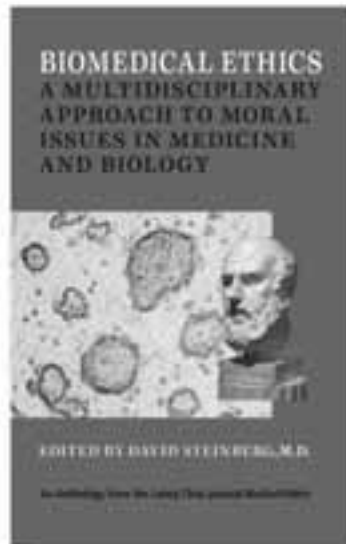


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Quote to note

“However elevated in power over the rest of life, however exalted in self-image, we were descended from animals by the same blind force that created those animals.”

— E.O. Wilson

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The minimally conscious state: ethics and diagnostic nosology

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Recently, my colleagues and I reported the use of thalamic deep brain stimulation in a 38-year-old man who had been in a minimally conscious state (MCS) for six years following an assault.¹ Before deep brain stimulation, he could respond intermittently with the movement of his thumb. He was dependent upon tube feeds through his stomach and was unable to control his secretions. He is now able to speak several words at a time and eat three meals a day. Most notably, he can interact with his family, having regained a degree of personal agency.

Media response to this case was gratifying, despite confusion about what MCS is and how it differs from other disorders of consciousness like coma or the persistent or permanent vegetative states. In this essay, I will explain why diagnostic clarity is critical in light of the therapeutic potential of deep brain stimulation in MCS. A failure of diagnostic precision has ethical implications because it will foster a therapeutic misconception of potential applicability to other similar, but biologically, distinct brain states.

To avoid such nosological errors, we need to start with a definitional primer of altered states of consciousness. *Coma* is an eyes-closed state in which the patient is unresponsive and unarousable. The most serious comas may progress to *brain death*, defined as the irreversible cessation of all clinical brain stem and higher brain functions.²

Comas can also evolve into a *vegetative state*, an eyes-open state of unresponsiveness. Jennett and Plum first described the vegetative state as one of “wakeful unresponsiveness” marked by autonomic brainstem function.

Vegetative patients exhibit nonpurposeful behaviors such as sleep/wake cycles, blinking, eye movements and even the startle reflex.³ They are neither conscious nor self-aware. By definition, the vegetative state becomes *persistent* once it has lasted for one month. By convention, it becomes *permanent* three months following an anoxic brain injury and 12 months after a traumatic injury.⁴

It is essential to distinguish MCS, in which the patient has episodic or intermittent consciousness, from other states.⁵ MCS patients demonstrate unequivocal, but fluctuating, evidence of awareness of self and the environment. They may say words or phrases and gesture. They also may show evidence of memory, attention and intention.

Once a patient is in an MCS, the possibility for additional recovery remains and can be, to some degree, open-ended, with further improvement taking place years and decades later.⁶ *Emergence* from MCS is taken to be the consistent and reproducible recovery of consciousness and an awareness of self, others and the environment. Once patients have emerged, they are better able to reestablish relations with family and interact with others.⁷

MCS—continued on page 2

MCS—continued from page 1

Diagnosing MCS

The diagnosis of MCS can be challenging when awareness behaviors are episodic. Family members may observe a behavior like tracking or command following indicative of MCS and then try to elicit it for clinical staff. When the behavior does not recur, family reports can be discounted as denial or hopefulness, not as a behavior pattern wholly consistent with the biology of MCS.

Such was the unfortunate case of Terry Wallis from Arkansas who sustained a severe head injury in 1984 in a motor vehicle accident.⁸ He lingered in a nursing home for nearly two decades before he emerged from MCS in 2003, regaining fluent speech. Before emergence, he had been misdiagnosed as being vegetative. A review of his behaviors indicated they were consistent with those seen in MCS. Nonetheless, his family's observations were discounted and staff denied their requests for expert consultation and imaging studies. His father told me he was told it would be too expensive and unhelpful for his son. (I have worked with the Wallis family and am grateful for their permission to write about their experiences.)

In retrospect, it is probable that, after acute hospital discharge, Wallis had migrated into MCS before his persistent vegetative state became permanent⁹ and that he had been in MCS for nearly two decades before he emerged. Lamentably, since Wallis's story was reported, more accounts of emergence are being reported of patients who have labored under inaccurate diagnostic assessment.

Sadly, such a societal "neglect syndrome" continues for many patients with severe brain injury once they are discharged from acute care facilities and placed into what is euphemistically described as "custodial care."¹⁰ Remarkably, it has been estimated that the diagnostic error rate of MCS patients as persistent vegetative state may be as high as 30–40%.¹¹ Wallis's story is a cautionary tale. Assessment of patients for MCS requires patience and multiple longitudinal exams lest they be misdiagnosed as vegetative.

The historic neglect of MCS patients such as Terry Wallis was all the more remarkable because recent studies of such patients is providing insight into mechanisms of brain recovery and that organ's residual capacity for function, even in the setting of severe injury.

Two findings bear special mention. The first was the wholly unexpected findings noted in Wallis's brain when he underwent neuroimaging scans at Weill Cornell. Using an MRI technique called diffusion tensor imaging, my colleagues reported interval changes in Wallis's brain, done after he emerged, which they speculated might have played a role in his recovery.¹² In interval studies taken after his emergence, the studies revealed what was described as the "sprouting" of new axonal connections. It was hypothesized that these new connections between surviving neurons might have played a role in the evolution of his brain state and his recovery.

The second area of inquiry is brain-imaging studies coupled to task completion, such as listening to spoken narratives. Such studies have suggested the capability of MCS patients to process language and semantic content.¹³ Subjects responded to narratives recorded by loved ones with activation of widely distributed neuronal networks, but did so only when tapes were played forward and not reversed. When the narratives were reversed, network activation did not occur, suggesting that it was language and semantic content that led to cortical network activation, not merely frequency spectrum, which remained constant. This was a remarkable finding because it suggested a retained ability of such patients, despite their marginalization by the broader human community from which they had been separated by loss of functional communication.

Despite the promise of these imaging techniques, it is critical that the assessment of MCS remains a *clinical* diagnosis done by a qualified practitioner who performs a skilled history and examination. Although neuroimaging is beginning to peer into how the injured brain recovers, the technique remains investigational. It is too early to apply these techniques in routine clinical practice. This is important to stress to families who may desire an "objective" diagnosis from an imaging study. Premature dissemination of imaging technology as an adjuvant to clinical diagnosis will lead to confusion in the short term, as we seek to correlate imaging findings with behaviors and brain state.

The real contribution of neuroimaging is, at this juncture, scientific. As noted, imaging studies indicate a degree of residual function in MCS patients that does not exist in patients who are vegetative. In contrast to MCS

patients who have integrated—but under-sustained—cortical function, vegetative brains are not integrated. In a sense, vegetative brains are dis-integrated, or severed from themselves. This distinction between the vegetative state and MCS is all the more salient because it is the integrative capability of the MCS brain that was supported and sustained in our recent deep brain stimulation trial.

Although the diagnostic distinction of the vegetative and minimally conscious states was a polemical one during the Terri Schiavo debate, it is now clear that the salient difference was always a scientific one.¹⁴ Today it is motivated by the emerging possibility of therapeutic instrumentality. □

¹Schiff ND, Giacino JT, Kalmar K et al. Behavioral improvements with thalamic stimulation after severe traumatic brain injury. *Nature* 2007;448: 600-603.

²Posner J, Saper C, Schiff ND and Plum F. *Plum and Posner's Diagnosis of Stupor and Coma*, 4th ed. New York: Oxford University Press, 2007.

³Jennett B. *The Vegetative State*. New York: Cambridge University Press; 2002.

⁴Medical aspects of the persistent vegetative state (1 and 2). The multi-society task force on PVS. *N Engl J Med* 1994;330:1499-1508 and:1572-1579.

⁵Giacino JT, Ashwal S, Childs N et al. The minimally conscious state: definition and diagnostic criteria. *Neurology* 2002;58: 349-353.

⁶Lammi MH, Smith VH, Tate RL et al. The minimally conscious state and recovery potential: a follow-up study 2 to 5 years after traumatic brain injury. *Arch Phys Med Rehabil* 2005;86: 746-754.

⁷Sherer M, Hart T, Nick TG et al. Early impaired self-awareness after traumatic brain injury. *Arch Phys Med Rehabil* 2003; 84(2):168-76.

⁸Schiff ND and Fins JJ. Hope for "comatose" patients. *Cerebrum* 2003; 5(4): 7-24. Reprinted as "A Cerebrum Classic" in *The Dana Foundation's Cerebrum* 2007. Read CA, Ed. New York: Dana Press; 2007, 185-203.

⁹Fins JJ. Clinical pragmatism and the care of brain injured patients: towards a palliative neuroethics for disorders of consciousness. *Prog Brain Res* 2005;150:565-582.

¹⁰Fins JJ. Constructing an ethical stereotaxy for severe brain injury: balancing risks, benefits and access. *Nat Rev Neurosci* 2003;4: 323-327.

¹¹Wilson, FC, Harpur J, Watson T et al. Vegetative state and minimally responsive patients—regional survey, long-term case

MCS—continued on page 5

Ask the ethicist:

Conflicting duties: an ethical dilemma in transfusion medicine

Question: A 24-year-old student from Asia was seriously injured in a car accident in Boston. He suffered massive internal bleeding and required many blood transfusions. His physicians deemed his situation hopeless and were prepared to stop treatment. They then received a message from his parents that they had arrived in San Francisco and were en route to Boston. They said it was extremely important to see their son before he died and requested that blood transfusion be continued despite the ultimately hopeless situation. The blood bank director currently has an ample supply to keep the patient alive and satisfy his family's emotional needs. However, in the unlikely event of an unanticipated emergency, another patient might suffer if the director exhausts the available blood on a patient who will not recover. Would you advise the blood bank director to continue to release blood for this hopelessly injured student?

Response: Transfusion medicine physicians are occasionally challenged by situations in which providing optimal care for one patient prevents the delivery of the same level of care to other patients. This problem derives from the multiple roles of such physicians—both as consultants assisting in the care of a particular patient and as stewards of the institution's transfusion resources. Boundless resources would prevent such dilemmas, but neither financial nor blood donor resources are so plentiful!

Thankfully, a situation as dramatic as this one occurs very infrequently. Very rarely would use of blood for one patient prevent another patient from having it available when needed. Occasionally, the issue arises in which a very rare blood type *isn't available*, but such a situation does not contain an implicit ethical question. More commonly, the clinical situation is similar to that described, in which the outcome is perceived as futile by experienced members of the clinical care team but not by family members who press for all measures to be taken to save their loved one.

Even when a hospital has enough of the correct blood component to transfuse to the doomed patient without endangering its ability to help other patients who have a more promising prognosis, would such use of blood break the moral contract with the blood donor? Altruistically motivated, non-remunerated blood donors gave of their own time and their own bodies to "help other people" and "save a life." While most donors would recognize that some recipients of their blood will succumb to their illnesses, would they regard their gift as having been appropriately used if it were transfused without any hope of the patient's recovery? Would the peace of mind that would accrue to the parents of the patient by being able to see him before death be regarded as "helping other people" as the donor intended?

Clearly, we cannot allow community blood donors to choose their recipients and authorize each potential transfusion. Instead, the transfusion system is operated under commonly understood principles of equality and fairness. Were transfusions to be used widely without medical logic and without patient benefit, one might expect the commitment of donors to dissipate. With only 5% of the eligible population donating each year, a reduction in support is something transfusion medicine cannot afford.

If unusual transfusion demands have depleted a facility's inventory faster than it can be replenished, the transfusion medicine specialist may be forced to adopt a prioritization or rationing scheme. Here, the physician is no longer acting in the best interest of a single patient but attempts to cause the least harm and achieve the greatest good for the greatest number of recipients—some of whom may be only theoretical patients who might appear in the emergency department or have an unexpected need for transfusion before the next blood shipment arrives. (This is common practice in many institutions with regard to platelets, which can quickly become scarce.) Questions to consider include: Are there alternatives that might alleviate or postpone the need for transfusion? What will be

the effect of Patient A vs. B vs. C not receiving their transfusion until later? When will additional supplies be available? What alternative care is available for a patient who may unexpectedly need a transfusion?

A similar case might provide additional opportunities to consider the impact of a decision whether to transfuse. The desire to see one's child might be framed in a religious or cultural context. Should acknowledgment of the family's religious beliefs alter a resource allocation decision? Does the claim of a religious basis of the desire to see the patient alive make it any more compelling than just an understandable request of a parent? Does a religious basis place this use of a scarce and potentially life-saving resource any higher on a prioritization scale than a use that actually would alter the course of another patient's care? Most transfusion medicine physicians would approach these situations by according the opportunity to save or meaningfully extend the lives of the greatest number of patients as the highest imperative.

We should also consider the student. In our analysis we assume that he is unable to make educated and informed decisions regarding his care. In such circumstances, and assuming he is unmarried, care decisions would fall to his next of kin, his parents. Do they have a legal precedent to insist on continued blood transfusions? What if he could make the decision for himself and, knowing the situation was futile, refused the transfusions requested by his parents? One would expect the patient's expressed wishes to be given paramount importance.

In the case proposed above, we would recommend fulfilling the family's wishes for continued transfusion until or unless other patients' more pressing needs arose.

Outcome: The blood bank director continued to release blood for the patient, but the patient suffered a cardiac arrest and died before his family arrived from Asia. □

Ask the ethicist—continued on page 7

The legal column: The Stark self-referral law

Ethical concerns about physicians making money while treating the sick have been voiced throughout the history of medicine. These concerns emerge from the general discomfort with physicians earning a livelihood for treating persons who are ill. In a fee-for-service environment, this concern is exacerbated by the possibility that physicians, particularly in procedural specialties, will perform more, or even unnecessary, services to earn more income. In a managed care environment, this concern is fueled by the possibility that physicians will personally benefit by providing fewer services, delaying referrals for costly tests or otherwise compromising quality by providing substandard care.

In recent years, the ethical concerns over how physicians may profit from the services they perform directly, whether in a fee-for-service or managed care environment, have been eclipsed by concerns over how and under what circumstances physicians should be permitted to earn a profit from diagnostic and therapeutic services they do not administer directly. This is the essential issue presented when physicians acquire ownership interests in, or enter into economic relationships with, facilities or organizations to which they refer patients for such services. This, too, is the specific conflict of interest addressed by the federal prohibition against certain self-referrals—the Stark Law.

Referrals by physicians to facilities in which they have an ownership interest have been a part of medicine since at least the inception of the modern hospital. In fact, early in the 20th century, many of the nation's smaller hospitals were little more than extensions of physicians' medical and surgical practices.

During the 1980s, several factors stimulated physician ownership of, and economic relationships with, health care providers to which these physicians referred patients and at which they might not have treated patients directly. However, one of the accelerants of this trend was the rapid development of diagnostic and therapeutic technology that accelerated the shift of many procedures from the inpatient hospital

setting to the outpatient one, and also enabled physicians and others to establish freestanding, nonhospital facilities at which a variety of diagnostic, therapeutic and surgical procedures could be performed. This trend continues today, as evidenced by the continuing growth in the number of freestanding surgery centers.

The Stark Law was a legislative regulatory response to a growing body of data that showed a correlation between physicians' ownership in businesses such as clinical laboratories and imaging centers and the volume of referrals by the physicians to them.

The original federal law prohibiting self-referrals was introduced by its namesake, Representative Fortney (Pete) Stark (D-CA), and applied only to clinical laboratories. Following the enactment of the self-referral prohibition to clinical laboratories, two additional reports fueled Congress's interest in expanding the self-referral prohibition beyond clinical laboratory services. First, the *New England Journal of Medicine* published a report in December 1990 comparing the frequency and cost of diagnostic imaging examinations performed by primary care physicians who used equipment in their offices with those of physicians who always referred patients to radiologists.¹ The report found that patients of physicians who owned their own equipment received imaging examinations 4.0–4.5 times more often than did patients referred to radiologists. A second report was released in 1991 by the Florida Health Care Cost Containment Board and found that doctor-owned, full-service clinical laboratories performed an average of 3.3 tests per patient versus an average of 1.7 tests per patient at “non-joint venture” laboratories.

In 1993, armed with fresh information concerning the impact of ownership on referral patterns, Congress extended the physician self-referral ban to a broad list of designated health services (DHS), including inpatient and outpatient hospital services, diagnostic imaging and home health.

Since 1993, Congress has continued to weigh in on the issue by becoming involved in the debate concerning the

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efficacy of specialty hospitals such as heart and surgical hospitals. In addition, the Centers for Medicare and Medicaid Services (CMS) has issued hundreds of pages of regulations, the most recent of which were issued on September 5, 2007.

Basically, the Stark Law prohibits self-referrals for DHS covered by Medicare. The Stark Law does not prohibit self-referrals for DHS covered by Medicaid or other federal health care programs, nor does it prohibit a DHS entity from submitting claims to state Medicaid programs for DHS. Rather, Medicaid law denies states federal matching funds for expenditures incurred as a result of referrals for DHS that would not have been payable by Medicare had Medicaid covered such DHS to the same extent and under the same terms and conditions as the state plan.

More specifically, the Stark Law generally prohibits a physician from making referrals for Medicare-covered DHS to an entity with which the physician or an immediate family member has a “financial relationship.” “Financial relationship” is defined as a “direct or indirect ownership or investment interest” or a “direct or indirect compensation arrangement.” In addition, an entity may not bill a patient, the Medicare program or anyone else for services rendered pursuant to a prohibited referral.

The Stark Law's broad ban on physician self-referrals is subject to numerous exceptions. Certain exceptions, such as those for in-office ancillary services and for academic medical centers, apply to both the ownership and compensation prohibitions. Other exceptions apply to either the ownership or the compensation prohibition, depending on the nature of the relationship. For example, physicians are generally permitted to have an ownership interest in an entire hospital, other than a specialty hospital, under an exception to the ownership prohibition. Similarly, physicians are permitted to be paid for professional or administrative services under a personal services exception to the compensation prohibition.

As a general matter, the Stark Law has had its desired effect and the preva-

Legal—continued on page 7

Ethics and the humanities: Slow Man

By J.M. Coetzee
New York: Viking, 2005, 263 pages

Since Susan Sontag's seminal works on language and illness, it has become something of an orthodoxy that we should be suspicious of representations of illness as having moral or social significance. Shakespeare's Richard the Third may ascribe his malevolence to his misshapen form and Dante's doomed spirits may be forever punished in somatic representations of their vices, but contemporary authors tend to avoid any such symbolism. Society and the environment as an external cause of illness is one thing; illness as a representation of a deformed inner being is another.

Nobel prize-winning author J.M. Coetzee is not willing to be sentimental about such matters. As one character in *Slow Man* puts it: “Your missing leg is just a sign or symbol or symptom, I can never remember which is which, of growing old, old and uninteresting.”

Slow Man tells the story of a photographer, Paul Rayment. Struck from his bicycle by an oncoming car, he is seriously injured; his leg cannot be salvaged and is amputated. Rayment refuses a prosthetic limb and insists upon living independently but compromised, nursing his own bitterness. He seethes under the ministrations of glib physicians and patronizing health care workers, during “the dragging, sleepless

nights in this hospital, this zone of humiliation with no place to hide from the pitiless gaze of the young.”

Returning home, he eventually comes under the care of Marijana Jokic, a sturdy Croatian nurse. Falling in love with her and responding to the care she provides him, Rayment offers to become a type of godfather to her family, paying for her son to attend university and protecting the daughters. Naturally, this is more complicated than Rayment could foresee. His hopes for a relationship with the Jokic family are put to the test by a reticent Marijana, a hostile husband and teenage children who are, well, teenagers. How the Jokic family ultimately addresses his disability—as a sign or symbol or symptom of him growing old and uninteresting—is the novel's surprisingly light, although by no means cheerful, climax.

There is, however, a twist running throughout the novel: the appearance of Elizabeth Costello, plucked from other writings by Coetzee. Her puzzling arrival raises all sorts of unanswered questions: Is she just another character? Is she a proxy for Coetzee? Is she there writing the novel of Paul Rayment and his unreciprocated love of Marijana, or is she writing *Slow Man* itself?

At the beginning of the novel, Rayment had expressed his disgust that he has become an object of care for the younger nurses and doctors: “*Better for the old to tend the old, the dying the dying!*” It is Elizabeth Costello, rather than any member of the Jokic family, who is his equal and with whom he can discuss and debate what it means for him to have suffered amputation, illness and aging.

Coetzee turns an unsentimental eye to their aging bodies—especially Costello's, whose varicose veins, cough, wrinkled skin and fragility are the “ugly” foil to the robust Jokic:

“By the time [Costello] gets to the door she is panting: a woman in her sixties, he would say, the later rather than the earlier sixties, wearing a floral silk dress cut low behind to reveal unattractively freckled, somewhat fleshy shoulders.”

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Coetzee's characters do not just experience their aging bodies or the pain of illness. They argue about whether there is meaning in injury and debilitation and decrepitude. In one of their quarrels, Rayment challenges Costello to “interpret your heart condition to me”; elsewhere, he rejects larger meanings about the loss of his leg, insisting that “blindness is a handicap pure and simple. A man without sight is a lesser man, as a man with one leg is a lesser man, not a new man.” And yet both Costello and Rayment wonder about these bodily changes and how, for example, Rayment's amputation signifies his mortality, childlessness and loneliness. In the midst of these discussions, Coetzee's characters stop to ponder and sometimes to debate the very words used to describe bodies and emotions. Rayment hears how Jokic pronounces a word that has meant so much to him: “*Prosthese*: she pronounces it as if it were a German word. Thesis, antithesis, then prosthesis.” At one point Costello says that she may be capricious, “but not as capricious as that. Capricious: goat-like, leaping from one rock to another. I am too old for leaping.”

Underlying these attempts to make sense of the metaphorical and linguistic experience of aging and physical corrosion are the characters' attempts to make sense of their duty to one another. The novel traces Rayment's relationships with his doctors and his nurses, then with his home care workers and the Jokics, and finally with Elizabeth Costello. Ultimately, the meaning of aging and decrepitude—the extent to which it is a symbol or representative of something internal—may be unanswerable or endlessly debatable, but one nevertheless becomes an object of care. At the close of the novel, Rayment accepts a gift from the Jokic family: a bicycle they have adapted so that he may ride it with his one leg. He is able to use the bicycle but not without giving up “his solemn airs” and becoming “a figure of fun.” The bicycle symbolizes both his recovery and the fact that he will never fully recover—either his leg or his dignity. □

MCS—continued from page 2

outcomes and service recommendations. *NeuroRehabilitation* 2002; 17: 231–236.

¹²Voss, H, Uluc A, Dyke J et al. Possible axonal regrowth in late recovery from the minimally conscious state. *J Clin Invest* 2006; 116:2005–2011.

¹³Schiff ND, Rodriguez-Moreno D, Kamal A et al. fMRI reveals large-scale network activation in minimally conscious patients. *Neurology* 2005;64:514–523.

¹⁴Fins JJ, Schiff ND, Foley KM. Late recovery from the minimally conscious state: ethical and policy implications. *Neurology* 2007; 68:304–307.

Dialogue: Nanotechnology in context

In July 2007, a specially convened task force of the U.S. Food and Drug Administration (FDA) concluded that size does in fact matter.¹ The focus of the task force was not on the importance of “largeness,” but rather on the technology of the unimaginably small—nanotechnology.

Nanotechnology is the technology of manipulating matter at near-atomic levels; typically, but not exclusively, within the size range of 1–100 nanometers. Working at this scale, it becomes possible to combine materials in ways and forms unimaginable more than a few decades ago.

According to the FDA task force, “properties of a material relevant to the safety and effectiveness of FDA-regulated products might change repeatedly as size enters into or varies within the nanoscale range.” But as Professors James H. Moor and John Weckert point out in “Nanotechnology and nanoethics,”² nanotechnology not only raises safety and regulatory issues, but ethical questions as well.

At the heart of the buzz surrounding nanotechnology is its potential to extend what can be achieved with conventional technologies, and the tantalizing possibility of developing radical new ones. Nanotechnology is a new way of doing things, a new technological tool kit. In the words of Moor and Weckert, “Nanotechnology offers us the general capability of material malleability.”

The idea of engineering at the nanoscale conjures up images of everyday mechanical objects shrunk to the scale of molecules; nanogears, nanoengines, even nanomachines—conventional engineering, but at a miniscule scale. Such nanoengineering would enable us to build complex devices from handfuls of atoms, increasing the performance and utility of human-scale products. It would also help use limited resources expediently—making products molecule by molecule, with minimal waste. In other words, this is a vision of nanotechnology that would emulate the biological world and lead to a *synthetic biology*; augmenting exist-

ing natural nanomachines and “molecular assemblers” that have evolved over billions of years, with an inorganic counterpart over which we have full control.

Eric Drexler envisaged such a world in his book *Engines of Creation: The Coming Era of Nanotechnology*.³ The chemist and Nobel Laureate Richard Smalley is credited with describing nanotechnology as “the art and science of building stuff that does stuff at the nanometer scale.” Scientists and technologists alike are drawn to nanotechnology because of the unconventional behavior exhibited by many nanoscale materials and their ability to “do stuff” in ways conventional materials do not. As atoms and molecules are formed into nanoscale structures, intrinsic material properties like conductivity, transparency and chemical reactivity diverge from those observed in the constituent molecules or the bulk material.

But engineered nanomaterials can also demonstrate unconventional behavior that is associated with extrinsic attributes like size and shape. For instance, engineering a material as discrete nanometer-diameter particles might make it easier to incorporate into products, deliver to specific areas of use or substantially increase the surface area to mass ratio. In these cases, the intrinsic physical and chemical properties of the engineered nanomaterial are not necessarily scale specific, but the ways in which the material is used *are*.

The scale-specific behavior of engineered nanomaterials takes on a special significance in interactions with biological systems and processes. Biology is inherently nanoscale, and purposely engineered nanoscale materials allow the possibility of modulating biological processes at a fundamental level. Nano-bio interactions may result from scale-specific physical and chemical properties intrinsic to some nanoscale materials. But they may just as likely result from nanoscale materials having access to biological processes that are inaccessible to larger-scale materials.

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In this way, nanotechnology provides a high-precision tool kit for exploring and influencing living systems. The biological utility of nanotechnology is demonstrated effectively through its use in potential cancer treatments. Researchers at Rice University, for example, are combining the scale-dependent photonic properties of nanometer-thick gold shells with the size-dependent biological properties of nanoscale particles to create composite particles capable of preferentially treating tumors. Gold-coated nanometer-diameter silica particles are introduced into the bloodstream, from where they preferentially pass through the leaky vasculature around tumors. Once sufficient material has accumulated around the diseased cells, irradiating the particles with a laser tuned to the gold nanoshells causes localized heating, destroying the growth while leaving healthy tissue unharmed.⁴

Researchers at the University of Michigan are developing multifunctional nanoparticles for treating specific cancers. Starting with generic nanoparticles, various functional components are added: ligands that attach to specific biological targets; contrast agents to allow particles to be tracked round the body; and sensitizing agents, enabling particles to receive and respond to external signals. With these components, nanoparticles are being developed that selectively target and destroy cancer cells, while minimally impacting the rest of the body.⁵

From relatively simple nanotechnology applications to the possibilities of synthetic life, nanotechnology provides tools for developing radical new processes and products. And with these tools come the social and ethical responsibilities to use them wisely. Concerns have already been expressed over potential new risks to humans and the environment that nanoscale-specific material behavior present. Little is known about how nanomaterials released into the environment will be transported, transformed and accumulated, or their impact on sensitive

ecosystems.⁶ Animal studies have demonstrated that nanoscale particles can enter and be transported within bodies in ways that larger particles cannot, and research suggests some nanomaterials are more potent in organs such as the lungs than their larger-scale counterparts.⁷ There are also early indications that nanoscale materials might interfere with protein conformation, and even lead to enhanced fibrillation rates in proteins associated with amyloid diseases such as Parkinson’s and Alzheimer’s.⁸

Studies remain inconclusive as to what might make nanomaterials harmful and what can be done to avoid harm. Recommendations have been made for better focused and funded strategic research.⁹ But the responsible use of nanotechnologies will depend on more than good risk management. Moor and Weckert suggest that nanotechnology has the potential to raise one of the ultimate ethical and medical issues: therapy versus enhancement. At what point do we cross the line between restorative biocompatible materials and implanted sensors (for instance), and the enhancements such technologies will offer to healthy individuals?

Already, there is serious discussion on how nanotechnologies might extend a person’s life span, or even be used to enhance an individual’s intelligence.¹⁰ But the ethical issues raised by nanotechnology go further: Who will receive the benefits of these new technologies, and who will pay the price? Will nanotechnologies widen social, economic and cultural divides, or close them? What are the implications of research into emulating biological systems? And what are the consequences of *not* grasping the opportunities being offered by nanotechnology?

Many of these issues are not unique to nanotechnology, but as Moor and Weckert intimate, the possibilities that nanotechnologies offer to *do things differently* throw them into sharp relief. Nanotechnology has the potential to improve living standards around the world, and offers solutions to some of the most pressing challenges we face: renewable energy, plentiful supplies of clean water, effective treatments for cancer, to name just three. If our aim is to improve quality of life and *do good*, it would be irresponsible and even unethical to deny the world what nanotechnology has to offer. Yet this potential for good must be weighed against the very real possibilities of

causing harm, widening equity imbalances and reducing autonomy. A future without nanotechnology would be a poorer, harsher place. But a world where nanotechnology is not developed within a clear ethical and social framework could be immeasurably worse. Either way, we have a challenge on our hands to move forward responsibly. When it comes to navigating through the implications of emerging technologies on our lives, size, it would seem, really does matter. □

¹U.S. Food and Drug Administration. *Nanotechnology. A report of the U.S. Food and Drug Administration Nanotechnology Task Force*. Washington, DC: Food and Drug Administration, 2007.

²Moor JH, Weckert J. Nanotechnology and nanoethics. *Lahey Clin Med Eth* 2007; 14(2):1–2.

³Drexler E. *Engines of Creation: The Coming Era of Nanotechnology*. New York: Anchor Books; 1986.

⁴O’Neal DP, Hirsch LR, et al. Photo-thermal tumor ablation in mice using near infrared-

absorbing nanoparticles. *Cancer Lett* 2004; 209:171–176.

⁵Koo YEL, Fan W, et al. Photonic explorers based on multifunctional nanoplatfoms for biosensing and photodynamic therapy. *Appl Opt* 2007;46:1924–1930.

⁶Oberdörster G, Oberdörster E et al. Nanotoxicology: an emerging discipline evolving from studies of ultrafine particles. *Environ Health Perspect* 2005;13(117): 823–840.

⁷Oberdörster G, Stone V, et al. Toxicology of nanoparticles: a historical perspective. *Nanotox* 2007;1(1):2–25.

⁸Linse S, Cabaleiro-Lago C et al. Nucleation of protein fibrillation by nanoparticles. *Proc Natl Acad Sci USA* 2007;104:8691–8696.

⁹Maynard AD, Aitken RJ et al. Safe handling of nanotechnology. *Nature* 2006;444: 267–269.

¹⁰Roco MC, Bainbridge WS, eds. *Converging Technologies for Improving Human Performance: Nanotechnology, Biotechnology, Information Technology and Cognitive Science*. Norwell, MA: Kluwer Academic Publishers; 2003.

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References

- Sazama K. The ethics of blood management. *Vox Sang* 2007;92:95–02.
Rogers, DM, et al. The approach to the patient who refuses blood transfusion. *Transfusion* 2006;46:1471–1477.

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lence of self-referrals has diminished greatly. However, the exceptions have proven to be fertile ground for the inventiveness of attorneys, promoters and other advisers for physicians and medical groups desirous of generating revenues from DHS. This has led to the use of condominium labs, block leasing, time-sharing and similar arrangements for imaging and various other DHS that are designed technically to satisfy the requirements of one or more exceptions to the application of the Stark Law, and thereby permit physicians and medical groups to continue to derive revenues from otherwise prohibited DHS.

In the end, the Stark Law and particularly the Phase III Regulations issued in September 2007 provide a complex minefield for physicians and their advisers. □

¹Hilman BJ, Joseph CA, Mabry MR et al. Frequency and costs of diagnostic imaging in office practice: a comparison of self-referring and radiologist-referring physicians. *N Engl J Med* 1990;323:1604–1608.