAL), a series of clinical trials taking place at University of Michigan School of Public Health (U-M SPH), Ann Arbor, with other sites including Harvard University, Boston, Howard University, Washington, DC, and the University of Pennsylvania, Philadelphia.

APOE testing is controversial in the medical com-

munity because the variant is neither necessary nor sufficient to cause Alzheimer's disease. This limitation, along with a general lack of treatment options for Alzheimer's, has raised concerns that the genetic information could burden rather than benefit patients. There have been numerous consensus statements and articles against using APOE genotyping for predicting Alzheimer's risk.

However, most of the study participants who took the test wanted to learn about their APOE test results and were not overtly distressed by them, said **Scott Roberts**, PhD, associate professor at U-M SPH and co-principal investigator of REVEAL, along with **Robert Green**, MD, MPH, fellow in genetics, professor of neurology, genetics, and epidemiology at Harvard University School of Medicine.

The National Society of Genetic Counselors and American College of Medical Genetics recently developed practice guidelines[1] for genetic counseling and testing for Alzheimer's disease. Roberts is one of the authors.

The guidelines provide clinicians with a framework for assessing their patients' genetic risk for Alzheimer's disease, identifying which individuals might benefit from genetic testing, and providing the key elements of genetic counseling. Alzheimer's disease is traditionally subdivided into early onset and late onset types. Early onset occurs before age 60–65 years and accounts for 1-5% of all cases, while late onset occurs after 60–65 years and is the predominant form.

REFERENCE

1. Goldman J, Hahn S, Catania J, et al. Genetic counseling and testing for Alzheimer disease: joint practice guidelines of the American College of Medical Genetics and the National Society of Genetic Counselors. *Genet Med* 2011; 13:597-605. ■

New ethics manual issued by ACP

The sixth edition of the *American College of Physicians'* (ACP's) *Ethics Manual* addresses ethical decisions in clinical practice, teaching, and medical research, as well as the underlying principles and the physician's role in society and with colleagues. The updated manual, approved by ACP's Board of Regents published in a recent issue of the *Annals of Internal Medicine*.[1]

The current update of the ACP's manual covers surrogate decision-making and end-of-life care, use of complementary and alternative medicine, physician-assisted suicide, relationship between physicians and industry, genetic testing, and research ethics.

The new edition also highlights the patient–physician relationship during health catastrophes, culturally sensitive care, research use of human biologic materials, social media and online professionalism, and industry-sponsored research. A first time topic for the manual is the challenges associated with offering care to "very important persons" experiencing unusual fame or prestige.

Other new or expanded sections include treatment without interpersonal contact, confidentiality and electronic health records, therapeutic nondisclosure, caring for oneself or persons with whom the physician has a previous nonprofessional relationship, boundaries and privacy, pay-for-performance, interrogation, attending physicians and physicians-in-training, the patient-centered medical home, protection of human subjects, placebo controls, and scientific publication.

REFERENCE

1. American College of Physicians Ethics Manual. *Ann Intern Med* 2012; 156:73-104. ■

Regulating transplants for troops and others

A proposed rule has been set forth by the Department of Health and Human Services (HHS) regulating face and hand transplants just as kidneys, hearts and other organs are already regulated. This development could mean the beginning of waiting lists and a national system to allocate body parts and donor testing.

Vascularized Composite Allografts (VCA) transplantation comprises transplants of a variety of body parts that are not currently regulated under the Organ Procurement and Transplantation Network (OPTN) final rule. The two most notable types to date have been hand and face transplants.

Although the body parts involved vary significantly, among their shared characteristics is the fact that they are susceptible to ischemia and that they

need revascularization, done through a surgical reconnection of blood vessels to accomplish the transplant, as opposed to secondary ingrowth of vessels. In viable vascularized transplants, immunosuppression is necessary to prevent or treat rejection. This immunosuppression has risks, which have been justified in patients needing organs as presently defined in the OPTN final rule because of their lifesaving potential.

Clinical demand for VCA transplantation appears to be increasing now that immunosuppression protocols have proven safer and support for military and veterans VCA transplantation programs continues to expand.

The secretary seeks comments from the public on the proposals made. To be considered, comments on this proposed rule must be submitted by Feb. 14, 2012. *(For information how to submit comments, see resources section, below.)*

The Health Resources Services Administration, which regulates organ transplants, has proposed expanding the regulation to cover other body parts. The new rules would take effect later this year or early next year.

RESOURCES

- Federal Register. Web: http://1.usa.gov/wgzhYH.
- You may submit comments, identified by RIN 0906-AA73, by any of the following methods: Federal eRulemaking Portal: http://www.regulations.gov., Agency Web site: http://www.hrsa.gov/, E-mail: VCATransplantation@hrsa.gov. Include RIN 0906-AA73 in the subject line of the message. ■

UK: Assisted suicide is legally possible

The Commission on Assisted Dying, Demos, London, United Kingdom, with members with expertise in law, medicine, social care, mental health, palliative care, theology, disability, and policing, published its final report after assessing more than 1,300 pieces of evidence on assisted suicide legality. The report suggests a framework that could allow people with a terminal illness the choice to end their lives while protecting those who are vulnerable.

The Commission on Assisted Dying, in addition to evaluating the strengths and weaknesses of the legal status quo, also set out to explore the question of what a framework for assisted dying might look like, if such a system were to be implemented in the UK, and what approach might be most acceptable to health and social care professionals and to the general public.

The report concluded that the current legal status of assisted suicide is inadequate and incoherent. While the current legal regime can be distressing for the people affected and their families, it is also unclear for health and social care staff, and it lays a deeply challenging burden on police and prosecutors, which could be eased by a new statutory framework, according to the report. A proposed legal framework for assisted dying is laid out in detail in the report, including strict criteria to define who might be eligible to receive assistance and robust safeguards to prevent abuse of any new law.

RESOURCE

- DEMOS – The Commission on Assisted Dying. Web: http://www.commissiononassisteddying.co.uk. ■

CME INSTRUCTIONS

To earn credit for this activity, please follow these instructions.

1. Read and study the activity, using the provided references for further research.
2. Log on to www.cmecity.com to take a post-test; tests can be taken after each issue or collectively at the end of the semester. First-time users will have to register on the site using the 8-digit subscriber number printed on their mailing label, invoice or renewal notice.
3. Pass the online tests with a score of 100%; you will be allowed to answer the questions as many times as needed to achieve a score of 100%.
4. After successfully completing the last test of the semester, your browser will be automatically directed to the activity evaluation form, which you will submit online.
5. Once the completed evaluation is received, a credit letter will be e-mailed to you instantly.

CME OBJECTIVES

Upon completion of this educational activity, participants should be able to:

- Discuss new developments in regulation and health care system approaches to bioethical issues applicable to specific health care systems.
- Explain the implications for new developments in bioethics as it relates to all aspects of patient care and health care delivery in institutional settings.
- Discuss the effect of bioethics on patients, their families, physicians, and society.

COMING IN FUTURE MONTHS

- ■ Advancing medical technologies affecting ethics consults
- ■ Complexities of the rules governing organ transplants
- ■ Improve handling of medical errors from ethical framework
- ■ The ethics of billing and coding

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CME QUESTIONS

1. According to Paul Hofmann, DrPH, the government survey regarding informed consent for egg donors confirms what ongoing problem with some forms of clinical research?
   A. That some embryos might be used for research, and even fewer informed consent documents mention stem cell research.
   B. Inconsistent and incomplete disclosure to individuals who must be informed if the person is, or might be involved in research activities.
   C. That because of the contentiousness of embryonic stem cell research, many women might want to know how their eggs might or would be used.
   D. None of the above.

2. True or False: Physicians Orders for Life Sustaining Treatment (POLST), was launched in Oregon almost 20 years ago and enables patients to document preferences to have or decline treatments in the form of medical orders.
   A. True
   B. False

3. A study published in the *Journal of Cataract and Refractive Surgery*, confirms that informed consent sheets that are written at what reading comprehension level, works well in helping patients understand the risks, benefits, and treatment alternatives?
   A. Eighth grade
   B. Sixth grade
   C. Second grade
   D. None of the above

4. What development could the new proposed rule regulating face and hand transplants bring?
   A. The beginning of waiting lists.
   B. A national system to allocate body parts and donor testing.
   C. Both A&B
   D. None of the above