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Perspective

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Of Tragedies and Miracles — Neonatal Organ Donation

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Baby K. was born at full term after an uncomplicated pregnancy, with sweet baby thighs, adorable little hands and feet, and a soft crown of wispy hair. But at 5 days of age, rather than snuggling with his mother and breast-feeding, he was lying on a cooling blanket in a neonatal intensive care unit (NICU), attached to a ventilator, monitors, and IV fluids. When his hypothermia therapy for encephalopathy ended that day, he underwent an EEG and an MRI. I'm sure his parents suspected what these tests would reveal, but it broke my heart to have to put their worst fears into words.

Over the years, I've had many difficult conversations with parents about devastating test results and the possibility of shifting an infant from curative care to comfort care. Some parents react with denial, some with anger. Others take the initiative in choosing redirection of care, and some quietly acquiesce to my guidance. As the team and I sat down to talk with Baby K.'s parents, I thought I'd seen the full spectrum of possible parental reactions.

But without waiting for my explanations or opinions, Baby K.'s father said something I'd never heard a newborn's parent say: "We would like to donate his organs."

Tears erupted from the few eyes in the room that had managed to remain dry.

Then we leapt into action — or tried to. This was my first experience with neonatal organ donation, and I had no idea how rarely that process took place. I was keenly aware that I didn't know what steps I needed to take, and that nobody else seemed to know either.

The first stumbling blocks we encountered were our own assumption that infants with significant organ injury could not be organ donors and our doubt about whether it was possible to diagnose brain death in a neonate — and if not, whether organs could be donated anyway. We learned that day that some level of injury to organs may be acceptable: neonatal organs are hard to come by, so transplant surgeons make case-by-case decisions based on the condition of both the organs and the recipient. A baby who would otherwise die soon may benefit from a less-than-healthy organ, whereas a baby who is stable may be better off waiting.

As the day stretched into night, I learned that what I'd been taught about neonatal brain death during training was incorrect. I'd believed that brain death can't be diagnosed in neonates for physiological reasons, but in fact there were simply no well-disseminated guidelines for this age group. The 1981 Guidelines for the Determination of Death covered pa-

tients 5 years of age or older, and the 1987 American Academy of Pediatrics (AAP) guidelines expanded the criteria to cover patients as young as 7 days old.

We spent that long night trying to reconcile the fact that the organ bank could not legally accept an organ from a patient who had not been declared dead with the fact that I could not conscionably declare a 5-day-old brain dead because it wasn't standard practice. We felt that we couldn't give up until we'd found a solution for Baby K.'s family. They were willing to give so much even as they were losing so much that I could not refuse their gift on the basis of technicalities. As we sat in the team room discussing options with the organ bank coordinator and our hospital risk manager, I remembered Thomas Edison's famous words: "I have not failed. I've just found 10,000 ways that won't work."

Then serendipity stepped in. The neonatology fellow on call that night had been a chief resident at a neighboring children's hospital. Wondering what the pediatric intensive care unit (PICU) at that hospital did in these situations, he contacted the on-call PICU attending. That intensivist happened to be on a committee charged with developing a new pediatric brain-death policy for the PICU, and she had just received a draft of it. She had not yet read it, but she was willing to share it with us. Although it was designed for an older population, the draft policy pointed us toward the AAP guidelines for the determination of brain death in children, an update to the 1987 recommendations that included guidelines on the determination of brain death from birth onward for infants born at 37 weeks' gestation or later.[1] Even the people we'd spoken to at the New England Organ Bank (NEOB) had not been aware of these 2011 guidelines.

Despite the guidelines, pediatricians' ability to define and apply the concept of brain death leaves substantial room for improvement,[2] so it's not surprising that cases of neonatal organ donation are rare. Between 1988 and 2013, there was a yearly average of 100 U.S. organ donors under 1 year of age. In the New England region, the average was 1.5 per year, according to the NEOB, and Women and Infants Hospital, home of the only level IV NICU in Rhode Island, had had no organ donations at all between 2000 and 2013. Furthermore, over the previous 28 years, only two neonatal organ donations had occurred in the entire New England region. All of this strongly suggests that before Baby K.'s parents proposed donating his organs, there had never been a neonatal organ donation in the state of Rhode Island.

As my colleagues and I worked to help Baby K.'s parents achieve their goal, I wondered whether neonatal organs are not being donated because NICU physicians are unaware of the donation criteria and so are missing many possible donors or whether there are actually few newborns who meet the criteria. Recent retrospective studies of theoretically suitable cases indicate that though it's unlikely that a large number of potential donors are being missed, there is room for improvement in physicians' awareness.[3,4]

Baby K.'s father asked me why he had to be the one to raise the question of organ donation. I think the complex answer is that we often believe that the family will find the idea too difficult to bear, we may be too uncomfortable ourselves to take the necessary steps, and we may assume that a given newborn wouldn't qualify as a donor.

Ultimately, the strength that Baby K.'s parents showed launched a cascade of unanticipated good. First and foremost, they saved another baby's life, thereby "saving another family from the anguish [they] were living through," as they put it. But they did more than that.

They allowed the NICU team to feel not just the sadness and failure that we experience when a baby dies under our care, but also the comfort of knowing that we were part of something miraculous. Although we could not save our patient's life, we played at least a small role in saving another baby's life — and so saw a faint light that we had not seen before. Baby K. and his family reminded us not only that miracles in medicine may sometimes arise out of the deepest tragedies, but also that patients and their families may offer their care providers such profound gifts as humility, strength, and inspiration.

And Baby K. and his parents challenged us to expand our clinical horizons beyond our comfort zone by educating ourselves. They thereby opened the door to future lifesaving donations: we now have a policy for neonatal organ donation and have been teaching our staff and trainees about the process.

During our final family meeting, Baby K.'s parents asked me to raise awareness about neonatal organ donation so that in the future more parents of dying newborns are offered the choice and more babies' lives can be saved. If we actively screen for qualified donors, perhaps we can avoid

missing so many opportunities to turn heartbreaking tragedy into bittersweet success.

Disclosure forms provided by the author are available at NEJM.org.

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The FDA Sentinel Initiative — An Evolving National Resource

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The Food and Drug Administration (FDA) Sentinel Initiative,[1] which was launched in 2008, has matured from a pilot program designed to assess potential drug-safety signals in insurance claims into a core component of the agency's evolving safety surveillance system. Sentinel is a flexible and robust program that provides evidence on the effects of medical products while protecting patient privacy; it uses a distributed data network that contains curated electronic health data covering more than 100 million people. The FDA regularly conducts safety analyses of the billions of hospital stays, outpatient visits, and pharmaceutical dispensings included in the Sentinel System.

To develop Sentinel, the FDA partnered with more than 200 health system leaders, pharmacoepidemiologists, clinicians, data scientists, patient representatives, and other experts from 31 health plans and academic organizations. Early on, the group focused on privacy and governance issues in order to support broad participation while addressing concerns related to confidentiality and proprietary information. The lead team then designed and built a secure querying system, created a very large rigorously curated and updated distributed health information data set, and developed tools permitting rapid, customized analysis.

Distributed data systems, in which data partners maintain physical and operational control over their data, provide a high level of protection for the privacy and security of patients' health information. Each data partner formats a copy of its data according to the specifications of the Sentinel Common Data Model and keeps the transformed data behind its existing firewalls. Neither the FDA nor the Sentinel Operations Center takes possession of these data sets; instead, questions in the form of executable computer programs are sent to each data partner. The partner returns only the results, which typically contain information such as counts of exposed people and outcomes of interest. Sentinel methodologists have developed and implemented techniques for performing sophisticated analyses such as propensity score matching and self-controlled analyses in a distributed environment. Scientists at each partner system also participate in this process, providing guidance on the best use of their data. Although data partners have chosen to respond to nearly all questions sent to them, their ability to opt out of specific queries remains an important contributor to their willingness to participate in the program.

Administrative claims data are the foundation of the Sentinel infrastructure because they are the most reliable and readily available source of complete longitudinal information about medication dispensing and medically attended events, regardless of where care is provided. The system is also able to link to registries and incorporate certain electronic health record data. In addition, when a specific analysis requires data available only in a medical chart, data partners are authorized to request this information from providers.

Sentinel data have informed many regulatory decisions made by the Center for Drug Evaluation and Research and, in the past 2 years, have eliminated the need for postmarketing studies on nine potential safety issues associated with five products (e.g., ustekinumab and serious infections). Such postmarketing studies typically require years to design and com-