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Ethical Issues in Neurology

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From the Editor

Thinking About Ethical Issues in Neurology

The theme editor introduces a special issue examining the ethical issues associated with the neurology specialty.

No medical specialty addresses fundamental ethical issues more frequently than does neurology. The reason is simple: the brain is so basic to human identity that even the language of transplants must be stood on its head when we talk about it—for who could argue that a "brain transplant" could be anything but a misnomer? If we ever did manage to take Charlie's brain and put it in Billy's head, would we claim that the resulting person was Billy, just because he looked like him, rather than Charlie, whose brain would then be running the show? When something happens that fundamentally changes the way the brain works—stroke, trauma, medication, disease—what does that do to the person whose identity is largely defined by that brain? And when we as clinicians intervene, what are our obligations when we explore the possibilities? What if we do the same to someone who isn't even sick? What intriguing, dangerous territory.

Each of the topics in the present issue of *Virtual Mentor* presents a dilemma that links it, directly or indirectly, to each of the others. Devastating brain damage evokes obligations of understanding and communication of facts and uncertainties that simply must be navigated for clinical decisions to be properly shared and made. If Eisenberg and Junge describe the legal consequences when such communication fails at the end of life, Truog goes on to challenge the very definition of death by neurological criteria altogether. How fascinating that he suggests that allowing families to permit lethal organ procurement before spontaneous death—effectively killing the donor for the purpose of procuring his organs—would "uncouple" the ethics of organ donation from the question of the determination of death. And how strange that he would describe the consequent main disadvantage as its necessitating a complete restructuring of "our ethical and legal approach to organ donation" rather than our ethical, legal, and clinical approach to euthanasia, assisted suicide, withdrawal of life-prolonging therapy, and most everything else we do as physicians.

Johnston's and Bascom's elegant discussions of patient-physician communication in physician-assisted suicide reminds me of a story I heard from Balfour Mount, the Montreal urologist who brought hospice to North America in the early 1970s in Montreal. While training at St Christopher's Hospice, he said, Cicely Saunders told him, "A bedpan thrown at you is not to be reacted to; it is to be interpreted." Would our interpretation of and response to requests for assisted death be altered fundamentally if organs might then be conveniently harvested? When Taylor discusses prognosis, uncertainty, and the importance of effective communication to establish goals of care consonant with the values of the neurologically devastated patient, it should be only too obvious that such communication might be fundamentally altered if the option of organ procurement became one component of at least one treatment option.

And so it goes with the minimally conscious and the vegetative, the latter of whom Cranford distinguishes from the minimally conscious by "the ability to visually track...in a consistent, sustained, and reproducible fashion"—defined further, oddly, rather like the obverse of Louis Armstrong's definition of jazz: "it is usually readily apparent to anyone seeing the patient." Why, then, do so many families refuse to accept what they see? And would the option of organ donation from those in a persistent vegetative state—whether "dead" by higher brain formulations, or merely "uncoupled" from the definition of death altogether—make things better or worse, easier or more difficult? Witness Lagay's discussion of our struggle over organ donation with anencephalic newborns whose higher brain is not permanently nonfunctional but altogether absent.

So what is the neurologist's job, after all? Garland's discussion of chronic pain treatment, devoid of ethical argument,

devoted exclusively to case management, is oddly if starkly appropriate. We should attach no greater stigma to appropriate treatment of pain, with or without opioids, than to treatment of any other disorder: complete history, exam, treatment plan according to realistic, agreed-upon goals. Period. Green's discussion of the promise, pitfalls, and risks of presymptomatic testing for degenerative diseases whose course cannot be significantly modified by existing treatment raises the bar for communication. For how many workaday neurologists are equipped to provide the kind of counseling and support needed to permit both truly informed decisions regarding the tests and adequate management of their aftermath? (Need we return to the previous paragraph to imagine how the conversation might be influenced by lethal organ donation?) Who is to train us, and how?

In "Cosmetic Neurology," Chatterjee challenges the easy distinction between therapy and enhancement and then describes the societal forces that make the proliferation of neuro-enhancements inevitable. Asking where physicians will fit into this market, like it or not, he poses a series of provocative questions that challenge us to question our own sincerity if we simply recoil at this possibility.

Farah's "Neuroethics" and Schwab's review of articles by Farah and Wolpe contain the most grist for the bioethicist's mill. Matters like mind and body, personhood, social equity, free will and determinism bubble rapidly to the surface in any discussion of "the myriad ways in which...neuroscience intersect[s] with social and ethical issues." Is the neuroethics discussed here the same as the ethics of neurology? Important, basic questions are begged in such brief discussions, but certainly must be hovering nearby. It is interesting that neurology textbooks are often called textbooks of clinical neuroscience and that neurology/neurosurgery units in hospitals are often named "neuroscience" units, despite not one iota of research or formal study being associated with them. So many questions of identity, yet unasked. Are we physicians, whose specialty is the treatment of persons with neurological disease, clinical neuroscientists, dispassionate students of the nervous system; or are we neurological engineers, who apply the fruits of the neuroscientists' labor?

Students, neurologists, neuroscientists: read on.

Sincerely,

James Gordon, MD, FRCPC

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Clinical Cases

Physicians' Role in Physician-Assisted Suicide Discussions

Physicians of patients who request physician-assisted suicide should not avoid the subject and should try to discuss the patients' specific concerns and fears with them.

Commentary by Wendy Johnston, MD, and Paul Bascom, MD

Four years ago, Jonathan Witlaw's internist referred him to neurologist Bob Ferris for a work up. At the time, Mr. Witlaw reported having stumbled on several occasions over the span of 6 or 8 weeks. At first, he paid no attention, thinking he was just being careless or not looking at the pavement, but then he stumbled in his own apartment and knew he needed to check it out.

The work-up, including nerve conduction and electromyographic studies confirmed that Mr. Witlaw had amyotrophic lateral sclerosis (ALS). When Dr. Ferris called Mr. Wiltlaw to the office to discuss the test results, he had much information to share about support services—physical, psychological, and social. He told Mr. Witlaw that the disease progressed a little differently in each patient, but he was honest about the stages of the disease, what Jonathan could expect, and what would, eventually, cause death. Dr. Ferris explained the sorts of interventions that could help—physical therapy, speech and swallowing therapy, counseling, and the pharmacologic agents that together would help him manage his illness.

It turned out that the rate of Jonathan Witlaw's ALS progress was on the slow end of the continuum, and he fought it with all he had. A computer applications designer who lived alone, Mr. Witlaw was able to continue going to work for many months. When his leg strength deteriorated but his arm control still allowed him to type, he worked from home for a few more months.

About 2 years after confirmation of his diagnosis, Mr. Witlaw went on long-term disability. He received a portion of his pay, and his medical bills were mostly covered. He had been working with his therapists and counselors and had consulted a lawyer to "get his affairs in order." His living will stated that he does not want to be put on a ventilator or to receive a feeding tube when he was no longer able to swallow.

Dr. Ferris sees Jonathan every few weeks. A home nursing agency provides someone to accompany Jonathan in his wheelchair to the neurology clinic. On one visit, Mr. Witlaw asks Dr. Ferris to prescribe a barbiturate and tell him how best to use it "just in case." He wants to be able to commit suicide before he loses the ability to do it on his own.

"I don't have any family," Jonathan says. "No one's pleading for me to stay alive for those last few months of deterioration. And my decision is not influenced by depression—you know me well enough to know that, Doc," Mr. Witlaw says. "What I'm suggesting is pretty sane, under the circumstances, isn't it?"

Not comfortable with participating in Mr. Witlaw's plan, Dr. Ferris said, "Well, I'm told you can get information from many of those death with dignity organizations. Is that true?"

"Yeah, probably, but you've been my doctor through all this and I trust you. Tell me what's the best thing to take and

then give me a prescription. I'll save them up from several prescriptions, if necessary. I won't make you look bad, I promise."

"Jonathan," Dr. Ferris said, compassionately, "I can't argue with anything you say, but, as a physician, I just can't participate in helping you commit suicide.

"Patient's best interest, Doc. Remember that?" was Jonathan's final attempt.

Commentary 1

by Wendy S. Johnston, MD

Patients with amyotrophic lateral sclerosis (ALS) have been prominent in the both the medical and public discussions of physician-assisted suicide.

ALS Is a relentlessly disabling disease that leads to death, in the majority of cases, within 5 years of diagnosis. Although generally perceived as a rare neurological illness, the annual mortality from ALS approaches that of HIV-related diseases in many states in the US.

In the course of the illness, the individual eventually loses all voluntary motor activity, including the use of all 4 limbs, the voice, and head control. Technology provides many ways to overcome the disabilities, but assistance from caregivers to access technology (eg, transferring from bed to wheelchair, setting up computer-assisted communication) is still necessary when the disease is advanced. Autonomy is possible, but can be compromised by insensitive or inexperienced caregivers or failures of technology. Supporting and maintaining autonomy is critically important to quality of life for many with ALS and can be a major factor in end-of-life decisions.

Unlike patients with many ultimately terminal disorders, those with ALS commonly are aware of their fate from the outset. The lack of significant disease-altering therapy and the steady, measurable losses impose the need for ongoing accommodation by both the patient and his or her loved ones. Awareness of the inevitability of dying, however, doesn't translate into actual knowledge about end-of-life care, and patients, families, and those caring for them frequently are unprepared for the decisions and symptom management in the final months. Even when living-wills are in place, the decisions to limit or forgo interventions may have been made with little or no discussion of how to manage without the unwanted intervention. Symptoms of respiratory failure may still prompt intubation and ventilation, in spite of an advanced directive, if no plan for symptom management is in place.

Therefore, any query on the part of patient or family about an end-of-life issue is an opening for discussion of care. A request for assisted suicide needs to be seen first and foremost as such a query.

Requests for assisted suicide are not uncommon. Of 100 ALS patient surveyed in Oregon and southwest Washington, 56 percent would consider PAS [1]. This interest is sustained through the last month of life [2]. Compared to other terminal diseases, those with ALS use assisted suicide and euthanasia at higher rates, as reported from jurisdictions where it is legal and statistics are available [3].

Interest in PAS correlated with higher education, less religious practice, male sex, and higher hopelessness scores in the earlier, cross-sectional study [1]. There was a corresponding lack of interest in other life-prolonging therapies, for example feeding tubes. There didn't seem to be a correlation with disease characteristics, current symptoms, suffering, or depression. Fears of future suffering and of being a burden were significant.

High levels of suffering overall were found in the last month of life; however, interest in hastening death correlated with poor symptom control [4]. Subsequently, Albert et al, in a prospective study of ALS patients followed in a hospice setting, found 23 percent hastened death, one by suicide [5]. Those who hastened dying reported poorer mood and were less religious; they were more likely to have depressive symptoms of clinical significance, and to feel less in control and more hopeless.

It is important to consider that the patient making the query may be suffering from depression, may fear uncontrolled

symptoms while dying, and may be misinformed about the terminal stages of the disease. Realistic concerns about loss of autonomy, privacy, and fear of being a burden may have arisen. Substantial losses of pleasurable activities, financial resources, and personal contacts may have already occurred.

Rather than focus on the legal or moral issues, the physician should take a step back, asking why the request was made. When Mr. Witlaw says, "You know me well enough" and "what I am suggesting is pretty sane" he is giving openings to Dr. Ferris to say something like, "I know you in some ways, but tell me why you think you will need this?" or "What is your understanding of the last months with ALS?" Dr. Ferris can be supportive ("Yes, you are sane"), without having to commit immediately to the request.

Mr. Witlaw is relying on Dr. Ferris, having seen him every few weeks throughout his illness, to take care of him in the terminal phase. Although the advance directives are done (living will) it appears that there has been little of substance discussed regarding his care. Mr. Witlaw, living alone, with an aide to bring him to appointments, may not see any other option but to take his own life.

On the other hand, Dr. Ferris, it would seem, may not be prepared to take care of Mr. Witlaw at the end of life. Neurology textbooks don't cover it; neurology residencies only recently added end-of-life care to the curriculum. CME courses are available, and there are on-line resources, but, frankly, they aren't much help when it comes to the actual face-to-face discussions. The issues facing Dr. Ferris are difficult for any solo practitioner to face in a busy practice. The issues and practicalities of his care may be best dealt with by a palliative care team, which may include or support Dr. Ferris in his care of Mr. Witlaw.

Dr. Ferris's response could be interpreted as fearful, and rejecting. In staking out his own values in opposition to Mr. Witlaw's perceived plan, he distances himself further from Mr. Witlaw's needs. Physicians should not feel compelled or coerced to comply with requests for assisted suicide. A physician can honestly state that he or she can't supply a lethal prescription. It is important to proactively attempt to understand the basis of the request and address the underlying concerns, rather than cut off discussion with too quick a denial.

Establishing the basis of quality of life in the present ("what do you live for now") as a bridge to what to continue to hope for in the future, addressing current concerns similarly, will strengthen the trust that allows for the best end-of-life care. For a minority of individuals, controlling the timing and means of death through suicide, assisted or not, may still be their final choice. For others, offering continuity of care to the end of life and the promise that they will receive the best of end-of-life care may be the answer to the question of assisted suicide.

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Commentary 2

by Paul Bascom, MD

Patient requests for physician-assisted suicide (PAS) are common. Fifty percent of patients with ALS report being willing to consider PAS. Far fewer ALS patients ultimately make an explicit request for PAS, and fewer still end their lives by PAS. Yet ALS patients are substantially overrepresented compared to patients with other terminal diseases in Oregon's experience with legal PAS.

Physicians need not initially respond to a patient request for PAS with a yes/no answer. In the case, Dr. Ferris's first response Mr. Witlaw's plan is to express his moral opposition to PAS by recommending that Mr. Witlaw seek information from death with dignity organizations. Dr. Ferris responds as if the patient's request were fixed and unyielding. Data shows, however, that many more patients consider, and even explicitly request, PAS than ultimately use PAS to end their lives. Therefore, the appropriate first response to a patient request for PAS is to explore the request further.

An exploration of the following areas will usually uncover some underlying motivation for the request, which, when addressed, will meet patient goals without PAS.

Expectations and fears. Mr. Witlaw states that he wants PAS "just in case." He worries about "those last months of deterioration." Dr. Ferris should explore what scenario Mr. Witlaw envisions for his future that would warrant him to end his life by PAS.

O*ptions for end-of-life care.* Mr. Witlaw has already indicated his desire for no tube feedings or mechanical ventilation. He would benefit from knowing that he will likely lose the ability to swallow as he deteriorates, and that the inability to take food and fluids will prevent the lingering deterioration that he seems to fear.

Patient goals. Medical treatments, even PAS, can be evaluated based on their ability to meet certain patient goals. The rare patient who chooses PAS to end his/her life often expresses the explicit goal of controlling the time and place of death. Mr. Witlaw expresses the wish to "commit suicide before he loses the ability to do it on his own." But it is not clear from the case whether the primary goal is control the time and manner of death or to avoid lingering deterioration.

Family concerns and burdens. Many patients fear being a burden on family. Mr. Witlaw reports "I don't have any family." As an independent spirit, Mr. Witlaw may fear becoming dependent on others for care.

Suffering and physical symptoms. Uncontrolled physical symptoms such as pain, rarely influence a desire for PAS. In some patients, fear of future pain may play a role.

Sense of meaning and quality of life. ALS is perhaps unique in that patient decisions about treatment will vastly affect longevity. The patient with ALS who chooses gastrostomy feeding and mechanical ventilation can live years longer than those who refuse such treatments. Some patients may continue to report meaningful life and good quality of life despite the extraordinary limitations imposed by their infirmity. Alternatively, others will find that even modest restrictions in independence will create such a poor quality of life that death is preferable, either by refusal of life-sustaining treatments or PAS.

Depression. Patients who request PAS do not have an increased prevalence of depression. Rather, they score high on ratings of hopelessness, of finding no meaning or purpose in ongoing life. Sometimes the direct question, "Are you depressed?" is as effective a screen for depression as multiple question instruments.

The ethical controversy over PAS will continue. There is no simple answer to Mr. Witlaw's assertion of his right to PAS as "patient's best interest." Is it in the patient's interest to hasten death? And if so, does the patient's individual

interest outweigh concerns that increased acceptability of PAS will cause harm to vulnerable populations?

Dr. Ferris should respond to the request with a detailed exploration with the patient of the areas noted above. Frequently, this exploration will lead to identification of concerns and goals that can be met without PAS. At times, requests for PAS will persist. The rare patient who chooses PAS usually has the goal of controlling the time and manner of death, and is motivated by the desire to avoid dependency. These are goals even the best medical intervention cannot help a patient accomplish. Death is by nature unpredictable, and, except for the rare sudden cardiac or traumatic death, requires one to be tended to by others. If indeed Mr. Witlaw persists in his desire for PAS, then Dr. Ferris may need to inform the patient that personal moral beliefs will prevent him from providing the prescriptions as requested.

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Clinical Cases

Helping Surrogate Decision Makers in the Face of Uncertainty

Physicians need to help surrogate decision makers to make treatment and end-of-life decisions for those with severe neurological damage by proving a realistic prognosis and maintain strong lines of communication.

Commentary by Robert Taylor, MD

Neurologist Dr. Biels was asked to evaluate Neal Boland, a 67-year-old, right-handed man with a long history of poorly controlled hypertension and hyperlipidemia. Mr. Boland was discovered by his wife to be sitting unresponsive in his armchair when she returned from an afternoon of shopping. Upon arrival of the EMT, he opened his eyes and moved his left arm and leg in agitation, but did not move his right. In the ER, he was mute and stuporous, unresponsive to voice, arousing only briefly to painful nailbed stimulation of the left hand and foot. Fundoscopic exam was normal. Pupillary responses, corneal reflexes, and gag were normal. Severe right facial weakness was noted. Occasional spontaneous left upper and lower extremity movements continued, but flaccid right hemiplegia persisted. Head CT scan was normal. His attending physician, an internist, consulted Dr. Biels, a neurologist, who documented a Glasgow Coma Score of 9 (eye 4, verbal 1, motor 4).

In the following days, Mr. Boland's neurological examination improved slightly. He began to have sleeping and waking periods and to open his eyes spontaneously. He occasionally seemed to smile when visitors or staff entered the room and squeezed his wife's finger several times, but not on command. His gag reflex remained weak, and a nasogastric feeding tube was placed. A follow-up CT scan 48 hours after admission confirmed a large left frontoparietal infarct with significant edema, likely resulting from left middle cerebral artery occlusion.

Mr. Boland's condition changed minimally over the next ten days. Caregivers were able to move him to a chair for short periods in the morning and afternoon. His wife, who was his only family member, became concerned at his lack of progress, since he still did not recognize her and could not communicate. Although Mr. Boland had no advance directive, Mrs. Boland said that they had discussed "that woman in Florida" when it was in the news—"lying there for years while her husband and parents fight over her." Neither of them wanted to be kept alive if they had to live "like that woman in Florida."

When Mrs. Boland asked about her husband's prognosis—specifically whether he would be able to eat, recognize her, and interact with his surroundings, "you know, watch television or play with our dog,"—the attending internist was optimistic, saying "it can take a long time for recovery and rehabilitation after a stroke like this." He cited Mr. Boland's stable vital signs and encouraged hope for some improvement. Mr. Boland's other health care team members reinforced this view. Mrs. Boland was told that her husband would have to have a percutaneous endoscopic gastrostomy (PEG) tube placed, to permit long-term feeding, and be transferred to a long-term nursing facility.

The next time Dr. Biels checked on her husband, Mrs. Boland asked his opinion. Based on several additional CT scans that showed extensive, irreversible hemispheric injury, and on the patient's lack of significant progress to date, Dr. Biels doubted that Mr. Boland would make significant neurologic gains, even with extensive rehabilitation efforts and nursing care. Moreover, his condition might worsen acutely if common infectious or cardiorespiratory complications were to occur, as is often the case in such severely impaired patients. If this occurred, Dr. Biels told Mrs. Boland, the

physicians would ordinarily employ aggressive medical therapies to give him more time to recover neurologically, but the outcome was not likely to be good, mortality in such cases being as high as 20-40 percent at 3-6 months in many studies. He shared this information compassionately with Mrs. Boland and answered her questions slowly and honestly. Mrs. Boland seemed to understand the prognosis, and then said that she felt overwhelmed by the decisions she had to make about his care. Dr. Biels asked whether she had talked to the chaplain or had a spiritual advisor who could help.

"It's not the spiritual part that bothers me," she said. "If he's going to stay like this, I know he would not want to. Are you certain he will stay like this? The other doctors seemed to think I should give him some more time to recover. I just want some advice about what to do. We've signed a DNR, but where do we draw the line? We can't just stop feeding him, can we? I just keep praying that he dies without us doing anything about it."

Commentary by Robert M. Taylor, MD

Unfortunately, Mrs. Boland's dilemma and the distress it causes her are not uncommon in today's hospitals. Mr. Boland's massive left hemispheric stroke has left him with global aphasia, right hemiplegia, and severe dysphagia. Although his internist appears to be optimistic about his long-term prognosis, his neurologist indicates he is unlikely to recover significant neurological function, and quotes a 3-6 month mortality of 20-40 percent, even with continued medical treatment. Faced with an uncertain prognosis for her husband, Mrs. Boland is understandably confused as to what decision to make, and even as to what decisions she can make.

Mr. Boland's global aphasia renders him unable to make decisions about his medical care. Because he has no advance directives, his wife is his appropriate surrogate decision maker. She should do her best to make decisions for him employing a substituted judgment standard. His statements about "that woman in Florida" (ie, Terri Schaivo) may well provide her some guidance in this effort. If she is unable to make a substituted judgment, she should make her decision based on what she perceives as his best interests. Mrs. Boland is faced with 2 major issues: first, what is Mr. Boland's prognosis and, second, what decisions can she and should she make with regard to his medical care.

Although Mrs. Boland appears to have received differing opinions on her husband's prognosis, the difference is really more a matter of emphasis than substance. His internist emphasized the hope for improvement after extended rehabilitation, without quantifying the probabilities. In contrast, while not excluding the possibility of significant recovery, Dr. Biels emphasized the far greater likelihood that he would fail to improve significantly, or even die. Better communication between the two doctors, and even a joint meeting with the 2 of them and Mrs. Boland, might have averted this problem and minimized her confusion. Unfortunately, almost all prognoses can only be given as probabilities, so it is important for physicians to acknowledge the uncertainty and to try to be as realistic about the probabilities as possible.

Mrs. Boland is confident that: "If [Mr. Boland is] going to stay like this, I know he would not want to." Yet she can't be certain that he will not improve significantly. Thus she finds herself in the uncomfortable position of facing difficult life-and-death decisions in the face of her uncertainty. What would Mr. Boland be willing to tolerate, and for how long, for a small chance of significant neurological recovery?

Before discussing particular treatment options, her doctors should help her to consider the goals of treatment. Once the goals of treatment are established, the physicians can recommend treatments that will help advance those goals and explain why other treatments are unlikely to be beneficial. Mrs. Boland's first goal, understandably, is that her husband recover all or most of his neurological function. Unfortunately that is unlikely to happen. If this goal is not achievable, she has indicated that he would not want to be kept alive indefinitely in his current debilitated condition. Although placing a PEG tube is necessary to permit whatever small chance he has for recovery, it is more likely to maintain him in his current condition. Not placing the PEG tube, in contrast, would eliminate any chance of recovery, but would permit him to die a natural death from the effects of his stroke.

The immediate therapeutic question, then, is whether to place the PEG tube to permit long-term artificial hydration and nutrition. Mrs. Boland has inquired of Dr. Biels: "We can't just stop feeding him, can we?" In fact, not placing a PEG tube is a legal and ethical option. Mr. Boland's dysphagia is the result of his stroke—he can no longer nourish himself

by eating and drinking. Thus, if the PEG tube is not placed, he will die from dehydration resulting from the effects of his stroke. The US Supreme Court, in the Cruzan case, established that artificial hydration and nutrition is a form of medical therapy and can be refused by competent or incompetent patients. Because, if competent, Mr. Boland would have a right to refuse the PEG tube, his wife, as his legal surrogate, likewise has a right to refuse it on his behalf [1].

Mrs. Boland should be advised that not placing the PEG tube and discontinuing artificial hydration and nutrition is, in fact, a legal and ethical option in this situation. She should also be informed that, if she refuses the PEG tube, Mr. Boland would die of dehydration, a process that can take as long as 1 to 2 weeks. If she refuses the PEG tube, palliative measures, including good mouth care and analgesic and sedative medications, should be provided to assure his comfort. She should be given the option of hospice care either in her home or in an extended care facility.

If she does decide to have the PEG tube placed and Mr. Boland is discharged to rehabilitation, she should be advised of the various decisions that she may need to face in the foreseeable future, so that she can begin to anticipate decisions rather than having to make them on the spur of the moment. For example, if he does develop an infection or other complication, she may refuse additional treatments, such as antibiotics, and palliative measures could be instituted at that time. Furthermore, a decision to place a PEG tube does not preclude the option of discontinuing tube feedings if the hoped-for outcome is not achieved. Thus, after a reasonable period of time, if Mr. Boland shows no significant neurological recovery, artificial hydration and nutrition could be discontinued, to avoid prolonging his life in a condition he indicated he would not want, and palliative care could be instituted.

Because stroke remains the third leading cause of death and a major cause of disability in the United States, families are often confronted with decisions regarding the appropriate treatment for patients like Mr. Boland. Keys to helping families make good decisions include maintaining effective communication among the treating doctors and with the family, providing realistic prognostic information, including the element of uncertainty, and understanding that surrogate decision-makers have the right, on behalf of the patient, to refuse any treatment that does not serve the goals of the patient as understood by the surrogate.

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Clinical Cases

Is Chronic Pain Treatment the Neurologist's Job?

Patients who are seeking pain management with opioids can be difficult for neurologists to manage.

Commentary by Erich Garland, MD

Dr. Fields has been a neurologist for 17 years. He has seen much improvement in pain management—particularly as part of palliative care at the end of life—over the course of his practice. Many challenges remain, however. Pain from inoperable lesions and pain that persists after surgery can be impossible to treat successfully. Patients with such pain can be in tremendous distress—often unable to continue at their jobs and sometimes unable even to rest without drugs that affect awareness and have other serious side effects.

One day a colleague of Dr. Fields, an orthopedic surgeon named David Burns, asks whether Dr. Fields will consent to see a patient of his. Dr. Burns relates an abbreviated history of his patient, Eleanor Mitchell, now 47 years old. Nearly 3 years ago, Mrs. Mitchell lost her balance while helping her husband carry a new air conditioning unit up the front stairs to their house. She experienced immediate lumbar pain. She called Dr. Burns who, after examination, prescribed a muscle relaxant and bed rest. Two weeks later, Mrs. Mitchell returned, still in pain. A subsequent lumbosacral MRI showed herniation of Mrs. Mitchell's L5-S1 disc with a small fragment compressing the left S1 root.

When Dr. Burns recommended surgery, Mrs. Mitchell rejected the idea. She had heard about mistakes in back surgery, she said. She also knew of someone her husband worked with who had injured his back at work and had as much pain after back surgery as before. He had to go on permanent disability. Mrs. Mitchell didn't want that. She decided instead to try physical therapy and "painkillers" and see how it went.

After 18 months, Mrs. Mitchell asked to be scheduled for surgery. She had missed a good deal of work and had been in moderate to severe pain "every minute of the day" except when sleeping—and getting to sleep wasn't so easy either. Dr. Burns performed surgery to remove the fragments and relieve the compression, and Mrs. Mitchell recovered without complication. After the appropriate recovery period, however, her pain persisted. In fact, it became more intense. She complained of pain in her left leg also. Upon Dr. Burns' recommendation, Mrs. Mitchell consulted another orthopedist and a neurosurgeon, both of whom found no other surgical indications. Now Dr. Burns was turning to his neurology colleague, Dr. Fields.

"She's had PT on and off without success and attended a pain clinic briefly but found that sympathetic and regional nerve blocks provided only transient—if any—relief. I think this is really more of a neurology case than an orthopedic case at this point," Dr. Burns said.

Dr. Fields, however, was reluctant to accept another patient with chronic pain.

"I have much sympathy for Mrs. Mitchell and others with her sort of intractable pain. You know I do, Dave. But it seems that all treatment doors have been opened and closed. She doesn't need a neurologist to write her a script every month for the rest of her life," Dr. Fields said. "Her internist can do that. Besides, I have quite a few patients who are being maintained on heavy-duty opioids, and I have to watch that. I could be escorted out of here in handcuffs some day. It's happened. Especially if the patient appears to be doctor-hopping," Dr. Fields said.

Commentary

Treatment of chronic pain is both an art and science. It requires that the treating physician have an understanding of the pathophysiology of pain and a history of treatments that have failed and those that have provided some relief. Physicians have traditionally been trained to diagnose and treat disease as the cause of pain, but few have the training to treat chronic pain effectively. In this case study the patient tried conservative management for 18 months before choosing surgery as an option. Postoperatively her pain persisted and eventually worsened. Although she consulted 2 other surgeons for opinions and attended a pain clinic, she continued to experience intractable pain.

Before accepting this patient, I would want to know why PT and a pain clinic could not provide Mrs. Mitchell adequate relief of her pain. Review of her medical records would be the most appropriate first step. Then I would offer Mrs. Mitchell an appointment to get a medical history, psychosocial history, and physical exam and determine what her expectations are before agreeing to provide long-tem opioid management. After a thorough history, physical exam, and psychosocial history, a diagnosis should be made, and all prior treatments and diagnostic tests verified; treating physicians and pharmacies used should also be confirmed. Goals for treatment such as return to work, less pain, and improved activities should be documented in the medical record. Treatment should be monitored and drug testing done when suspicion of inappropriate use arises. Patients must be informed about the side effects associated with chronic opioid use, and their informed consent must be obtained. One physician and one pharmacy must be chosen for the opioid prescriptions. A written contract is the best way to document this process. Patients receiving opioids should be seen by the physician on a regular schedule. The physician should prescribe long-acting opioids on a time schedule, document treatment outcomes in the medical record, and reevaluate the benefits and risks of continued opioid use periodically. Taking these steps will alleviate the concerns Dr. Biels expresses in his reluctance to take on the care of Mrs. Mitchell.

Opioids are not the only treatment option. Optimal pain management also includes physical conditioning, non-opioid medications, and coping skills to obtain the best quality of life from the treatment plan. Recovery from chronic pain requires educating the patient for a life without pain. This can entail major psychological adjustment to overcome fear, anger, shame, loss of self-esteem, loss of respect, and codependency. Finally, psychiatric disorders are a common co-morbidity with chronic pain, a fact that makes treatment difficult and non-rewarding for physicians to manage.

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Journal Discussion

Ethical Issues in the Application and Prescription of CNS Interventions

A neuroscientist and a sociologist discuss the ethical concerns with common neurological medicines that are used to enhance or change behavior.

Abraham P. Schwab, PhD

Farah MJ. Emerging ethical issues in neuroscience. *Nature Neuroscience*. 2002;5:1123-1129.

Farah MJ and Wolpe PR. Monitoring and manipulating brain function: new neuroscience technologies and their ethical implications. *Hastings Center Report.* 2004;34(3):35-45.

As our understanding of the brain and nervous system has advanced and as CNS treatments expand and improve, normal individuals have begun to use therapeutic treatments to enhance their existing capabilities. Neuroscientist Martha J. Farah has published 2 articles [1] (1 with sociologist Paul Root Wolpe [2]) that start some meaningful conversations about the ethical issues raised by this developing practice as well as the growing use of brain-reading (translating neuroimages to psychological characteristics).

Neuroscience enhancements have been available for quite some time, and drug experimentation has long been a part of human history. Nonetheless, more effective CNS interventions have been recently produced, selective seratonin reuptake inhibitors (SSRIs) have diminished some previously nasty side-effects, and supplementary medications have been developed that effectively counteract others (ie, sildenafil for sexual dysfunction). Currently, CNS interventions are available in 3 general areas: appetites (sex, sleep, and hunger), mood, and cognition (attention and memory) [3].

The primary ethical concern involved in the use of neural interventions for enhancement is safety. While not entirely unique to neuroethics, safety (especially long-term safety) is of special concern in neuroethics for two interrelated reasons: (1) because "neuroscience-based enhancement involves intervening in a far more complex system [than other comparable elective treatments]" [4] and (2) because of an increased likelihood of long-term use. For example, some individuals may use methylphenidate (Ritalin) to enhance attention for 40 or more years (their working adult life). The appropriate response to safety concerns is the deliberate completion of the appropriate research. Farah and Wolpe note, however, that, "drug safety testing does not routinely address long-term use, and relatively little evidence is available on long-term use by healthy subjects" [4]. Because many of these neural interventions are not intended to be used as enhancers, and research does not generally address long-term risks, the use of neuroscience-based interventions for enhancement will include unknown risks for the foreseeable future.

Farah and Wolpe initiate an important discussion about a constellation of ethical concerns centered on challenges to our conceptions of personhood and responsibility that are raised by the use of neuroscience-based interventions for enhancement. As they admit, these concerns are complex, and their discussion, not fully developed. For example, they offer the following: "Improving behavior pharmacologically seems to detract from the responsibility of the person for his or her own actions" [3]. This statement seems to assume (1) that individuals who are not enhancing their behavior pharmacologically have substantial control over their moods, cognitive abilities, and appetites, and (2) that pharmacological interventions diminish this control and, subsequently, individual responsibility. If these assumptions

are true, Farah and Wolpe may be right. If individuals, however, can only marginally control their mood, etc., when compared to the control available through CNS interventions, then it seems we should hold them more responsible because now they are in better position to control their moods, cognitive abilities, and appetites. For example, we might hold a cigarette smoker more responsible for not quitting now that Zyban (a CNS intervention) has been shown to at least triple the success rate of individuals trying to quit smoking.

Wolpe and Farah also assert that, "Maximizing the performance capabilities of an already healthy, functional person can be viewed as commodifying human abilities" [4]. Yet, we already commodify human abilities and attempt to maximize performance (ie, paying to receive advanced training on the hopes of receiving more income; determining pay scales, in part, by type of degree and other qualifications). The difficulties Farah and Wolpe encounter in discussing these and other potential challenges to our conceptions of personhood and responsibility illustrate that we do not yet have an adequate grasp on whether or how the causal physiological processes of the brain affect psychological states and abilities. As our understanding of this relationship improves, the challenges, to our existing conceptions of personhood and responsibility will become more tractable, and the discussion of these challenges, more substantive.

Issues of personal responsibility also arise in Farah's discussion of court-ordered CNS interventions. Just as courts currently order anger management and parenting classes, and some convicted sex offenders are required to use antiandrogen treatments (which have been shown to lower serum testosterone levels and reduce recidivism), Farah asserts that safe and effective neural interventions may be used as punishment/ rehabilitation techniques [5]. She notes that this will infringe on personal freedom, but that that alone does not raise a new ethical challenge [5]. We regularly compromise freedom for concerns of public safety—convicted criminals are confined for long-term incarceration. Even so, the effects of neuroscience-based interventions demand caution in their application. The convict is free to react in thought and attitude to her condition however she chooses (insomuch as she can choose), but the same cannot be said for a medicated individual. Farah uses the following example to reflect this point: an individual may attend but ignore the content of an anger management class, but he cannot avoid the effects of a required neuroscience-based intervention [5]. As Farah suggests, because court-ordered CNS interventions may illegitimately violate personal freedom to "think one's own thoughts," court-ordered uses of these interventions should be carefully considered and cautiously applied.

Farah and Wolpe spend a good deal of time discussing brain-reading and its possible applications. Brain-reading is essentially the attempt to accurately translate physiological activity in the brain (available through neuroimaging) into psychological information (eg, personal information, personality, and preferences). Though its potential, like that of genetics, appears limitless, its usefulness to date has been restricted by its diagnostic limits. Brain-reading only reliably distinguishes between groups and, in some cases, distinguishes the most extreme individuals with a given characteristic. For example, neuroimaging correctly distinguishes groups of recently detoxified cocaine addicts from non-addicts when they are shown drug-related pictures, but in one study that Farah and Wolpe cite, only half of the recently detoxified cocaine users could be identified individually [6]. This uncertainty leads to the primary ethical concern about brain-reading—its over-application. Any attempt to apply brain-reading to individuals would provide information that has only "illusory accuracy" [7]. If/when brain-reading accuracy improves to the point of reliable individual diagnosis, it will raise serious concerns about privacy. Even an accurate interpretation of individual physiological data could be more revealing than necessary, and may undermine the individual's right to privacy.

In closing, let's note and expand on the ethical concern about equity raised by Farah in her earlier article. She foresees that neuroscience-based enhancements might not be distributed fairly [8]. She responds to this concern by noting the number of inequities we leave untouched (and seem to endorse). What warrants some attention here is that there are limits to justifiable inequity, and effective neural interventions used for enhancement may breach them. An unequal distribution of educational opportunities already exists, and our market system generally pays less talented and less capable individuals less money. Given these existing structural inequities, any exacerbating effect of neural interventions should be discussed and evaluated explicitly.

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Questions for Discussion

1. Do you agree with the authors that our conceptions of personhood and responsibility are challenged by the use of neuroscience-based interventions for the enhancement of mood, cognitive abilities, and appetites? Do some of these interventions challenge our conceptions of personhood and responsibility more than others?
2. Does the use of neuroscience-based interventions for enhancement exacerbate existing inequalities such that individual freedoms to use them should be limited?
3. Should a physician participate in an individual's court-ordered involuntary CNS intervention?

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Clinical Pearl

Diagnosing The Permanent Vegetative State

Neurologists need to understand and be able to identify the most distinguishing features of permanent vegetative state.

Ronald Cranford, MD

Modern medicine and newer life-saving treatments have not only resulted in the saving of an untold number of lives and preservation and restoration of health but, as an unfortunate and unavoidable by-product, they have created syndromes of severe brain damage rarely seen, if at all, prior to these advances in medical therapy. These syndromes include brain death, the minimally conscious state, locked-in syndrome, and, probably the most widely known example, the permanent vegetative state. In the middle of the last century, most physicians would have thought it strange to envision a neurological syndrome wherein the patient manifests sleep-wake cycles with periods of eyes open and yet possesses no consciousness whatsoever during those wakeful periods. This state—the permanent vegetative state—is a condition of wakeful unawareness, a form of permanent unconsciousness. Originally described and named by Fred Plum and Brian Jennet in 1972, this neurological syndrome is now well known to most doctors who treat neurological disorders. Furthermore, many of the landmark right-to-die legal cases in the United States have involved patients in a permanent vegetative state, beginning with Karen Quinlan, the first major termination-of-treatment case in the US to reach the state supreme court level (in New Jersey, 1975); Nancy Cruzan, the first right-to-die case to reach the United States Supreme Court (1990), and, more recently, the widely publicized case of Terri Schiavo, now pending before the Florida Supreme Court. Although cases of the permanent vegetative state were undoubtedly rare prior to the 1960s, the Multi-society Task Force on the Persistent Vegetative State estimated in 1994 that there were 10,000 to 25,000 adults and 4,000 to 10,000 children in persistent vegetative states in the United States.

The reason why these patients experience periods of wakeful unawareness is readily explainable by the underlying characteristic neuropathological changes present in most patients. Whatever the primary cause of the vegetative state, such as hypoxic-ischemic encephalopathy secondary to a cardiac or pulmonary arrest, or shearing injuries in brain trauma, there is extensive damage to the higher centers of the brain, with relative preservation of the brain stem structures. Hence, the cognitive functions of the cerebral cortex are absent, while the arousal system (the reticular activating system) in the brain stem is intact.

Making the PVS Diagnosis

Given this situation, the clinical diagnosis of PVS can be a difficult, and scary, diagnosis to make, unless a physician has adequate experience and expertise in evaluating neurological syndromes. To the families and loved ones, and to inexperienced health care professionals, PVS patients often look fairly "normal." Their eyes are open and moving about during the periods of wakefulness that alternate with periods of sleep; there may be spontaneous movements of the arms and legs, and at times these patients appear to smile, grimace, laugh, utter guttural sounds, groan and moan, and manifest other facial expressions and sounds that appear to reflect cognitive functions and emotions, especially in the eyes of the family.

But the cardinal features that distinguish the vegetative state from other syndromes of lesser brain damage, such as the minimally conscious state, are the absence of sustained visual pursuit (visual tracking) and visual fixation. The eyes do not follow objects or persons, nor do they fixate on these objects or persons. And, when patients do emerge from the vegetative state, almost invariably the first and most reliable sign of improvement is the ability to visually track objects

or persons in a consistent, sustained, and reproducible fashion. The question is often asked, what exactly does "consistent, sustained, and reproducible fashion" *mean* in this context? None of the guidelines in the literature precisely defines these terms, but when the patients do develop sustained visual pursuit, it is usually readily apparent to anyone seeing the patient, families and health care professionals alike, and it is so consistent and reproducible that it is present almost 100 percent of the time during the periods of wakefulness.

Persistent and Permanent Vegetative States

Extensive dialogue and debate has centered on when the vegetative state becomes permanent. Originally, and in common usage today, the term "persistent" was equated with "permanent." But the 2 terms should be distinguished, because some persistent vegetative state patients, especially those with traumatic head injuries, may gradually improve to higher levels of cognitive and motor functions in the first few months. It is now well established in the literature and among clinicians with over 3 decades of experience in this condition that, for both children and adults in vegetative states secondary to hypoxic-ischemic encephalopathy, the chance of any meaningful recovery beyond 3-6 months is negligible. In patients with traumatic brain injuries, the chances of meaningful recovery are practically nonexistent beyond one year. Reports of dramatic "miracle" recoveries surface in the lay press on a regular basis every few years, but these cases, when thoroughly investigated, have not substantially undermined the recovery period statistics given above. So the term "persistent" should be restricted to patients in a vegetative state of at least 1-month duration, while "permanent" should be used when it can be determined with an extremely high degree of certainty that the condition is irreversible.

The diagnosis of the permanent vegetative state is primarily clinical, with repeated neurological examination necessary over a period of time to establish absence of cognitive functions and irreversibility. Laboratory studies may be useful and confirmatory in some cases. For example, EEGs will show severe background slowing. When monitored over a few years, CT scans and MRIs will show progressive cerebral cortical atrophy. While the degree of cerebral cortical atrophy does not necessarily correlate with the complete loss of cerebral cortical functions, it does, however, help to confirm that the underlying process, given the severity of destruction seen on these neuroimaging studies, is irreversible, thus establishing to a high degree of certainty that the condition is permanent. Clinical studies evaluating the usefulness of PET (positron emission tomography) have confirmed the absence of consciousness in these patients by conclusively demonstrating levels of oxygen and glucose metabolism in the cerebral cortex consistent with deep levels of coma, and other forms of deep unconsciousness.

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Health Law

Words Count as Much as Deeds

Physicians must maintain strong communication lines and document discussions with patient surrogates to avoid confusion regarding end-of-life care and decisions for patients with irreversible brain damage.

Leah Eisenberg and Melissa Junge

Mrs. Milos was brought to the emergency department at Middlesex Hospital one evening, unconscious but breathing on her own. The 76-year-old woman had been transported there by ambulance from the skilled nursing facility where she had resided for the last 3 years. She moved into the facility after a stroke left her with neurological deficits that rendered her unable to speak or care for herself independently. She retained the ability to understand speech, and she enjoyed TV as well as being talked to or read to. Until the night she was taken to the ED, she still recognized her son, smiled at her fellow residents, and liked to be walked around the nursing facility in a wheelchair. However, on the night in question, Mrs. Milos had pressed the "panic button" in her room, and when an aide responded to her call, he found her unconscious on the floor and summoned the paramedics.

Shortly after arriving in the ED, Mrs. Milos went into cardiac arrest. Since she did not have any DNR orders, CPR was performed. The physicians treating her were able to restore her heartbeat in roughly twenty minutes, but Mrs. Milos remained unable to breathe on her own. Therefore, she was intubated before being transferred to the ICU in a deep coma.

The next morning, the attending physician, Dr. Mosher, called in Dr. Henry, a neurologist, to examine Mrs. Milos and to assess her neurological condition. Dr. Henry found Mrs. Milos to be unresponsive, with fixed, nonreactive pupils, no purposeful movement, and no spontaneous or reflex eye movements. Her son, George, was present during this examination, and Dr. Henry was not optimistic about Mrs. Milos's prognosis. He ordered a CT scan and left until the next morning. At that time, he found Mrs. Milos's condition to be unchanged. He told Dr. Mosher that Mrs. Milos was irreparably brain damaged and that there was no hope for neurologic recovery. He spoke to George Milos again, and told him that, based on the CT scan and the exam he had conducted, his mother had no remaining brain function. Most of this conversation took place between just the two of them, since Dr. Mosher was called away early on in the discussion.

Dr. Henry recommended a trial of patient-assisted ventilation in order to confirm his diagnosis. He explained to George that if Mrs. Milos made any attempt to breathe on her own, the patient-assisted ventilator would sense her efforts and deliver a breath for her. Should she fail to make such an attempt, however, the ventilator would not function, and then they could conclude that no brain function remained. George agreed that they should try the patient-assisted ventilation, and the ventilator settings were adjusted accordingly. Just then, Dr. Henry was called away from the ICU, and a nurse was left to observe the trial. The nurse did not see any evidence that Mrs. Milos was attempting to breathe on her own, but did not call a code. The nurse did call Dr. Mosher, and by the time he arrived, Mrs. Milos's heart rate and blood pressure had slowed. Twelve minutes later, she became asystolic, and Dr. Mosher declared her dead based on cardiac criteria. When he informed George that Mrs. Milos had just died, George was shocked. He said that he had only agreed to try the patient-assisted ventilation because Dr. Henry had led him to believe that his mother was already "brain dead" and that, if he had known she wasn't, he would never have agreed to change the ventilator settings. He was also furious that Dr. Mosher had done nothing to save his mother when he arrived and saw that she was failing to breathe on her own.

George Milos filed two lawsuits; he sued Dr. Mosher and Dr. Henry for fraud, and he sued Middlesex Hospital for malpractice.

Legal Analysis

The 2nd Circuit Court of Appeals addressed similar claims in the 2001 case of *Law v Camp* [1]. The basic facts in *Law v Camp* were similar to those in the Milos case—James Law sued the hospital where his mother died, as well as the physicians who treated her there, for malpractice and fraud, respectively. The 2 actions were later consolidated by the district court. In the *Law* case, as in the case above, a DNR was never signed, and part of the ruling discusses the implications of removing a patient from life support without such a directive. *Law v Camp* never went to trial, and the court focused more on procedural matters than on an adjudication of facts.

James Law asserted that the defendant physicians who cared for his mother, one of whom was Dr. Camp, violated a Connecticut statute when they withdrew Mrs. Law from life support before she had been declared brain dead, and that in so doing they also disregarded the hospital's own protocols, which established the medical standards for determining brain death. Mr. Law wanted these violations recognized as negligence *per se*, the negligence that arises automatically from the breach of a public duty. Since Mr. Law maintained that the statute prohibited the removal of a person from life support unless brain death had been established, and since Dr. Camp testified that he had not told James Law that his mother was brain dead, Mr. Law believed negligence per se was apparent. Therefore, he moved for summary judgment, a court decision made on the basis of pleadings, depositions, and other evidence presented for the record without a trial. Depriving a party of a trial violates the Constitutional guarantee of due process, so a court will only grant a motion for summary judgment when it determines that reasonable people could not differ as to their interpretation of the material facts in the case.

The district court ultimately rejected Mr. Law's motion for summary judgment. Key to its decision was the fact that Law failed to offer expert testimony supporting his interpretation of the Connecticut statute, while the defendant physicians offered an expert who stated that the standard of care does not demand a determination of brain death prior to placing a patient in Mrs. Law's condition on a patient-assisted ventilator. The fact that the defendant physicians presented an expert, while Law did not, sunk his claim of negligence per se and therefore his motion for summary judgment.

Expert testimony is generally required in all medical malpractice proceedings in order to establish that the alleged negligence was the proximate cause of the injury in question. Law asserted that expert testimony was not needed in this case, and that the cause of his mother's death was not at issue, since it was "undisputed" that she was not brain dead before life support was removed, and that she died as a result of its removal. The court rejected his reasoning, holding that the cause of Mrs. Law's death was far from certain. Instead, it declared that, in order to find in Mr. Law's favor, the court would have to have evidence that Mrs. Law was not brain dead when life support was removed and that its removal was the proximate cause of her death. Since Mr. Law failed to offer expert testimony supporting a single claim against the defendant physicians, and since the defendant physicians backed up their own assertions, the district court granted the physicians' counter-motion for summary judgment.

Implications for Physicians

This case focuses on communication (or lack thereof) between the physician and the patient's decision maker. It is not an all or nothing situation of either no communication or completely accurate communication. The problem arises from the extent of the communication between the physician and the patient's family or surrogate.

First and foremost, physicians in situations similar to that of Dr. Camp must follow the hospital or health care institution's policy regarding the determination and confirmation of brain death. However, as exemplified in the case, much confusion can arise regarding the use of terminology such as "irreversibly unconscious," "brain death," "no brain function," and "persistent vegetative state." There are aspects of the terminology upon which even physicians disagree. [See this month's *VM* article, "Brain Death: At Once 'Well Settled' and 'Persistently Unresolved"] Determination of death by neurological criteria is definitely not a topic that is simple or straightforward for a patient's family or

surrogate to understand.

The *Code of Medical Ethics* provides guidance on the underlying issues of patient communication and informed decision making. Opinion 2.20, "Withholding or Withdrawing Life-Sustaining Medical Treatment," states that "Physicians should provide all relevant medical information…" [2]. Opinion 2.215, "Treatment Decisions for Seriously Ill Newborns" adds pertinent language which applies to an adult surrogate of a patient who is either brain dead or irreversibly brain damaged. It states that "Physicians must provide full information…regarding the nature of treatments, therapeutic options and expected prognosis with and without therapy, so that [surrogates] can make informed decisions for [the patient] about life-sustaining treatment" [3].

The challenge for physicians is to provide the information about the patient's condition and the implications of various treatment options in language that the family or surrogate can understand. In *Law v Camp*, it is quite obvious that there was a miscommunication or, at the very least, a misunderstanding between the patient's family member and the physician. Ultimately, a lack of communication and understanding leaves the family or surrogate feeling confused, frustrated, and potentially betrayed.

When speaking with the patient's family or surrogate, the physician should follow the guidelines of Opinion 8.081, "Surrogate Decision Making." Opinion 8.081 states that "Physicians should recognize the proxy or surrogate as an extension of the patient, entitled to the same respect as the competent patient. Physicians should provide advice, guidance, and support; explain that decisions should be based on substituted judgment when possible and otherwise on the best interest principle; and offer relevant medical information as well as medical opinions in a timely manner" [4]. After this discussion with the patient's family or surrogate, the physician should clearly document the discussion, including the information presented, implications discussed, and the family or surrogate's questions and decision(s).

Given the absence of a Do Not Resuscitate (DNR) order or advance directive, it is surprising that the absence of efforts to resuscitate Mrs. Law was not considered a material issue in the *Law v Camp* case. Generally, in the absence of a DNR order, efforts *are* made to resuscitate the patient, inasmuch as his or her preference to the contrary has not been expressed or documented. The *Law v Camp* case indicates that Dr. Camp discussed the absence of a DNR or an advance directive for Mrs. Law with her son. Her son replied that his mother would not wish to be kept alive in a state of irreversible brain damage. Perhaps this discussion sufficed to make clear that Mr. Law did not want efforts made to resuscitate his mother, should she "fail" the patient-assisted ventilator test. Nevertheless, a physician who has this type of discussion with the family should at least document the patient's preferences as expressed by the surrogate, if not establish the order accordingly. Preferably, the physician would take the next step and see that the DNR was entered into the patient's chart. Opinion 2.22, "Do-Not-Resuscitate Orders" provides guidance by stating that "[i]f a patient is incapable of rendering a decision regarding the use of [resuscitative efforts], a decision may be made by a surrogate decision maker, based upon the previously expressed preferences of the patient or, if such preferences are unknown, in accordance with the patient's best interests" [5]. The Opinion also states "[i]f, in the judgment of the attending physician, it would be inappropriate to pursue CPR, the attending physician may enter a DNR order into the patient's record."

In life-and-death situations, clear and complete communication, coupled with clear evidence that the surrogate understands the situation and treatment options will go far toward decreasing the number of cases such as *Law v Camp* where the patient's family or surrogate is left with confusion and frustration about the end-of-life care of the patient.

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Policy Forum

Brain Death: At Once "Well Settled" and "Persistently Unresolved"

The use of neurological criteria to determine brain death has ethical implications for prospective organ donors.

Robert Truog, MD

Bioethicist Alexander Capron began a recent article on the subject of brain death by noting that "If one subject in health law and bioethics can be said to be at once well settled and persistently unresolved, it is how to determine that death has occurred" [1]. The "well settled" aspect is easy to understand—thousands of deaths are diagnosed daily on the basis of cessation of pulse and respiration. A much smaller number are diagnosed on the basis of neurological criteria—so-called brain death. Brain death requires the patient to be comatose, to have no detectable brainstem reflexes, and to have no neurological drive to breathe, even when high levels of carbon dioxide are allowed to accumulate in the blood (as happens during the required "apnea test"). Following the diagnosis of brain death, patients may be taken to the operating room while their body is still being perfused by a beating heart for recovery of organs like the heart, lungs, and kidneys.

The "persistently unresolved" aspect of death is more subtle, and becomes apparent only on closer inspection of the definition of brain death [2,3]. According to laws in the United States, brain death requires the "irreversible cessation of all functions of the entire brain, including the brain stem" [4]. Currently accepted guidelines for diagnosing brain death examine many, but not all, testable brain functions [5]. Not surprisingly, the closer one looks at brain function, the more one is likely to find. One brain function that is often present in patients diagnosed as brain-dead is the secretion of anti-diuretic hormone (ADH) from the posterior pituitary in response to changes in blood volume and osmolality. This may seem like nit-picking, but one of the most important reasons for equating the death of the brain with the death of the person is that the brain is seen as the "central organizer" of the body, such that when the brain is dead the body can no longer sustain physiologic integrity. Many of the components of the brain death exam measure functions that contribute nothing to physiologic integrity (such as determining whether the pupils react to light), yet functions that are critical to maintaining physiologic integrity (such as the regulated secretion of ADH) are ignored. The problem, in sum, is that current testing for brain death focuses on tests that have been selected because they are straightforward and easy to perform at the bedside, rather than focusing on functions that are essential to physiological integrity and that would truly answer the question of whether there is "the complete absence of all functions of the entire brain," as required by law.

Neurologist Alan Shewmon has performed careful neurological examinations on many patients who have fulfilled all of the legal requirements for brain death and yet who have "survived" for long periods of time (I have put "survived" in quotes, because all of these patients are legally dead). In the most dramatic case, he has documented the "survival" of a patient for more than 14 years following the diagnosis of brain death [6].

Cases like these highlight the ways in which brain death can be very counterintuitive to our common-sense understanding of death. Consider, for example, the following table that compares features of patients who are alive, brain-dead, and heart-dead (by heart-dead, I mean patients declared dead on the basis of loss of pulse and respiration). The point of the table is to show that brain-dead patients share many more features with living persons than they do with heart-dead persons.

Features	Living persons	Brain-dead	Heart-dead
Heart-beating, warm, well-perfused	Yes	Yes	No
Breathing	Yes	Yes	No
Functioning vital organs (liver, kidneys, etc.)	Yes	Yes	No
Capable of reproducing	Yes	Yes	No
Capacity for consciousness	Yes	No	No

(Note – some might quibble with my claim that brain-dead patients breathe, since one of the requirements for diagnosing brain death is the loss of the neurological drive to breathe. While it is true that brain-dead patients require a ventilator in order to breathe, so do many other patients who are not brain-dead. Christopher Reeve and other individuals with high spinal cord injuries cannot breathe without a ventilator, yet we do not consider them to be any less alive than those who breathe on their own.)

The table also shows that the one feature that clearly differentiates brain-dead patients from living individuals is loss of the capacity for consciousness. This fits with the very commonly held view that once a person has permanently lost the capacity to be conscious, life is no longer worth living. Some philosophers have taken this logic to the next step and proposed that once patients have been diagnosed with the permanent loss of consciousness, they should be considered dead for all ethical and legal purposes. This idea is the basis for the so-called "higher brain death standard," since patients who are permanently unconscious are generally understood to have lost function of the upper brain (the cortex and associated structures) but not necessarily function of the lower brain (the brainstem).

This view has been very popular in the medical and philosophical literature for decades, but suffers from one very significant problem. Patients who have been diagnosed with the persistent vegetative state are thought to be permanently unconscious, yet thousands of these patients are living in nursing homes throughout the world, breathing on their own, and fed through tubes that have been surgically placed in their stomachs. Under the "higher brain death standard," all of these patients would be legally dead, and we would be logically committed to treating them in the ways that we treat dead people, including burial and cremation. Yet few, if indeed anyone, would be willing to bury or cremate a person who was still breathing. Although there are other problems with the higher brain death standard, this reason alone is sufficient to show that such an approach, no matter how philosophically appealing, could never be implemented in our society.

Given all of these problems with the concept of brain death, what are possible solutions? The current approach is simply to ignore all of these problems and inconsistencies. Surprisingly, perhaps, this approach has much to recommend it. Our primary strategy for organ procurement and transplantation relies heavily upon the diagnosis of death by neurological criteria. Any serious disruption in the transplantation enterprise could jeopardize opportunities to save the lives of those in need of vital organs. As epitomized in the name of the old game show "Truth or Consequences," sometimes it is better to sacrifice devotion to the truth in order to optimize important consequences [7].

On the other hand, we could take a fresh look at the foundations of the ethics of organ transplantation. One approach, which I have explored in more detail elsewhere [3], would reexamine the ethical requirements for organ donation. We

currently require all organ donors to be diagnosed as dead, but as shown in the discussion above, diagnosing death is not as straightforward as it may first appear. Alternatively, we could allow patients and their families to request to be organ donors only in circumstances where the death of the patient that would *follow* the procurement of vital organs would be seen by the patient and family as a small loss in comparison to the opportunity to give life to others. Obviously, this would only be the case for patients with extremely profound neurological damage or patients within moments of death from cardiac or pulmonary failure. The main advantage of this approach is that it would "uncouple" the ethics of organ donation from the problematic determination of death. The main disadvantage of this approach is that it would require a complete restructuring of our ethical and legal approach to organ donation. This is unlikely to happen, as long as the "persistently unresolved" issues discussed above remain quietly ignored in relation to the "well settled" aspects of the diagnosis of death and the procurement of transplantable organs.

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Medicine and Society

Presymptomatic Genetic Testing for Neurodegenerative Diseases

Presymptomatic genetic testing for neurodegenerative diseases can help patients make effective treatment decisions, but the medical profession needs to ensure that the increasing use of the tests is done responsibly.

Shane K. Green, PhD

A few years ago, I was asked by someone very close to me whether I, as her genetics-savvy friend, thought she should undergo genetic testing to determine carrier status for a particular polymorphism that has been linked to Alzheimer's disease (AD), namely the e4 allele of apolipoprotein E (APOE). She had witnessed her father's slow deterioration and eventual death from AD, and feared, as she still does, that the same fate awaited her many years down the road. Having read a news item—or was it a website?—describing, or rather overstating, the link between APOE e4 and AD, she was considering facing her fear head-on by going to be tested for Alzheimer's.

"You're asking the wrong kind of doctor," I thought. So I advised her to seek the guidance of her physician, but not before directing her to numerous consensus statements issued by neurologists, geneticists, and medical ethicists that universally recommend against presymptomatic APOE genotype testing because of its low predictive value [1]. Though she decided not to pursue testing, her story has left me thinking ever since about the similar choices facing growing numbers of people as our understanding of the genetic underpinnings of disease continues to make great strides forward.

If, for example, you could have a genetic test—that is, obtain a clinical analysis of your DNA—that would tell you whether or not you were likely to be stricken with a terrible disease later in life, would you want to?

To state the obvious, most people have these tests in hopes of negative results (ie, absence of disease-causing genes). Sadly, but inevitably, such hopes are often dashed by tests that come up positive. But many others—in particular, those in families with a history of disease—choose to be tested so that, in the event of a positive test, they can make lifestyle changes or pursue clinical interventions that may alter the course of the disease(s) to which they are predisposed.

A woman in a family with a history of breast cancer, for example, may wish to be tested for an inherited mutation in the BRCA1 gene, which can lead to the development of breast (and ovarian) tumors. A positive test may prompt her to undergo more frequent mammograms to catch tumor development at an early stage when it may be more responsive to treatment or to undertake more drastic measures to protect against cancer developing at all, namely, prophylactic double mastectomy. While these are not enviable options, at least they are options; that is, in such cases, a positive genetic test is accompanied by a choice of preventive or even curative treatments.

This is not true of genetic testing for Huntington disease (HD) or Alzheimer's disease, both neurodegenerative conditions for which there is no treatment that stops the progression of the disease. Individuals considering being tested for either of these diseases must therefore answer another, in some ways more challenging, question:

If you could have a test that would tell you whether or not you were likely to be stricken with an incurable, fatal

disease later in life, would you want to?

Genetic Testing for HD and AD: A Primer

Huntington disease (sometimes referred to as Huntington's chorea) is caused by an autosomal dominant genetic variation with 100 percent penetrance—in other words, everyone who inherits an HD gene *will* eventually develop the disease. Because people have 2 of every autosomal gene (ie, 2 alleles), only 1 of which is passed on to their offspring, children of parents with 1 or 2 HD genes have a 50 or 100 percent chance, respectively, of developing it themselves.

Approximately 30,000 Americans have HD and another 150,000 are at risk of inheriting it from a parent [2]. Symptoms generally begin in affected individuals' 30s or 40s, and last for a mean duration of 17 progressively more difficult years before the disease proves fatal, barring earlier death from other causes. The test for the HD gene is fast, relatively inexpensive, and highly sensitive, with positive and negative predictive values approaching 99 percent.

Unlike HD, there is no single genetic cause of all cases of Alzheimer's disease, which currently affects 4.5 million Americans. Familial, early-onset (before age 65) AD comprises about 10 percent of all AD cases, 50 percent of which (or 5 percent overall) are caused by a heritable mutation in the gene encoding one of 3 proteins: presenilin-1 (PS1), -2 (PS2), or amyloid precursor protein (APP). Like the HD gene, mutations in these genes are dominant, causing AD to develop in nearly 100 percent of people possessing them. Hence, positive tests for these genes, as for the HD gene, are predictive rather than merely suggestive. Unlike the HD test, however, a negative PS1 (or PS2 or APP) test does not rule out the future development of AD with a different genetic etiology.

Indeed, the vast majority of AD cases are late-onset and not linked to the aforementioned genes, but instead are believed to be caused by the interaction of multiple genetic and environmental factors; recent twins studies suggest that genes are, in fact, less important than environmental influences in the development of AD [3]. Though studies have identified a number of putative genetic linkages that warrant further examination [4], only the APOE e4 allele has been validated as an AD risk factor. Individuals who are heterozygous (ie, have 1 allele) or homozygous (have 2 alleles) for APOE e4 have increased lifetime risks of developing AD of about 3-5 or 8-18 times, respectively; however, not all patients with late-onset AD possess the APOE e4 allele, and not all persons possessing the allele develop AD. Simply put, a genetic test for APOE e4 has little predictive value.

Why choose genetic testing for HD or AD?

With the exception of the APOE e4 risk factor, a positive DNA test for HD or (early-onset) AD means that, if the person lives to middle or late middle age, the disease *will* manifest, and will be unstoppable once it does. This unfortunate fact is the primary reason why only about 15-25 percent of people at risk for HD get tested [5]. For example, when asked why she has not been tested, Nancy Wexler, PhD, a prominent HD researcher who led the effort to identify the HD gene and herself a member of a family with a history of HD, blamed the lack of available treatment, wondering, "Why do we want this? What's on the plus side" [6]?

In the absence of a possible clinical response, a test confirming or even suggesting future development of a fatal neurodegenerative condition can have a devastating psychological impact on the patient. Moreover, pursuing such a test may strain relationships with and put undue burdens on other family members (eg, identical twin siblings) for whom the patient's test could reveal unwanted information. For the patient and other potentially affected individuals, a positive test could also have a detrimental effect on employment and insurance status. It should be noted, however, that more than 40 states currently have some form of genetic non-discrimination legislation to prevent such an occurrence [7] and federal legislation is pending [8].

This is not to say, however, that no benefit can come from testing. Even a positive test can be of emotional and psychological benefit to patients for whom knowing what lies ahead is preferable to the anxiety born of uncertainty. Foreknowledge can, for example, profoundly influence patient decision making with respect to finances (eg, providing for inevitable hospice care), family planning (eg, marriage or reproduction), and fostering personal relationships. Having insight into one's likely future health status can be empowering, helping to put control over these decisions squarely in one's hands.

Weighing the risks and benefits of these genetic tests is a decidedly personal endeavor. Hence, guidelines concerning presymptomatic genetic testing for HD and AD generally include the following:

- patients must be fully informed and as free as possible from coercive influences (eg, from family members, health care professionals, or direct-to-consumer pharmaceutical advertising) in consenting to be tested;
- only the individual being tested may provide consent (ie, no proxy consent);
- pre-test counseling should be provided to explain the implications of positive and negative results, and to assess family dynamics, cultural issues, financial support, and the emotional and psychological stability of the patient;
- post-test counseling should be provided to help the patient interpret and cope with test results;
- minors should *not* be tested;
- strict privacy and confidentiality must be maintained.

Looking Ahead

Genetic research and clinical medicine will continue to build greater understanding of these diseases and their causes, and, in the not-too-distant future, will undoubtedly develop ways to affect and ameliorate how they manifest in patients. As these are discovered, presymptomatic genetic testing will play an increasingly important role in helping patients decide what prophylactic interventions and treatments they can and should make use of, or even what clinical trials of such measures to enroll in.

It is entirely possible, if not likely, that, as with BRCA1 carriers, those with AD genetic risk factors or HD alleles will be forced to weigh the desirability of interventions that are highly toxic, or disfiguring, or otherwise physically or emotionally burdensome against their risk of disease. They will, therefore, become increasingly dependent on the guidance of clinicians and genetic counselors in making these difficult choices.

Already, there is evidence to suggest that the present capacity for genetic counseling is inadequate and will soon be overwhelmed as more people begin to require those critically important services [9]. Let this be a call to the medical profession, then, to put in motion whatever efforts are necessary to ensure that, as presymptomatic genetic testing is used more frequently, it is used as effectively and responsibly as possible.

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The Living Code

Considering Organ Donation by Anencephalic Neonates

The history of the AMA's policy on anencephalic newborns as organ donors is a living example of what medical science can do sometimes conflicts with society's support or nonsupport of those possibilities.

Faith Lagay, PhD

The AMA's *Code of Medical Ethics* – the living code

The mission of the AMA's 157-year-old *Code of Medical Ethics*—and its authors—is to set standards for the ethical and professional conduct of physicians within the ever-changing context of medical practice. There are at least 2 distinct aspects to the "context of medical practice"; one is the panoply of treatments and enhancements that medical science and biotechnology provide. These range from artificial life support and organ transplantation to in vitro fertilization and preimplantation genetic diagnosis. Such technologies change how we are born, how long we live, and how we die, and, in so doing, they place new demands on ethical decision making.

The second contextual component that the *Code* and its authors must consider is the environment in which physicians practice—society's understanding of emerging treatments and its inclination to accept or reject them as well as the system for the delivery and financing of medical care. Often these 2 components—what medical science can do and society's support or nonsupport of those possibilities—come into conflict. The conflict arises, for example, in legal arguments about withdrawal of life-sustaining treatment; public refusal to fund many forms of mental health treatment, and, to take the latest case, the debate over use of embryonic stem cells in research. Because of its contract with society, the medical profession must balance its interest in what science can do with what society is willing to support and fund. The *Code of Medical Ethics* sits at the fulcrum of this balancing act.

Reproductive medicine and neurology are often at the center of conflicts over treatments made possible by medical science and society's sense of how those treatments may support, challenge, or perhaps violate deeply held moral and social values. Between 1988 and 1995, the AMA's Council on Ethical and Judicial Affairs, stewards and authors of its *Code*, struggled along with society to balance the value of hope for organ recipients with the interests of anencephalic newborns, that is, infants born with no cerebral cortex.

The context for organ donation decisions

A convergence of medical trends set the context for this struggle. Ventilators prolonged the lives of those who could not breathe on their own; improved methods for artificial nutrition and hydration extended the lives of individuals with conditions that claimed their ability to swallow; advances in surgical techniques and immunosuppressant drugs contributed to the success of organ transplantation. And, confronted with the new circumstances in which individuals who could no longer breathe on their own could be "kept alive" mechanically, the medical profession and the US government undertook separate efforts to redefine "death" itself and the criteria for determining it. The Ad Hoc Committee of the Harvard Medical School to Examine the Definition of Brain Death published its report in *JAMA* in 1968, proposing that death could be declared on the basis of irreversible cessation of brain function even while

ventilators might be maintaining respiration and circulation in the patient [1]. During the next 12 years, a good deal of confusion reigned concerning which criteria to use for determination of death—the Harvard report's neurological criteria, referred to in short as "brain death" by the profession and the public alike, or the previous standard which was irreversible cessation of circulatory and respiratory functions [2]. The President's Commission on the Uniform Determination of Death institutionalized the ambiguity rather than resolving it by simply adding the Harvard committee's neurological criteria for death to the existing standard and asserting in 1981 that death could be declared on the basis of either "(1) irreversible cessation of circulatory and respiratory functions, or (2) irreversible cessation of all functions of the entire brain, including the brain stem" [3].

Thus, advances in medical technology and the policies that had sprung up to manage them set the stage for the Council on Ethical and Judicial Affairs' attention to organ donation by anencephalic neonates. Following successful transplants of the kidney, pancreas, liver, and heart in the late 1960s, the *Code* carried the AMA's first opinion on organ transplantation in its 1969 edition [4]. The 7-point "Guidelines for Organ Transplantation" emphasized that, though new, organ transplantation procedures were subject to all existing rules governing the patient-physician relationship; the prospect of donation was "no justification for a relaxation of the usual standard of medical care." Death of the donor, it continued, "shall have been determined by at least one physician other than the recipient's physician" and based upon "all available, currently accepted scientific tests" [5]. Though not stated explicitly in the *Code*, currently accepted scientific tests would have included neurological as well as cardio-pulmonary criteria in 1969. The 1969 *Code's* guidelines on organ donation have remained essentially the same over the years, even to the present.

Anencephalic Newborns as Organ Donors

In June 1988, 2 resolutions concerning organ donation were brought before the AMA House of Delegates and referred to the Council on Ethical and Judicial Affairs (CEJA) for investigation. One requested the AMA to reexamine the criteria used to select organ donors. The other sought ethical guidelines to address the use of prenatal diagnoses and organ "harvesting"; both concerned the transplantation of organs from anencephalic infants, some of whom were now able to survive for up to several days. The implicit question in the resolutions was this: Is it ethical to declare organ donor status for anencephalic newborns on the basis of prenatal diagnosis and, with parental consent, to procure the organs before the infant died of its neurologic devastation? In December 1988, CEJA reported its recommendation to the House of Delegates. The answer was, "No." Here are CEJA's words:

> [CEJA] supports the voluntary donation of organs in appropriate circumstances. However, the Council does not view the use of organs of anencephalic newborns prior to a determination of death, ie, the complete and irreversible cessation of all brain function, as appropriate for transplantation purposes" [6].

The 1989 edition of the *Code* contained no separate entry on anencephalic neonates as organ donors.

The first separate opinion on anencepahlic neonates as donors appeared in the 1992 edition, giving public voice to the view expressed in the 1988 report. The new opinion stated that the newborns could be kept on ventilators and provided other treatment to sustain "organ perfusion and viability until such time as a determination of death can be made in accordance with accepted medical standards and relevant law." The opinion went on to emphasize that retrieval of organs was "ethically permissible only after such a determination of death is made" [7].

By 1994, things had changed. In June 1994, "after more than a year of deliberation," the Council issued a lengthy report, a version of which was subsequently published in *JAMA* [8]. The extensively researched and documented report grounded its conclusions on 3 facts or assumptions: anencephalic newborns faced certain death, usually within 3 days; they lacked any degree of consciousness; and parents of such newborns often requested that their children's organs be donated. The Council reached the conclusion that, with prior consent of the newborn's parents, it *was* ethically acceptable to transplant the organs of anencephalic neonates without waiting for them to die naturally.

The 1994 report examined 5 objections to the policy it was proposing: (1) the new position violated the prohibition against removal of life-necessary organs from living persons, (2) the diagnosis of anencephaly might be incorrect, (3) the proposed practice could open the door to considering other living people as organ donors, eg, those in persistent vegetative states or the severely disabled, (4) the infrequency of cases in which anencephalic newborns could actually

be donors, and (5) anticipated harm to the public's trust in organ donation. The Council argued each of these points, some at great length. In each case, justification for permitting retrieval of organs from anencephalic newborns before they had been declared dead seemed to outweigh the arguments against doing so. The Council's recommendation was accepted by the House of Delegates and replaced the former opinion on organ donation by anencephalic neonates in the 1994 edition of the *Code*. After defining anencephaly, the new opinion stated:

> It is ethically permissible to consider the anencephalic as a potential organ donor, although still alive under the current definition of death only if: (1) the diagnosis...is certain and confirmed by two physicians who are not part of the organ transplant team; (2) the parents of the infant desire to have the infant serve as an organ donor and indicate such in writing; and (3) there is compliance with the Council's Guidelines for the Transplantation of Organs [9].

The opinion went on to say that some parents who wished their anencephalic newborns to be donors might choose alternative means and "provide the infant with ventilator assistance and other medical therapies " to keep it alive until death was determined by current standards and relevant law [9]. Finally the opinion drew special attention to the fact that its new opinion marked a noteworthy exception to its guidelines on donation of organs necessary for life because these infants have "never experienced and will never experience consciousness" [9].

Reaction to the report and opinion was immediate, widespread, and highly critical. During the year following the opinion's release, the AMA and CEJA received protests from individual parents and physicians, advocacy groups such as the Anencephaly Research & Help Line, the American Association of Pro-Life Pediatricians, the Christian Medical and Dental Society, and medical specialty societies. And the Council became aware that its new opinion on anencephalic newborns as organ donors was incompatible with the policy of the United Network for Organ Sharing (UNOS), the organization established by the US Congress in 1984 to administer the nation's Organ Procurement and Transplantation Network. UNOS policy stipulates that organ procurement must occur after declaration of death by medical and legal standards.

The Council on Ethical and Judicial Affairs considered the clear message it had received from members of the profession and the public. Society was not about to tolerate alteration of principles derived from the closely held value it placed on the sanctity of life, no matter how damaged that life might be. If the owner of that life, himself or herself, vehemently refused treatment to sustain it, that was one thing, but others who had never known the will of the person in question should not end its life. In its December 1995 report entitled, "The Use of Anencephalic Neonates as Organ Donors—Reconsidered," the Council rescinded its 1994 opinion, pointing to concerns about accurate diagnosis of anencephaly and incomplete understanding of the possible level of consciousness in these newborns [10]. The report urged the scientific community to continue to investigate the consciousness of neonates and provide knowledge to guide future policy making on this topic. Promising to continue assessing relevant information, the Council recommended—and the House of Delegates approved—reinstating the 1992 opinion. Nearly a decade later, the 1992 opinion remains in the *Code*.

This history of the AMA *Code's* opinion on anencephalic newborns as organ donors is an "action shot" of the social contract and professional self-regulation. In this case, the message from the public and some members of the profession was that medicine had taken a step beyond the point to which society was willing to go. Upon reflection and renegotiation, the profession reassumed its former stance, one with which the entire profession and its contractual partner could agree.

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Op-Ed

Cosmetic Neurology: For Physicians the Future is Now

Medications for brain enhancement raise many ethical concerns regarding the roles of personal autonomy and responsibility.

Anjan Chatterjee, MD

Basic neuroscience and neuropharmacology are beginning to yield therapies for cognitive disorders. While we can eagerly anticipate treatments for dementing illnesses, stroke, traumatic brain injury, and developmental abnormalities, these very treatments raise uncomfortable questions. If we can improve cognitive systems in disease, can we also do so in health? Should we practice cosmetic neurology?

The possibility of "better brains" has captured the imagination of the press, policy pundits, and ethicists [1-10]. With few exceptions, physicians have not contributed to these discussions, despite their central role in this unfolding drama [11,12].

Cosmetic neurology includes the use of botulinum toxin to brush away wrinkles. However, it also alters how we function and feel, rather than just how we look. Many interventions to improve cognitive and emotional systems are available now, and others are on the horizon. The risks and benefits of newer medications remain to be worked out. However, we can assume that some version of these medications will be relatively efficacious and safe. The accompanying article on neuroethics by Martha Farah reviews the anticipated pharmacopeia of cosmetic neurology and the deep ethical concerns raised for individuals and society (also see [12]). The focus here is on the role of the physician in managing the use of cosmetic neurologic interventions.

Framing the Issue: the Purpose of Medicine

Ethical discussions of cosmetic neurology often frame the issue as one of therapy versus enhancement [6,13]. Therapy treats disease and enhancement improves normal abilities. Most people consider therapy desirable. By contrast, many pause at enhancement. Francis Fukayama, for example, opines, "the original purpose of medicine is to heal the sick, not turn healthy people into gods" [14]. He suggests that public policy should restrict research for enhancement.

For 2 reasons, the distinction between therapy and enhancement is less useful than one might hope. First, notions of disease often lack clear boundaries. For example, if individuals of short stature can be "treated" with growth hormone [15], does it matter whether they are short because of a growth hormone deficiency or because of other reasons [13]? Second, promoting research for therapy and restricting it for enhancement ignores the simple fact that research in one often applies to the other.

The therapy versus enhancement distinction also obscures what for physicians may be the critical question: What is the purpose of medicine? The strength of allopathic medicine has been its scrutiny of disease mechanisms. Understanding the biology of malfunction provides insight into how to fix that malfunction. Despite its undoubted successes, this approach has limits. Most notably, the quality of patients' lives does not always correspond well to biomarkers and symptoms of disease. The symptoms of Parkinson's disease that are most responsive to dopamine agonists are not those that bother patients most [16]. Measures of disease activity may not be the best indicator of the impact of multiple sclerosis on patients [17]. Recognizing the limits of clinical and pathological indices, assessing patients' quality of life is now a routine practice in therapeutic trials. Such assessments seem eminently reasonable. After all,

the point of treating a disease is to improve patients' quality of life. However, if a purpose of medicine is to improve quality of life for people who happen to be sick, then why not apply medical knowledge to improve the quality of life of those who happen to be healthy?

Inevitability

Cosmetic neurology raises several serious ethical concerns. These interventions challenge fundamental notions of character and individuality; it is *likely* that they will be used coercively, and cosmetic neurology will not lessen the burden of distributive justice in a country in which the quality of health care is polarized by economic class. It is improbable, however, that cosmetic neurology will be restrained significantly by journalistic consternation, religious admonition, and government regulation. More likely, such restraints will be overwhelmed by free markets and military innovations.

The market. Pharmaceutical companies stand to make substantial profits and will probably support social pressures that encourage wide use of cosmetic neurology. According to Carl Elliott, in 2001 GlaxoSmithKline spent $91 million dollars in direct advertising to consumers for its medication Paxil [8], more than Nike spends on its top shoes. Advertisements for better brains would undoubtedly prey on an insecure public. Gingko Biloba, despite underwhelming effects on cognition [18], is a billion dollar industry. Pharmaceutical companies are not oblivious to the marketing possibilities of new "interventions" that could apply to the entire population [19,20]. Sadly, the academy is *unlikely* to restrain Industry. Scientific leaders who discover new therapeutic possibilities are quick to stake biotech claims [20]. Joint ventures between universities and pharmaceutical companies are increasingly common.

The military. Imagine a soldier who is stronger, faster, more enduring, learns more quickly, needs less sleep, and is not hampered by disturbing combat memories. The military's deep interests in cognitive enhancements date back to "go-pills" (amphetamines) for World War II soldiers [20], and continue to the present [20,21]. For example, military investigators found that modafinil [a wakefulness-promoting agent] has its greatest effects in helicopter simulation performances at the combined nadir of sleep deprivation and circadian troughs [22]. Relevant findings from military research are likely to trickle down to civilians. Over-fed Hummer vehicles maneuver through the cobbled streets of Philadelphia. Perhaps Hummer brains are around the corner.

The Role of Physicians

Americans believe that the pursuit of happiness is an inalienable right. This pursuit assumes we know what constitutes happiness [23]. Fame and fortune have been standard proxies for happiness in American culture. Better brains may very well join the list, either as a means to fame and fortune or as a direct source of happiness [24].

Scientific, economic, marketing, and regulatory forces are likely to shape the role physicians will play. The details are difficult to predict, but what is certain is that physicians will engage in cosmetic neurology. This practice will be complicated by the fact that physicians will not be able to rely on the conventions of traditional practice. Neurologists may have special understanding of the potential risks and benefits of quality of life interventions that work through the nervous system, but they have no special insight into the underpinnings of happiness.

One plausible scenario is that physicians will become quality-of-life consultants. Physicians might offer a menu of options, with the likely outcomes and the incumbent risks stated in generalities. The role would be to provide information while abrogating final responsibility for decisions to patients. Abrogation of such responsibility is promoted by current practice norms. Financial incentives in medicine are now driven by paper trails and diagnostic studies, rather than by personal engagement with patients. A comfortable stance would be to let people decide for themselves. After all, isn't autonomy what patients want?

It turns out that the degree of autonomy patients want is not so clear, especially when they are sick (as reviewed in [25]). Furthermore, the bewildering array of choices available to American consumers in almost every domain of life is a source of considerable anxiety [26]. A practice of medicine that encourages patients to be consumers is in danger of compounding these anxieties. I am not advocating that physicians become disengaged purveyors of quality-of-life elixirs. I am suggesting that this role is a distinct possibility given current trajectories of medical practice. In a litigious

society, many physicians would gladly shed the irksome traditional mantle of beneficence.

Where do you stand?

Since 1997, the FDA has permitted direct marketing to consumers. Physicians can anticipate facing questions from "patients" and advocacy groups in which distilling principle from prejudice is not easy. To make these issues concrete, I invite readers to consider the following questions.

1. Would you take a medication with minimal side-effects half an hour before Italian lessons if it allowed you to learn the language more quickly?

2. Would you give your children a medication with minimal side-effects half an hour before piano lessons if it allowed them to learn better?

3. Would you pay more for flights whose pilots were taking a medication that made them react better in emergencies?

4. Would you want residents to take medications after call nights that would make them less likely to make mistakes in caring for patients because of sleep-deprivation?

5. Would you take a medicine that selectively dampened disturbing memories?

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Op-Ed

Neuroethics

An overview of the burgeoning field of neuroethics, which encompasses the myriad ways in which developments in basic and clinical neuroscience intersect with social and ethical issues.

Martha Farah, PhD

Five years ago the word "neuroethics" was rarely used, and when it was it denoted the classic issues of clinical bioethics—informed consent, resource rationing and the like—in the context of neurology. Recently the word has gained wider currency and its meaning has changed. In this brief article I will review the burgeoning field of neuroethics and highlight one particular issue likely to affect practicing neurologists in the very near future.

Neuroethics encompasses the myriad ways in which developments in basic and clinical neuroscience intersect with social and ethical issues. The field is so young that any attempt to define its scope and limits now will undoubtedly be proved wrong in the future, as neuroscience develops and its implications continue to be revealed. At present, however, we can discern 2 general categories of neuroethical issue: those emerging from *what we know*, and those emerging from *what we can do*. In the first category are the ethical problems raised by our growing understanding of the neural bases of behavior, personality, consciousness, and states of spiritual transcendence. In the second category are the ethical problems raised by advances in functional neuroimaging, brain implants and brain-machine interfaces, and psychopharmacology.

The "What We Know" Issues

Responsibility and blame. The idea that behavior is determined is hard to reconcile with the intuitive notions of free will and moral agency on which our legal systems are based. Although many people believe that, in principle, human behavior is the physical result of a causally determined chain of biophysical events, most of us also put that aside when making moral judgments. We don't say "but he had no choice—the laws of physics made him do it!" However, as the neuroscience of decision making and impulse control begins to offer a more detailed and specific account of the physical processes leading to irresponsible or criminal behavior, the amoral deterministic viewpoint will probably gain a stronger hold on our intuitions. Whereas the laws of physics are a little too vague and general to displace the concept of personal responsibility in our minds, our moral judgments might well be moved by a demonstration of subtle damage to prefrontal inhibitory mechanisms wrought by, for example, past drug abuse or childhood neglect. This has already happened to an extent with the "disease model" of drug abuse.

Science and the soul. Most people are Cartesian dualists: they believe that body and mind are not made of the same "stuff." Until recently, neuroscience did not pose a strong challenge to this view. Revealing the neural mechanisms of color vision puts color vision in the realm of the body, as opposed to the mind, but so what? You can still believe in what Arthur Koestler called "the ghost in the machine" and simply conclude that color vision is carried out by the machine for the benefit of the ghost. However, as neuroscience begins to reveal the mechanisms of personality, character, and even sense of spirituality, this Cartesian line of interpretation becomes strained. If these are all features of the machine, why have a ghost at all? By raising questions like this, it seems likely that neuroscience will pose a far more fundamental challenge to religion than evolutionary biology.

The "What We Can Do" Issues

Imaging and mental privacy. Functional neuroimaging has evolved from clinical use to an indispensable tool for basic neuroscience, and in recent years has been applied to the understanding of personality. With these developments comes a serious potential threat to privacy. The ability to estimate someone's personality, attitudes, and preferences would be welcomed by employers and marketers. The search for better lie detection and behavior prediction has led the intelligence and criminal justice communities to pursue fMRI (functional MRI) and ERP (event-related potentials, derived from EEG) methods These trends raise new questions about whether, when, and how to ensure the privacy of one's own mind.

Of course, to the extent that functional neuroimaging is not up to the task of reliably delivering such information—and at present it is not—another problem arises: the high-tech aura of brain images leads many people to accept them uncritically. We must work to give the public more accurate and accessible explanations of functional neuroimaging.

Cyborg brains. Two lines of research are paving the way for the possibility of electronic brain augmentation. The first is research on brain and vagus nerve stimulation, currently at various stages of clinical utility and acceptance in the treatment of Parkinson's disease, epilepsy, and depression. These methods are capable of affecting mood and cognition, and in the future may gain wider use for those purposes. The second line of research is on brain-machine interfaces, carried out mainly but not exclusively in animals. Here the goals are primarily to enable information from the world to be transduced into neural activity and to enable neural activity to be transduced into information that is externally useful for communication or robotic control. Although both lines of research conjure up futuristic and frightening science fiction scenarios for many people, the ethical issues they raise are of a familiar nature, from informed consent for patients undergoing invasive treatments to the enhancement-related problems discussed in the next section.

Medical enhancement (as opposed to therapy). Many neuropsychiatric illnesses occur along a spectrum that includes normal variations of functioning, and this raises the question: if treatment X can relieve a clinically significant deficit of psychological function Y, what can it do for normal healthy people? To be more specific, if we can treat depression with SSRIs and ADHD with stimulants, can we enhance the mood or attention of normal people by the same means? And should we? This is the topic of the remainder of the present article as well as Anjan Chatterjee's companion article, "Cosmetic Neurology."

In his article, Dr. Chatterjee focuses on the aspects of brain enhancement that are most directly relevant to medicine as a profession, asking how enhancement relates to the goals of medicine and the role of physicians. I will cover a complementary set of issues here, relevant to physicians and lay people alike.

Enhancing Brains: Current Capabilities and Their Bioethical Implications

Peter Kramer's popular book, "Listening to Prozac" first drew society's attention to the potential of psychopharmacology for enhancing the lives of healthy people. The patients he described, though far from satisfied with their lives, were not clinically depressed. Yet Prozac helped many of them to feel better. Surprisingly little is known about the effects of SSRIs on people who are not depressed. It seems clear that SSRIs are not happy pills, shifting depressed people to normalcy and normal people to bliss. Rather, for most people they seem to leave positive affect unchanged while attenuating negative affect—for example, reducing the subjectively experienced "hassle" factor.

In addition to mood, vegetative functions such as sleep, eating, and sex can be influenced pharmacologically, and there is a large demand for ways of enhancing these functions. The wakefulness-promoting agent modafinil, approved in the US for treatment of certain sleep disorders, is prescribed off label for a panoply of other conditions and is said to be favored by some ambitious professionals as a way of packing more work into a day. Although a safe and effective appetite suppressant is at present just a goal, such a drug will undoubtedly find a huge market when it comes along. Even after it became clear that the Phen-Fen combination could be fatal and it was pulled from the market, there was a constituency of consumers that fought for continued access to it. Finally, although currently popular medications for erectile dysfunction do not achieve their effects by altering brain function, newer neurally active drugs are in

development, aimed at improving both male and female libido. If society's experience with sildenafil (Viagra, eg) is any indication, many people without sexual dysfunction will seek these drugs to enhance their sex lives.

The treatment of cognitive disorders has also begun to shade into cognitive enhancement for healthy people. Two main cognitive systems have become targets for enhancement, attention or executive function (an umbrella term for flexible attentional control of cognition and necessary for organization, planning and problem-solving) and memory. Stimulant medication, which has been shown to improve the executive function of individuals with ADHD, also enhances normal performance on a variety of executive function tasks. Although methyphenidate (Ritalin) and amphetamine (Aderall) are ostensibly prescribed mainly for the treatment of ADHD, sales figures suggest that they are not uncommonly used for enhancement. Methylphenidate is currently widely used by college students, many of whom obtain it from friends or campus dealers as a recreational drug and study aid.

The most commonly used method of memory enhancement involves manipulation not of memory circuits per se but of cerebrovascular function. Herbal supplements such as Gingko Biloba affect memory mainly by increasing blood flow within the brain. However, a huge research effort is now being directed to the development of memory-boosting drugs. The candidate drugs affect various stages in the molecular cascade that underlies memory formation, including the initial induction of long-term potentiation and the later stages of memory consolidation. Although this research is aimed at finding treatments for dementia, there is reason to believe that some of the products under development would enhance normal memory as well, particularly in middle and old age when a degree of increased forgetfulness is normal.

Ethical Issues in Enhancement

The ethical issues surrounding brain enhancement can be grouped into 3 general categories. The first is practical: safety. Side effects and unintended consequences are a concern with all medications and procedures, but in comparison to other comparably elective treatments such as cosmetic surgery, neuroscience-based enhancement involves intervening in a far more complex system. We are therefore at greater risk of unanticipated problems when we tinker. In addition, drug safety testing does not routinely address long-term use, and relatively little evidence is available on long-term use by healthy subjects.

The second category of ethical issue is social: how will the lives of all individuals, including those who choose not to enhance, be influenced by living in a society with widespread enhancement? In competitive situations such as SAT testing, we may end up needing the equivalent of the regulations surrounding performance-enhancing drugs at sports events. Even in everyday work and school contexts, enhancement is likely to touch all of us.

The freedom not to enhance may be difficult to maintain in a society where one's competition is using enhancement. American courts have already heard cases involving parents coerced by schools to medicate their children for attentional dysfunction. Given that in some school districts the proportion of boys taking methylphenidate exceeds the most generous estimates of ADHD prevalence, it seems likely that some parents feel their child will be at a disadvantage in school without stimulant medication, whether or not they have a diagnosis of ADHD.

Conversely, barriers such as cost will prevent some people who would like to enhance from doing so. This could exacerbate the disadvantages already faced by people of low socioeconomic status in education and employment.

The third category of ethical issue could be called philosophical, in that it concerns our values and our sense of self. Cosmetic neurology raises many profound questions at this level. We generally view self-improvement as a laudable goal. At the same time, improving our natural endowments for traits such as attention span runs the risk of commodifying those traits. We generally encourage innovations that save time and effort, because they enable us to be more productive and to direct our efforts toward potentially more worthy goals. However, when we improve our productivity by taking a pill, we may also be undermining the value and dignity of hard work, medicalizing human effort, and pathologizing a normal attention span. The self-transformation we effect with a mood-enhancing drug can be seen either as self-actualizing or as eroding our personal identity. Neither the benefits of brain enhancement nor the dangers are trivial.

A final point concerning all 3 types of ethical problem is that many of the same issues arise when more familiar substances are used for enhancement, for example drinking coffee or smoking tobacco to focus attention or drinking alcohol to relax.

Conclusions Regarding Enhancement

Many of the patients now taking stimulants to improve attention and antidepressants to improve mood would not have been considered reasonable candidates for medication 2 decades ago because of the mildness of their complaints. By the standards of the 1980s, such patients are practicing enhancement. Even by today's diagnostic standards there is now an active market for attention enhancement. Is this good, bad, or a mixture of the two?

I do not believe that the answer to this question can be discovered a priori by reflecting on general principles such as "people have a right to do what they want to their own brains" or "people should not interfere with the basic design of humanity." Rather, I believe that the answer will emerge as we learn more about the long-term safety of these medications, the ways in which users in fact come to incorporate them into their work and family lives, the success with which society can rise to the challenges of equalizing access to enhancement and protecting the rights of people who choose not to enhance, and our ability to preserve a sense of personal autonomy, responsibility, and identity even as we experiment with unprecedented methods of self-transformation.

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