

cular risks of rosiglitazone led to a major change in FDA policy regarding the approval of all new diabetes drugs. From a cardiovascular perspective, rosiglitazone, saxagliptin, and alogliptin appear to be relatively safe. It is disappointing, however, that neither intensive glycemic control nor the use of specific diabetes medications is associated with any suggestion of cardiovascular benefit. Thus the evidence does not support the use of glycated hemoglobin as a valid surrogate for assessing either the cardiovascular risks or the cardiovascular benefits of diabetes therapy.

Patients with type 2 diabetes and their physicians currently have numerous treatment options, and additional drugs are in development. Perhaps the recent experience with rosiglitazone will allow the FDA to become more targeted in its adjudication of the car-

diovascular safety of new diabetes drugs, focusing the considerable resources needed to rule out a cardiovascular concern only on drugs with clinical or preclinical justification for that expenditure. New therapies targeting glycemic control may have cardiovascular benefit, but this has yet to be shown. The optimal approach to the reduction of cardiovascular risk in diabetes should focus on aggressive management of the standard cardiovascular risk factors rather than on intensive glycemic control.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

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This article was published on September 2, 2013, at NEJM.org.

1. The ACCORD Study Group. Long-term effects of intensive glucose lowering on cardiovascular outcomes. *N Engl J Med* 2011;364:818-28.
2. Nissen SE, Wolski K. Effect of rosiglitazone on the risk of myocardial infarction and death from cardiovascular causes. *N Engl J Med* 2007;356:2457-71. [Erratum, *N Engl J Med* 2007;357:100.]
3. Guidance for Industry: diabetes mellitus — evaluating cardiovascular risk in new antidiabetic therapies to treat type 2 diabetes. Silver Spring, MD: Food and Drug Administration, 2008 (www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm071627.pdf).
4. Home PD, Pocock SJ, Beck-Nielsen H, et al. Rosiglitazone evaluated for cardiovascular outcomes in oral agent combination therapy for type 2 diabetes (RECORD): a multicentre, randomised, open-label trial. *Lancet* 2009;373:2125-35.
5. Kaul S, Diamond GA. Is there clear and convincing evidence of cardiovascular risk with rosiglitazone? *Clin Pharmacol Ther* 2011;89:773-6.

DOI: 10.1056/NEJMp1309610

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The Dead-Donor Rule and the Future of Organ Donation

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The ethics of organ transplantation have been premised on “the dead-donor rule” (DDR), which states that vital organs should be taken only from persons who are dead. Yet it is not obvious why certain living patients, such as those who are near death but on life support, should not be allowed to donate their organs, if doing so would benefit others and be consistent with their own interests.

This issue is not merely theoretical. In one recent case, the parents of a young girl wanted to donate her organs after an accident had left her with devastating brain damage. Plans were made to withdraw life support

and to procure her organs shortly after death. But the attempt to donate was aborted because the girl did not die quickly enough to allow procurement of viable organs. Her parents experienced this failure to donate as a second loss; they questioned why their daughter could not have been given an anesthetic and had the organs removed before life support was stopped. As another parent of a donor child observed when confronted by the limitations of the DDR, “There was no chance at all that our daughter was going to survive. . . . I can follow the ethicist’s argument, but it seems totally ludicrous.”¹

In another recent case de-

scribed by Dr. Joseph Darby at the University of Pittsburgh Medical Center, the family of a man with devastating brain injury requested withdrawal of life support. The man had been a strong advocate of organ donation, but he was not a candidate for any of the traditional approaches. His family therefore sought permission for him to donate organs before death. To comply with the DDR, plans were made to remove only nonvital organs (a kidney and a lobe of the liver) while he was under anesthesia and then take him back to the intensive care unit, where life support would be withdrawn. Although the plan was endorsed by the

clinical team, the ethics committee, and the hospital administration, it was not honored because multiple surgeons who were contacted refused to recover the organs: the rules of the United Network for Organ Sharing (UNOS) state that the patient must give direct consent for living donation, which this patient's neurologic injury rendered impossible. Consequently, he died without the opportunity to donate. If there were no requirement to comply with the DDR, the family would have been permitted to donate all the patient's vital organs.

Allegiance to the DDR thus limits the procurement of transplantable organs by denying some patients the option to donate in situations in which death is imminent and donation is desired. But the problems with the DDR go deeper than that. The DDR has required physicians and society to develop criteria for declaring patients dead while their organs are still alive. The first response to this challenge was development of the concept of brain death. Patients meeting criteria for brain death were originally considered to be dead because they had lost "the integrated functioning of the organism as a whole," a scientific definition of life reflecting the basic biologic concept of homeostasis.² Over the past several decades, however, it has become clear that patients diagnosed as brain dead have not lost this homeostatic balance but can maintain extensive integrated functioning for years.³ Even though brain death is not compatible with a scientific understanding of death, its wide acceptance suggests that other factors help to justify recovery of organs. For example, brain-dead

patients are permanently unconscious and cannot live without a ventilator. Recovery of their organs is therefore considered acceptable if organ donation is desired by the patient or by the surrogate on the patient's behalf.

More recently, to meet the ever-growing need for transplantable organs, attention has turned to donors who are declared dead on the basis of the irreversible loss of circulatory function. Here again, we struggle with the need to declare death when organs are still viable for transplantation. This requirement has led to rules permitting organ procurement after the patient has been pulseless for at least 2 minutes. Yet for many such patients, circulatory function is not yet irreversibly lost within this timeframe — cardiopulmonary resuscitation could restore it. So a compromise has been reached whereby organ procurement may begin before the loss of circulation is known to be irreversible, provided that clinicians wait long enough to have confidence that the heart will not restart on its own, and the patient or surrogate agrees that resuscitation will not be attempted (since such an attempt could result in a patient's being "brought back to life" after having been declared dead).

Reasonable people could hardly be faulted for viewing these compromises as little more than medical charades. We therefore suggest that a sturdier foundation for the ethics of organ transplantation can be found in two fundamental ethical principles: autonomy and nonmaleficence.⁴ Respect for autonomy requires that people be given choices in the circumstances of their dying, including donating organs. Nonmaleficence requires protecting patients from harm. Accordingly,

patients should be permitted to donate vital organs except in circumstances in which doing so would harm them; and they would not be harmed when their death was imminent owing to a decision to stop life support. That patients be dead before their organs are recovered is not a foundational ethical requirement. Rather, by blocking reasonable requests from patients and families to donate, the DDR both infringes donor autonomy and unnecessarily limits the number and quality of transplantable organs.

Many observers nevertheless insist that the DDR must be upheld to maintain public trust in the organ-transplantation enterprise. However, the limited available evidence suggests that a sizeable proportion of the public is less concerned about the timing of death in organ donation than about the process of decision making and assurances that the patient will not recover — concerns that are compatible with an ethical focus on autonomy and nonmaleficence.⁵

Although shifting the ethical foundation of organ donation from the DDR to the principles of autonomy and nonmaleficence would require creation of legal exceptions to our homicide laws, this would not be the first time we have struggled to reconcile laws with the desire of individual patients to die in the manner of their own choosing. In the 1970s, patients won the right to have ventilator use and other forms of life support discontinued, despite physicians' arguments that doing so would constitute unlawful killing. Since that time, physicians have played an active role in decisions about whether and when life support should be withdrawn, and the willingness of physicians

to accept this active role in the dying process has probably enhanced, rather than eroded, the public trust in the profession.

Our society generally supports the view that people should be granted the broadest range of freedoms compatible with assurance of the same for others. Some people may have personal moral views that preclude the approach we describe here, and these views should be respected. Nevertheless, the views of people who may freely avoid these options provide no basis for denying such liberties to those who wish to pursue them. When death is very near, some patients may want to die in the process of helping

others to live, even if that means altering the timing or manner of their death. We believe that policymakers should take these citizens' requests seriously and begin to engage in a discussion about abandoning the DDR.

The views expressed are those of the authors and do not necessarily reflect the policy of the National Institutes of Health, the Public Health Service, or the Department of Health and Human Services.

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1. Sanghavi D. When does death start? *New York Times Magazine*. December 16, 2009 (http://www.nytimes.com/2009/12/20/magazine/20organ-t.html?pagewanted=all&_r=0).
2. Bernat JL, Culver CM, Gert B. On the definition and criterion of death. *Ann Intern Med* 1981;94:389-94.
3. Shewmon DA. Chronic "brain death": meta-analysis and conceptual consequences. *Neurology* 1998;51:1538-45.
4. Miller FG, Truog RD. *Death, dying, and organ transplantation: reconstructing medical ethics at the end of life*. New York: Oxford University Press, 2012.
5. Siminoff LA, Burant C, Youngner SJ. Death and organ procurement: public beliefs and attitudes. *Kennedy Inst Ethics J* 2004;14:217-34. DOI: 10.1056/NEJMp1307220

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Life or Death for the Dead-Donor Rule?

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The increasing disproportion between the supply of donor organs and the demand for transplants as well as the tragic deaths of patients awaiting organs have encouraged the development of creative solutions to increase the donor supply. In the domain of donation from deceased donors, the protocols for organ donation after the circulatory determination of death (DCDD) have been one such response. Most U.S. organ-procurement organizations have seen organs from DCDD protocols account for a growing percentage of all organs donated from deceased donors (see graph). In England, DCDD organs currently constitute a greater percentage than organs donated after the determination of death by brain criteria ("donation after the brain determination of death," or DBDD).

Another innovative strategy is the kidney-donation protocol re-

cently proposed by Paul Morrissey of Brown University.¹ This protocol permits a lawful surrogate decision maker for a patient with a severe, irreversible brain injury (but who is not "brain dead") to authorize withdrawal of life-sustaining treatment and pre-mortem donation of both kidneys. Whereas DCDD protocols entail removal of organs after the cessation of life-sustaining therapy and the subsequent declaration of death, the Morrissey protocol provides for procuring organs while the patient remains alive. Life-sustaining treatment is withdrawn after the donation has been accomplished. The patient dies of the respiratory complications of the original brain injury, which is fatal in the absence of life-sustaining treatment.

Some commentators have claimed that Morrissey's protocol violates the dead-donor rule (DDR). The DDR is not a law but

an informal, succinct standard highlighting the relationship between the two most relevant laws governing organ donation from deceased donors: the Uniform Anatomical Gift Act and state homicide law. The DDR states that organ donation must not kill the donor; thus, the donor must first be declared dead. It applies only to organ donation from deceased donors, not to living donation, such as that of one kidney or a partial liver. Morrissey's protocol does not violate the DDR because it is a type of living organ donation that does not kill the donor. The donor dies not as a result of the azotemic consequences of the donation of both kidneys but earlier, of respiratory arrest.

That the act of organ donation must not kill the donor has been regarded as the ethical and legal foundation of organ donation from its earliest days. John Rob-