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INSIDE

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Ethical Controversy Erupts Over Human-animal Embryo Research

Proposal would lift ban on federal funding

Do animals with partly human brains, or producing human embryos, sound like science fiction? Some worry that creating "chimeras"— embryos with cells from more than one species — opens the door to just such possibilities.

"The most basic ethical concern is whether the value of human life will be degraded by this research," says **Karey A. Harwood**, PhD, associate professor of religious studies at North Carolina State University in Raleigh.

Years ago, some ethicists raised the same concern about in vitro fertilization. "They worried that turning reproduction into a process of manufacture would somehow put the product of that effort — the child — on a lesser moral plane from its parents," says Harwood.

The issue is now being raised regarding scientific research that deliberately mixes human and animal cells. "The concern about reducing humans to their component parts, to be used instrumentally for some distant end, will very likely reawaken these same worries, perhaps for good reason,"

EXECUTIVE SUMMARY

The National Institutes of Health has proposed lifting a moratorium on funding of certain controversial experiments using human stem cells to create animal embryos that are partly human. Some ethical concerns include the following:

- Once research is underway, scientists could find reasons to cross additional ethical boundaries.
- Research might not live up to the public's expectations for curative treatments in the short term.
- The issue of making chimeras hasn't been the focus of widespread public debate.

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says Harwood.

Thomas V. Cunningham, PhD, MA, MS, medical bioethics director at Kaiser Permanente West Los Angeles, says that there are both practical and theoretical issues with chimeras. An important theoretical question is their "moral status." "Just as we might ask about the moral status of human embryos produced by fertilization in vivo or in vitro, we can now consider the same question for human-nonhuman embryos," he says.

The National Institutes of Health (NIH) recently proposed lifting a moratorium on funding of certain controversial experiments that use human stem cells to create animal embryos that are partly human.

"Formation of these types of human-animal organisms, referred to as 'chimeras,' holds tremendous potential for disease modeling, drug testing, and perhaps eventual organ transplant," NIH's associate director for science policy and director of the Office for Science Policy, **Carrie Wolinetz**, PhD, recently wrote in a blog about the draft chimera policy.[1] However, multiple ethical concerns are raised by such research. NIH is establishing an internal steering committee to provide input on funding decisions for research that include the following:

- Human pluripotent cells are introduced into non-human vertebrate embryos, up through the end of gastrulation stage, with the exception of non-human primates, which would only be considered after the blastocyst stage.
- Human cells are introduced into post-gastrulation non-human mammals (excluding rodents), where there could be either a substantial contribution or a substantial functional modification to the animal brain by the human cells.

Any research falling inside this scope will trigger the review of the steering committee. "That's not a restriction and it's not a prohibition. It's just another look, a careful consideration of the research, to make sure we are being thoughtful about animal welfare and ethical considerations," Wolinetz said during a media phone call. She expects scientists to confront difficult ethical issues for years to come. "There are no hard and fast lines," she said. "I expect this is going to be an evolving set of thinking as we understand more about the human brain."

Where to Stop?

Once research on chimeras begins, there could always be medical or scientific reasons to push the boundary still further, experts say. "There is no obvious place to stop. For that reason, it's an extreme step for civilization to do this," says **Stuart A. Newman**, PhD, professor of cell biology and anatomy at New York Medical College in Valhalla.

If researchers start making animals that are partly human, there might be some incentive to make animals that are more human, or even mostly human. "There have been proposals to make chimeras with animal brains so that tissues can be harvested from a human body even without a human brain present," says Newman.

Many people believe that the possibility of finding cures for diseases justifies crossing some ethical boundaries. "They might say, that to really do this work thoroughly and scientifically, they need to put a whole human brain in a sheep or pig," Newman says. While such research might be abhorrent to many, he says, "there are always going to be people who see benefits in taking

it further than most people are comfortable with."

Down the line, researchers might contemplate doing things they previously thought were unacceptable. "People who have reservations about taking a technique further can be depicted as old-fashioned, anti-science, or just not getting with the program," says Newman.

In 2015, the U.K. Parliament approved a controversial "three-parent" procedure to prevent mitochondrial disease. "The public was sold on that, even though it's a very extreme procedure which created potentially harmful gene combinations that could be passed to future generations," says Newman. "People who had reservations about it were called anti-progress."

Newman sees a parallel in research on nuclear chain reactions which ultimately lead to the development of the atomic bomb. He points to the 70 scientists who signed a letter urging President Truman not to use the atomic bomb on Japan before that nation had been given a chance to surrender.

Newman says that similarly, today's bioethicists need to bring to light the possible unintended consequences of chimera research.

"Unless we put on the brakes in some way and describe these things for what they really are, people are going to wake up and find out things are going on that they never would have approved of," says Newman.

In the U.S., there are no laws prohibiting use of animal or human embryos for research. Even without NIH funding, other organizations are funding chimera research, including the Oakland-based California Institute of Regenerative Medicine.

"It really is kept off the public agenda in some ways," says Newman. "Most people don't have opinions about embryos, except if they are talking about abortion." The separate issue of using embryos for research or making chimeras has, thus far, not been the focus of widespread public debate. "If the issue were truly discussed openly, I think you would have great differences of opinion," says Newman.

The unresolved question is which ethical lines are morally acceptable to cross. Ideally, this distinction is made on the basis of careful reasoning and good evidence. Harwood says, however, "more often, it seems to be based on the evolving, arbitrary, and unpredictable comfort level of the popular majority and mainstream media."

> "THERE ARE ALWAYS GOING TO BE PEOPLE WHO SEE BENEFITS IN TAKING IT FURTHER THAN MOST PEOPLE ARE COMFORTABLE WITH."

It's unrealistic to assume that the purpose of chimera research is self-evident to everyone. "There is always great potential for the public to misunderstand the basic scientific facts underlying an ethical issue," Harwood says, noting that heart transplants were originally met with strong resistance. "For this issue to get a fair hearing, the scientific community will need to educate the public."

Cunningham expects some groups to paint chimera research as "heinous, frightening, and a slippery slope to genetic engineering and eugenics."

When Cunningham and colleagues recently examined how policymakers and scholars talked about embryo experimentation from the 1970s through the present day, they found attitudes had changed quite a bit.

"There appears to be more support for the research by these groups than there was in the past," he says. "Yet, there also appears to be a consensus that these practices need to be carefully regulated."

Not All Benefits Practical

Researchers might fall short of the public's hopes for curative treatments in the short term, and instead, simply gain knowledge. "Sometimes things we learn about now don't pay off for many years," says Cunningham.

If the practical payoff of chimera research is remote, that makes it difficult for the public and policymakers to understand why it's necessary. "Unless one is quite savvy in understanding the history of scientific progress and the regulatory environment, then it is easier to see this research as superfluous and overly risky, rather than seeing it as incremental progress that may lead to a paradigm shift," says Cunningham.

If research on chimeras is hindered by lack of funding without adequate justification, scientific and medical progress could be unnecessarily thwarted. "The worry is that if we do not allow regulated research to proceed, then we will not learn valuable information that would help us as a society," says Cunningham.

He points to recent research showing how somatic cell nuclear transfer could be used to create

embryonic stem cells in both primates and humans — procedures that, in theory, could be used to treat mitochondrial disease.[2]

"This team uses methods that some would find morally objectionable," says Cunningham. "Yet others find their work extraordinarily promising." ■

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Intense Competition, Inadequate Assessment are Factors in Research Misconduct

Institutions should create a climate of research integrity, experts say

The number of retractions in scientific journals has increased significantly in recent years, according to research.[1] Sometimes, it's due to honest mistakes — researchers realize they made an error and want to correct the scientific record.

"But there is also misconduct," says **Zubin Master**, PhD, assistant professor at Albany (NY) Medical College's Alden March Bioethics Institute. While some journals publish the reason for retraction of a clinical trial's finding, others do not. "There isn't a day that I don't hear about a case of misconduct. There is always some type of research integrity issue going on," says Master.

Data are Largely Self-reported

A 2015 study found 1.97% of scientists admitted to have fabricated, falsified, or modified data or results at least once; up to 33.7% admitted other questionable research practices.[2] Such data is largely self-reported, however.

"We're asking research scientists if they've ever engaged in misconduct, or seen others engage in misconduct," says Master. "Obviously, there will be some bias."

James M. DuBois, DSc, PhD, Steven J. Bander Professor of Medical Ethics and Professionalism at Washington University School of Medicine in St. Louis, is not convinced that research misconduct is actually increasing. "It is far easier today to detect plagiarism, fabricated data sets, and falsified images," he says.

DuBois believes the movement toward increasing the rigor and reproducibility of science is likely to decrease instances of data falsification and fabrication, even if more instances are discovered in the short-term. "It is much more likely that individuals will get caught when they engage in research misconduct — at least, once suspicions arise," says DuBois.

As data sharing continues, peer oversight is also likely to increase. "We may see another rise in detected misconduct, but not necessarily misconduct itself," says DuBois. He names the following approaches:

- ensure researchers know the rules surrounding misconduct, and how seriously society takes them,
- increase transparency by providing adequate institutional server space for all research data, and requiring data sharing, and
- increase oversight of research staff, post-doctoral trainees, and peers by principal investigators, including review of raw data.

"However, this is often difficult as science grows more complicated, and individuals possess unique skills that others on the team lack," says DuBois. The following are ethical issues involving research misconduct:

• Definitions of research misconduct may vary.

The U.S. Department of Health and Human Services' (HHS') Office of Research Integrity defines misconduct as "falsification, fabrication, and plagiarism."

"Not every nation has such narrow

definitions," says Master. "Other nations have a broader definition of scientific dishonesty." Some include conflict of interest violations, or ethics violations involving authorship of publications or bad recordkeeping.[3]

• Intense competition can create a culture that incentivizes misconduct.

"Everybody is ready to blame the bad apple, as if they are morally corrupt. But it's the environment that pushes people, ethically," Master says.

Under this kind of pressure, an investigator might decide to publish a study's findings prematurely. "Right now, the research environment is at a state of hypercompetition. People are scrambling for grants and jobs," says Master.

Researchers don't always take that extra step to make sure the data are reproducible, he says. "Or maybe the data doesn't fit the hypothesis, so they justify removing it and only show certain results," says Master.

Conflict of interest in clinical trials sponsored by pharmaceutical companies gets a lot of attention. "But we've got to remember, academic scientists also have vested interests in their careers," says Master.

In one study, researchers analyzed 40 cases of falsification, fabrication, and plagiarism. They identified poor ability to cope with research pressures as a contributing factor.[4]

"The reasons for misconduct are highly diverse," says DuBois, the study's lead author. Reasons can include the following:

- researchers with personality disorders who seek fame,
- being under a lot of pressure to obtain funding,
- recklessness with data,
- experiencing personal stress that clouds judgment,
- not realizing how seriously U.S. society takes plagiarism, and
- fear of peer reviewers, which could lead to minor falsification rather than wholesale fabrication of data.

"The diversity of reasons is part of why it is difficult to craft a one-size-fits-all solution," says DuBois.

• Research institutions typically react only after misconduct cases are reported in the press.

"The university tries to save its reputation and wants to make sure that the behavior isn't prevalent, so they react and do a bunch of different things in response to a publicized case of misconduct," Master says. The following are practices that, instead, can create a climate of research integrity:

1. Institutions can reduce the number of "soft money" positions, which require scientists to pay their own salaries with grant money.

"'Hard money' positions are becoming extinct," says Master. "This kind of environment is ripe for research misconduct."

2. Research funders can limit how many students and fellows are hired with a grant.

If a principal investigator gets a grant for several years, the usual approach is to hire many students and fellows to do the work. "When they graduate and become principal investigators, the system becomes saturated. Resources are limited, creating competition," Master says. Limiting this number would encourage universities to hire research scientists as permanent employees, he says.

3. Institutions can do a better job of assessing the integrity of their research environment.

Keith Baggerly, PhD, a biostatistician at the University of Texas MD Anderson Cancer Center in Houston, says, "Most do not assume that their faculty are doing things in a fraudulent way. The baseline assumption is that everybody is trying to do things correctly."

In one case, there initially appeared to be some honest mistakes made in data analysis. "But over time, when it persisted, we got more suspicious there was substantial fraud involved," says Baggerly. The biggest problem was that after concerns were raised about the quality of the raw data, those concerns were largely ignored or dismissed, he says.

While some institutions do the bare minimum to promote a culture of research integrity, others do it really well. Master suggests using the indirect costs from grant funding for this purpose. "If you are doing well, great," he says. "But if the climate of research integrity is underserved, ramp it up to do what you can."

4. Institutions can recognize there is increasing recognition that reproducibility and reliability rates are not as high as they should be.

EXECUTIVE SUMMARY

Retractions in scientific journals — some due to research misconduct — have increased significantly in recent years. This is likely due to such factors as intense competition, institutions' inadequate assessment, and improved detection, some experts say. Some ethical issues include the following:

- The data on misconduct is largely self-reported.
- Perpetrators of fraud may receive inadequate punishment, even though patients were harmed.
- Pressure to publish findings incentivizes researchers to take shortcuts.

"If you are aware that this is a big problem — and it is — addressing it is fairly easy," says Baggerly, who teaches a course on reproducibility of research.

Several journals have begun to ask for the data used to produce results, but don't go so far as to check the results. "What is easy and fast is simply checking existence of the data. Checking accuracy is not as simple," Baggerly says.

One problem is that researchers tend not to question whether another factor could have been responsible for a given finding. "Instead, people say, 'Oh my gosh, how brilliant I was to run this experiment.' People get excited when they see a cool result," Baggerly says.

Batch effects also result in misleading findings — in some cases, due to improperly set calibration. "Randomizing the run order can minimize batch effects," notes Baggerly. "Good design can separate the batch effects from the biological effects that we actually want to find."

Wide availability of image comparison tools has also contributed to the increase in retractions. "If you can see if it matches, that becomes a lot easier to check," says Baggerly. "The ability to detect it is getting better."

Too-light Penalties

Penalties for egregious research fraud are often viewed as too light — for both the investigator and the institution. "If an individual is found guilty of research fraud, a separate assessment needs to be done to determine the degree of culpability on the part of the institution," says Baggerly.

If fraud is discovered, the institution is supposed to report it to the HHS Office of Research Integrity if grant funding is involved. "But I don't believe they've ever acted or imposed sanctions on the institution — it's wholly on the individual," Baggerly says.

Typical penalties include suspension of grant funding, and barring the investigator from serving on various NIH committees. "This might be sufficient to get a bad actor out of the research community, but can be too light if there have been substantial real-world consequences," says Baggerly.

In one highly publicized case, a prominent cancer researcher at Duke University was found to have falsified data in multiple published studies. His punishment was a five-year ban from federal grant funding.[5]

Baggerly co-authored an editorial noting that the researcher misused taxpayer dollars and put patients at risk.[6] "In that case, I don't think suspension from grant funding was adequate because it resulted in people being incorrectly treated in clinical trials," he says.

Except when it is clear the institution engaged in cover-up or was negligent in some fashion, DuBois strongly opposes punishing institutions for the wrongdoing of investigators.

"Doing so is likely to increase the motivation of institutions to cover up wrongdoing," he explains. "It may also increase an 'us-them' dynamic between institutional officials and researchers."

Both of these consequences would serve to hinder, rather than promote, research integrity. "The airline safety movement has important lessons for the world of research integrity in terms of focusing on root cause analyses and problem-solving, rather than blame of institutions," says Dubois. ■

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Physicians Have New Guidance on Ethics of Telemedicine

Patient/physician relationship is central focus

A patient asks her physician, whom she's never seen previously, a particularly sensitive medical question. How does this interaction differ if the patient is at home, viewing the doctor's response on a computer screen?

"Telemedicine services can change communication and power relationships between clinicians, between patients and clinicians, and between family members," says **Bonnie Kaplan**, PhD, FACMI, Yale Interdisciplinary Bioethics Center Scholar and faculty in the Yale Center for Medical Informatics at the School of Medicine at Yale University in New Haven, CT.[1]

A telemedicine physician may never meet the patient or others involved in caring for that person. "So physicians may not get to know the patient's situation, and that can affect care," Kaplan says.

New ethical guidance from the American Medical Association (AMA) aims to help physicians understand how their fundamental responsibilities may play out differently when patient interactions occur through telemedicine instead of in-person.[2]

BJ Crigger, PhD, the AMA's director of ethics policy and secretary for the AMA's Council on Ethical and Judicial Affairs (CEJA), explains, "As the public becomes increasingly fluent in utilizing novel technologies in all aspects of daily life, evolving applications in healthcare are altering the contours of when, where, and how patients and physicians engage with one another."

Crigger describes the practice of medicine as "inherently a moral activity." This is founded in a covenant of trust between patient and physician. "No matter what the model for care, physicians' fundamental ethical responsibilities do not change," she says.

Patient/Physician Relationship

The ability to maintain privacy and confidentiality is one oft-cited ethical concern with telemedicine. "Others 'off-camera' at the patient site and unknown to the physician may be able to hear or observe the interaction taking place," says **David A. Fleming**, MD, MA, MACP, director of University of Missouri's Center for Health Ethics in Columbia.

Fleming names the following three issues as other central ethical concerns:

- preventing harm to the patient by ensuring standards of care equal to in-person visits,
- avoiding the entrepreneurial temptation of deploying telehealth primarily in the interest of profit, or in situations where it's inappropriate, and
- ensuring the technology being used does not serve as a barrier to maintaining the trust and integrity of the physician-patient relationship.

Kaplan says that ethical policies for the use of telemedicine should include the following:

- Familiarize everyone involved with a realistic assessment of its benefits and limitations, and current ethical and practice guidelines.
- Train people for the change in their roles and responsibilities.
- Address the burgeoning area of commercially available smartphone apps.
- Develop guidelines for incorporating telehealth data into patient records.
- Involve patients in designing telehealth and telemedicine services.
- Promote shared decision-making for each patient's use of telemedicine services.
- Set up policies for patient consent when possible consequences are unknown, because the technology or services are so new.
- Prevent assumptions built into computer software algorithms, hardware, or telemedicine from

EXECUTIVE SUMMARY

A new ethical guidance from the American Medical Association focuses on how the physician's fundamental responsibilities play out differently with the use of telemedicine. Some considerations include the following:

- Telemedicine changes the way patients and clinicians communicate.
- Some telemedicine physicians don't ever meet the patient in person.
- Others 'off-camera' may be able to hear or observe the interaction.

replacing clinical judgment, patient autonomy, and human values.

• Evaluate telemedicine services to make them better, improve health and well-being, support patients, caregivers, and clinicians.

• Weigh this use of resources against better or more cost-effective ways to improve health.

• Ensure that patients' decisions are freely made. "Patients should not be pushed into unwanted monitoring or other forms of remote care by their well-meaning children, clinicians, or caregivers," says Kaplan.

Fleming says that bioethicists can offer education for providers who will be using telehealth about its potential ethical pitfalls. Bioethicists can also make themselves available if questions arise during clinical encounters, or if there are questions about appropriate telehealth utilization.

"The ethics team can provide an invaluable service to systems that are establishing telehealth services," says Fleming. ■

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People with Mental Illness Often Excluded from Clinical Trials

Misconceptions about capacity to consent are problem

If a medication for major depression has a dangerous adverse interaction with a different medication that's being studied in a clinical trial, will it be discovered by researchers and reported in the literature? Not likely, if no one enrolled in the study has major depression.

"We need to make sure that the people we study are like the people we treat," says **Keith Humphreys**, PhD, a professor of psychiatry and behavioral sciences at Stanford University. "The healthcare system takes care of many people with psychiatric disorders all over the system, not just in psychiatry."

Previous research has shown that women and older people are often disproportionately excluded from research. "We wanted to see if the same was true of people with mental illness. It's an important question to ask, because people with mental illness are just as likely, or even more likely, as the general population to have serious medical problems," says Humphreys.

The researchers found that half of 400 highly cited randomized trials across 20 common chronic disorders reported possible or definite psychiatric exclusion criteria.[1] Negative attitudes about people with mental illness are one likely reason, researchers found. Another is that researchers make blanket assumptions about lack capacity to give consent.

"The problem is that research then doesn't generalize as well to people with psychiatric problems as it does to the rest of the population," says Humphreys, the study's lead author.

EXECUTIVE SUMMARY

People with mental illness are disproportionately excluded from participation in clinical trials, due in part to misconceptions about their capacity to consent, experts say. The following can ensure enrollment practices are ethical:

• Obtain advance directives for eventual participation in research.

• Give patients time to consider whether they want to participate.

• Check comprehension with open-ended questions, and provide corrective feedback.

Misconceptions on Capacity

When enrolling patients with psychiatric disorders in research, it's ethically important to "balance research opportunities with research protection," says **Cynthia M.A.**

Geppert, MD, MPH, chief ethics consultant at New Mexico Veterans Affairs Health Care System in Albuquerque.

"In areas where psychiatric patients may have vulnerabilities such as impairments in executive functioning, efforts should be made to minimize risks and maximize the benefits of participation," Geppert says.

Previous research indicates that patients with serious mental illness want the opportunity to express their altruism and autonomy through research participation.[2] "These patients should be not prevented from enrolling in research based on misconceptions about capacity," says Geppert.

The presumption that many psychiatric patients are incapable of providing informed consent for research is still prevalent. "This is despite empirical work demonstrating that the majority of patients are able to provide informed consent for research participation," Geppert says. For the small number of psychiatric patients who lack the capacity to consent, she suggests that proxy decision-making can safeguard patients' welfare while permitting participation.

Marilyn A. Fisher, MD, MSBioethics, associate professor at the Center for Biomedical Ethics Education & Research at Albany (NY) Medical College, says, "Because patients who are decisionally incapacitated may seem to be convenient, gullible, and exploitable research participants, they have the right to be afforded extra protections from the dangers of participating in research." The following are two primary ethical concerns:

• People with psychiatric conditions are particularly vulnerable to coercion.

Coercion may cause an institutionalized person to consent to participate in a research study for reasons other than wanting to contribute to scientific knowledge to help others, due to fear of retribution, says Fisher.

"In order to minimize effects of coercion, the potential study subject should clearly understand that participation will not be rewarded and non-participation will not be punished," says Fisher.

Barton W. Palmer, PhD, professor of psychiatry at University of California, San Diego, notes that a cornerstone of ethical research is that it be voluntary. This means participants cannot be coerced or unduly influenced.

"This can raise complex issues when the investigator also wears the hat of clinical provider, and is recruiting his or her own clinical patients into a protocol," says Palmer. While this is not necessarily unethical, the potential for undue influence needs to be carefully considered, he says.

• People with psychiatric conditions may have a permanent, or fluctuating, lack of capacity.

"The informed consent process should be carried out in a way that is understandable to the potential research subject, and at a time when he or she has the most capacity for understanding the information discussed," Fisher says.

Upon diagnosis of a psychiatric illness, during a period of lucidity, advance directives can be sought for eventual participation in the research study, suggests Fisher. "The patient should have the opportunity to contemplate the study over a period of time, to ask questions about the study, and to discuss it with his or her support people," says Fisher.

To declare all patients who are decisionally incapacitated ineligible to participate in clinical trials violates the ethical principle of justice, says Fisher. "This is because other diseases are having active research performed in hopes of finding their cures, so cures should also be actively being sought for psychiatric disease," she says.

Certain psychiatric disorders are associated with greater risk of impaired decisional capacity. However, says Palmer, "a large body of research has shown that there is considerable within-group heterogeneity — such that it would be inappropriate to equate a psychiatric diagnosis with impaired capacity."

Moreover, it is not a person's general decisional capacity that is at issue — rather, the capacity to make a very specific decision. "A person may retain capacity to make a decision about a straightforward protocol with a good risk/benefit ratio, but have questionable capacity to decide in regard to a more procedurally complex protocol, or one in which the risk/benefit considerations are more complicated," says Palmer. Therefore, capacity must be evaluated on a situation-specific basis, he says.

"It is important to consider that the comprehension of a potential participant is influenced not only by his or her decisional capacity, but also by the quality of the consent process," adds Palmer.

Except perhaps with very high-functioning individuals, it is generally inappropriate to simply have the person read and sign the consent form. "Rather, consent should be conducted as an interactive process," says Palmer. This includes checking of participant comprehension with open-ended questions, provision of corrective feedback, and further assessment of comprehension.

"When decisional capacity is in question, formal assessment with an established tool should be considered," Palmer adds. ■

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Close Ties Between Surgeons and Device Reps Raises Ethical Concerns

"I often felt like I'm driving up the costs of the healthcare system … We used to sell an implant that has 99% survivorship at 15 years, which is great, right? We were told to not ever market it to anybody … If a doctor asked for it by name, we would give it to him. We want to market the newer, the better technology. I'm not certain I ever thought the newer technology was better. There certainly wasn't data on it … I was uncomfortable with those sorts of things."

This statement was made by a medical device representative during a recent focus group held by researchers. "We believe that there is an inherent conflict of interest, and therefore an ethical problem, in having the surgical sales representatives present in advisory capacities in the OR," says **Bonnie B. O'Connor**, PhD, the study's lead author and professor emerita of pediatrics at Brown University's Alpert Medical School in Providence, RI.

Researchers also held focus groups with ear, nose, and throat surgeons and hospital-based attending orthopedic surgeons. While most surgeons said that medical device representatives improved efficiency within the OR, some were uncomfortable with certain aspects of the representative's role, researchers found.[1]

Device reps can make surgeries more "efficient" in terms of length of time spent completing the surgical procedure. "This, along with sales techniques that rely on sophisticated use of social psychology data, helps to create a sense of indebtedness on the part of physicians," says O'Connor.

In the case of drug reps, this is well-demonstrated to affect physicians' choices and prescribing practices. "We believe the same factors are at work in the selection of medical devices," says O'Connor.

Adriane Fugh-Berman, MD, associate professor in the department of pharmacology and physiology at Georgetown University Medical Center in Washington, DC, is another of the study's authors. She notes that some surgeons didn't realize that devices did not have to be tested in humans before being approved.

"Newer devices not only cost more, but they are relatively untested," says Fugh-Berman. "Untested devices have caused many problems." In the U.S., devices can be approved based on "substantial equivalence;" many have never been tested in humans before being surgically implanted in patients.

"Add to that surgeons' conflicts of interest with device companies, and the question of whether patients are aware that a device rep will attend their surgery, and the ethics issues increase exponentially," says Fugh-Berman.

Close relationships develop when device reps provide services to individual surgeons. "They act as a part of the surgical team," says Fugh-Berman. "However, these are not health professionals who have the patient's best interests in mind."

Rather, the reps are industry employees who make money from every device from their company that is implanted into a patient. "They should not be part of the surgical team. Everyone in an operating room should be there to benefit the patient," says Fugh-Berman.

While device reps offer services that surgeons are grateful for, says Fugh-Berman, these services should be provided by the hospital — not

someone who is profiting from surgeons' choices.

O'Connor says, "Surgical sales representatives are understandably biased in favor of their companies' proprietary devices, and so are trying to 'convert' surgeons to use them." Commissions earned on sales can significantly increase the compensation of successful reps.

"This creates a powerful incentive for reps to persuade physicians to choose newer and more expensive devices, irrespective of how much benefit they confer for patients by comparison with established and less expensive devices," says O'Connor.

The American College of Surgeons' guidelines for informed consent of patients regarding the presence of device reps in the OR state the patients should be clearly informed, and their agreement or disagreement with having reps present documented and followed.

"The majority of the surgeons we interviewed were not aware that this is a recommended part of the pre-surgical informed consent content and process," says O'Connor. The surgeons didn't know if it was part of their hospital's informed consent process.

"Some believed it was not necessary to inform patients, since the choice to have a rep present rested with the surgeon," says O'Connor. Some believed patients would not be equipped to make the decision in an educated way. "One believed it would only confuse patients to be asked about it, at a time when they were already stressed enough," says O'Connor.

Others expressed concern at informing patients about the practice because they believed that patients would refuse it if it were specifically pointed out. "Deciding not to inform patients of a practice because you believe they will say no if you tell them about it, is an obvious signal of an ethical problem," says O'Connor.

Lydia Dugdale, MD, assistant professor of medicine and associate director of Yale School of Medicine's Program for Biomedical Ethics, says that even if the devices pushed by reps are equivalent in efficacy to older options, they typically cost more — and the patient bears this cost.

"The relationships between doctors and medical device or pharmaceutical reps also raise questions of conflict of interest and informed consent," says Dugdale.[2]

If a surgeon plans to use a brand-new device for a joint replacement, for example, should the patient be told that an older, cheaper, similarly efficacious device is available? "There has been a growing trend, among academic physicians, at least, to disclose financial conflicts of interest in publications or before a public lecture," notes Dugdale.

Should the patient's consent to surgery include the patient being privy to the surgeon's relationship with the device company? "If we doctors are to be wholly consistent, we should consider making similar disclosures to our patients who might benefit, or not, from physician relationships to drug and device reps," says Dugdale.

While there is growing awareness of the untoward influence of drug reps on physicians' practice, notes Fugh-Berman, the same is not true of device reps. "A few places make them wear different colored surgical caps," she notes.

A few device companies are trying out a "rep-less" approach, with hospital employees trained to provide the technical assistance instead. But, according to O'Connor, device reps "still aren't getting even a tiny percentage of the push-back and refusal that drug reps have in recent years." ■

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CME/CE QUESTIONS

1. Which is true regarding research misconduct, according to Zubin Master, PhD?

A. Retractions in scientific journals have markedly decreased in recent years, due to improved detection of actual fraud.
B. Self-reported data on misconduct is believed to be most reliable.
C. Punishment for fraud should not differ depending on whether patients were harmed.
D. Pressure to publish findings incentivizes researchers to take shortcuts.

2. Which is true about ethical considerations involving use of telemedicine, according to Bonnie Kaplan, PhD, FACMI?

A. A lower standard of care for some aspects of the visit is permissible than would be expected for in-person visits.
B. Shared decision-making is not realistic because the technology is too new for patients to adequately assess the risks and benefits.
C. It is acceptable for computer software algorithms to supersede clinical judgment and patient autonomy in many cases, in order to maximize efficiency and prevent harm.
D. Providers should weigh this use of resources against better or more cost-effective ways to improve health.

3. Which is true regarding enrollment of people with mental illness in clinical trials, according to recent research?

A. Large numbers of study participants with mental illness are routinely enrolled despite clear lack of capacity.
B. Although there is consensus that mental illness should be an automatic exclusion from the majority of clinical trials, some studies wrongly categorize it as only a possible exclusion.
C. People with mental illness are often disproportionately excluded from research.
D. People with serious mental illness are more likely to be included in some types of clinical trials than the general population.

4. Which is true regarding relationships between surgeons and device representatives, according to a recent study?

A. The majority of surgeons have discontinued such relationships altogether, due to a growing awareness of the untoward influence of device reps on surgeons' clinical practice.
B. All of the surgeons reported feeling comfortable with the representative's role, mainly because of improved patient care.
C. None of the device reps reported perceiving any conflict of interest.
D. Most surgeons reported that the device reps improved efficiency.