EDITORIALS

Cardiac Transplantation in Infants

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For children born with inoperable congenital heart disease or advanced cardiomyopathy, cardiac transplantation is the only therapeutic option. Each year in the United States, approximately 400 heart-transplantation procedures are performed in children and adolescents. In about two thirds, the indication is complex congenital heart disease, and in the remainder it is cardiomyopathy. During the past decade, the procedure has proved lifesaving for thousands of children.

Of the 400 pediatric heart transplantations performed annually, about 100 are in infants under the age of 1 year. The 15-year survival rate among these infants is greater than 50%, increasing to 80% among those who survive for the first 5 years after transplantation. Thus, cardiac transplantation in infants is a highly successful procedure that has saved the lives of many babies with terminal heart disease.

But not all the news is favorable. Each year, as many as 50 infants are placed on the waiting list for cardiac transplantation but die while waiting, owing to the lack of a suitable donor heart. Although in recent years the rate of death among patients awaiting cardiac transplantation has declined in most age groups, the single exception is infants under 1 year of age. Infants in fact have 10 times the risk adults have of dying while waiting for an organ. Thus, a shortage of donor hearts among infants is a serious matter and contributes to a substantial number of otherwise preventable deaths. There is an urgent need for more infant donors, but meeting this need while being mindful of the ethical considerations has been challenging and complex.

According to the "dead donor rule," before donation organ donors must be declared dead, on the basis of either brain-death criteria (i.e., irreversible cessation of all brain functions) or cardiac-death criteria (i.e., irreversible cessation of cardiocirculatory function). Donation after cardiocirculatory death, previously called non-heart-beating donation, typically involves donors who have suffered devastating neurologic injury (yet are not brain dead) but who have normal cardiac function if maintained on life support.

In donation after cardiocirculatory death, life support is withdrawn, the heart stops, death is declared, and organs are then removed for transplantation. To ensure that autoresuscitation (the heart starting again on its own) will not occur, protocols for donation after cardiocirculatory death also require that a suitable period elapse after the cessation of cardiocirculatory function before organs are removed from the donor. The length of that period is a key variable.

A 1997 report from the Institute of Medicine (IOM)[1] suggested that 5 minutes should elapse between cardiocirculatory death and organ retrieval, but the report also recommended further study of the validity of this interval. A second IOM report in 2000[2] reassessed the time interval and stated that "The empirical data available indicate that cardiopulmonary arrest becomes irreversible within a shorter time interval — 60 seconds or less." But the report also stated that "existing empirical data cannot confirm or disprove a specific interval at which the cessation of cardiopulmonary function becomes irreversible," and it concluded that "this is an area in which well-considered judgments continue to differ."

Given these differing judgments, some protocols for donation after cardiocirculatory death have shortened the waiting period after the cessation of cardiocirculatory function to 2 minutes. Although there must be certainty that autoresus-

citation will not occur, it is also critical for the benefit of the recipient that the donor organs be protected by minimizing the period of warm ischemia. The 2000 IOM report concluded, "These variations suggest that even with a strong commitment to ethical practice and a reliance on the best clinical data available, there is room for significant differences of opinion on non-heart-beating donation practices."

In this issue of the *Journal*, Boucek et al.[3] report on three successful heart transplantations in infants that involved donation after cardiocirculatory death, a report that is likely to provoke controversy. After informed consent was obtained from the parents and approval granted by the institution's ethics committee, physicians not involved in the transplantation procedures withdrew life support from three prospective infant donors who had sustained severe neurologic injuries but who did not meet brain-death criteria; all had normal cardiac function while receiving life support. The unambiguous separation of the decision to withdraw life support and the decision to donate organs, which is an essential element of all transplantation protocols, rendered this approach acceptable.

After the withdrawal of life support from the three infants, there was cessation of cardiocirculatory activity after an average of 18 minutes. For the first patient, an additional 3 minutes was permitted to elapse before removal of the heart for transplantation was begun. For the other two donors, this interval was shortened to 75 seconds. The basis for the shortened time interval used in this investigational protocol will be questioned by some, but to a certain extent it is consensus, not definitive scientific evidence, that has determined the intervals used. The 2000 IOM report indicated that "it is a decision point at which different options may be followed, but the grounds for selecting one option over another should be clearly specified." In accordance with this requirement, Boucek et al. indicate that the ethics committee recommended "a period of observation of 75 seconds . . . based on the longest reported period before autoresuscitation in a child or adult, 60 seconds."

We are publishing the article by Boucek et al. to foster discussion of donation after cardiocirculatory death in general and its application to infant heart transplantation in particular. To initiate the discussion, in this issue of the *Journal* we also publish three Perspective articles,[4-6] along with a video roundtable discussion[7] available at www.nejm.org.

In his Perspective article, Veatch[4] takes the position that since it was possible to restart the three donor hearts in the recipients after transplantation, there was not irreversible cessation of cardiac function and therefore the criterion for cardiac death had not been met. In his article, Bernat[5] points out that the investigational protocol of Boucek et al. tests the permissible boundaries of organ procurement, and he expresses the view that the 75-second interval that they used will ultimately not be found acceptable by the medical community. Truog and Miller[6] believe that it is time to reassess the dead donor rule and refocus criteria for organ donation on "valid informed consent under the limited conditions of devastating neurologic injury."

The video roundtable[7] was moderated by Atul Gawande, and the panelists were George Annas, Arthur Caplan, and Robert Truog. In this interactive session, they explore a number of ethical issues.

The opinions of each of these experts are controversial and may be challenged. We hope that the articles and roundtable discussion will stimulate debate on organ donation in infants and lead to a consensus that not only meets a high ethical standard but also addresses the urgent shortage of donor organs. The development of standard criteria for pediatric heart donation is a vital goal. In the report by Boucek et al., one conclusion is clear. As a result of their investigational protocol, three babies are now alive; had the procedures not been performed, it is virtually certain that all six babies would be dead.

1. Non-heart-beating organ transplantation: medical and ethical issues in procurement. Washington, DC: National Academy Press, 1997.
2. Non-heart-beating organ transplantation: practice and protocols. Washington, DC: National Academy Press, 2000.
3. Boucek MM, Mashburn C, Dunn SM, et al. Pediatric heart transplantation after declaration of cardiocirculatory death. N Engl J Med 2008;359:709-14.
4. Veatch RM. Donating hearts after cardiac death — reversing the irreversible. N Engl J Med 2008;359:672-3.
5. Bernat JL. The boundaries of organ donation after circulatory death. N Engl J Med 2008;359:669-71.
6. Truog RD, Miller FG. The dead donor rule and organ transplantation. N Engl J Med 2008;359:674-5.
7. Gawande A, Annas GJ, Caplan AL, Truog RD. Organ donation after cardiac death. July 23, 2008. (Available at www.nejm.org.)