Medicine

Assisted Reproduction Technology

Two articles appearing in the journal *Human Reproduction* concern negative aspects of assisted reproductive technology (ART). In the first article, "Admission to Hospital of Singleton Children Born following Assisted Reproductive Technology" (*Human Reproduction*, June 2008), Michèle Hansen and colleagues investigated hospital admissions for all singleton children born between 1994 and 2000 in Western Australia. There were 162,350 children born as singletons following spontaneous conception and 1,328 born as singletons following ART: ART procedures included in vitro fertilization, intracytoplasmic sperm injection, and gamete intrafallopian transfer. Compared with the spontaneous-conception group, ART children were three times more likely to be born at or before thirty-two weeks' gestation or to weigh less than 1,500 grams; they were almost twice as likely to have a major birth defect, 60 percent more likely to be stillborn, and twice as likely to die before their first birthday.

In the second article, "Women's Experiences of Childbirth and Postnatal Healthcare after Assisted Conception" (*Human Reproduction*, July 2008), Karin Hammarberg and colleagues used telephone interviews and self-report questionnaires to investigate women's experiences of childbirth and postnatal health care following ART. The study design was prospective and longitudinal, and there were 166 evaluable women who had delivered following ART. Of these women, 51 percent had cesarean births, compared with 25 percent of other Australian women, indicating that the risk of cesarean (surgical) birth after ART is double the risk after spontaneous conception. Compared with women who delivered vaginally, women who had cesarean births were statistically less likely to report having an active say about what happened during birth, being pleased with the birth experience, or being able to hold the baby soon after birth, and they were more likely to report severe postnatal pain and a need for more help and advice with infant feeding. Despite information about

increased risks and undesirable features of ART, individuals' pursuit of reproductive choices and so-called freedom are not likely to be deterred.

In the same journal, two other articles about ART convey more positive aspects. In "Mental and Psychomotor Development of Two-Year-Old Children Born after Preimplantation Genetic Diagnosis/Screening" (*Human Reproduction*, July 2008), Julie Nekkebroeck and colleagues report findings from a study of three matched cohorts, each of seventy two-year-old singleton children who were evaluated in terms of mental and psychomotor development, by a trained psychologist using standardized assessment tools. The cohorts were children born following (1) preimplantation genetic diagnosis or screening (PDG/PGS), (2) intracytoplasmic sperm injection, or (3) natural conception. The authors report no differences among the groups with respect to mental and psychomotor development. Limitations of the study include the relatively small sample size at a single center and the unblinded design. (The psychologist was only partially blinded, as the natural-conception group was evaluated at day care or in a pediatrician's office.)

In a second article, "Socio-emotional and Language Development of Two-Year-Old Children Born after PGD/PGS, and Parental Well-Being" (*Human Reproduction*, August 2008), the same group of investigators reported additional observations on the same cohorts of children, although the sample sizes were smaller—fifty-two, fifty-four, and sixty-nine children in the PGD/PGS, intracytoplasmic sperm injection, and natural conception groups, respectively. Using a series of standardized questionnaires and established assessment instruments, the authors found no differences among the groups with respect to socio-emotional or language development, and no differences among the parents with regard to well-being (or stress index) scores. Both papers present neutral features of ART, but the faithful should be reminded that such reproductive techniques are immoral. Regarding the children born of such technology, however, it is also important to remember that every child who comes into the world must be accepted as "a living gift of the divine goodness" and brought up with love (*Donum vitae*, II [B], 5).

Turning attention to the perinatal outcomes of twin births following ART, Sheree Boulet (from the National Center on Birth Defects and Developmental Disabilities) and her colleagues reported outcomes from 1,446 ART twin deliveries and 2,729 non-ART twin deliveries ("Perinatal Outcomes of Twin Births Conceived Using Assisted Reproduction Technology: A Population-Based Study," *Human Reproduction*, August 2008). They found that twin deliveries following ART were no riskier than other twin deliveries. In the subset of women giving birth for the first time (primiparous deliveries), the ART deliveries were less likely than non-ART deliveries to be very pre-term, the babies were less likely to have very low birth weights or Apgar scores less than 7, and there were fewer infant deaths. The authors suggest that the apparent risk attenuation in the ART group may be related to heightened monitoring and care during the prenatal and perinatal periods.

Neonatology

The genetic abnormality trisomy 18 is reported to affect approximately one in eight thousand live-born infants, and the median life expectancy of an affected infant is two to ten days if the child is not treated with intensive care. First-year mortality

rates are between 90 and 100 percent, the vast majority of infants apparently die in the first month, and those who live more than a year have severe impairments. Until recently, the medical community agreed universally that that it is not in the best interest of infants with trisomy 18 to pursue aggressive or invasive therapy after birth.

In the June 2008 issue of *Pediatrics*, Melanie McGraw and Jeffrey Perlman report the results of a study of the attitudes of neonatal providers toward delivery room resuscitation of a thirty-six-week fetus with confirmed trisomy 18 and congenital heart disease ("Attitudes of Neonatologists toward Delivery Room Management of Confirmed Trisomy 18: Potential Factors Influencing a Changing Dynamic," *Pediatrics 2008*). A description of the clinical scenario was sent with a multiple-choice questionnaire to neonatologists in the New York City area. The authors explored whether neonatologists would consider initiating resuscitation and, if so, what factors would influence them to do so. There were 54 respondents, of whom 44 percent indicated that they would consider resuscitation. Maternal preference was given as the primary reason to initiate resuscitation, with the appearance of the infant (appearing vigorous or having a heart rate of 100 beats per minute or more) and legal concerns given as the second and third most important factors, respectively. This small study suggests that there may be a change in the approach taken by neonatologists toward this fatal condition. Specifically, it suggests that the best-interest standard is being trumped by parental autonomy.

Infants' best interests may or may not accord with parents' decisions about medical care. The findings of this study seem to reflect an increasing emphasis on individual autonomy regardless of what is medically appropriate. Patient autonomy—in this case the autonomy of the parents of a gravely ill infant—cannot be absolute. Autonomy must be balanced by a sound, properly formed moral conscience, admittedly not an easy task.

Organ Transplantation

Physicians at the Children's Hospital of Philadelphia report on pediatric donation after cardiac death (DCD) in the June 2008 issue of *Critical Care Medicine* ("The Children's Hospital of Philadelphia's Experience with Donation after Cardiac Death"). Maryam Naim and colleagues studied the charts of twelve children from one to seventeen years of age who were organ donors following cardiac death. Eight of the children suffered hypoxic ischemic encephalopathy, and four had severe traumatic brain injury. Twenty-four kidneys, eight livers, four lungs, and one pancreas were procured from these children, and twenty-three kidneys, four livers, and one pancreas were transplanted. (Four lungs and four livers were donated to research, mostly because they were unsuitable for transplantation).

Conversations about organ donation were initiated by the child's family in nine cases, by a physician in one case, and by a physician and representative of the organ procurement agency in two cases. All the conversations occurred after decisions to withdraw life-sustaining therapy were made. Withdrawal of LST occurred in the operating room in ten cases and near the operating room (in a holding area or post-anesthesia care unit) in two cases. Family members were invited to be present for the withdraw of LST, and were present in eight of the twelve cases. The time from

removal of LST (extubation) ranged from 4 to 30 minutes (mean, 14.5 minutes), and organ procurement began no earlier than 7 minutes after asystole (no electrical activity in the heart) developed. Sedative and narcotic medications were used for patient comfort prior to withdrawal of LST, and no muscle relaxants were used prior to LST removal. The only medication specifically given to improve chances of organ viability was the anticoagulant heparin, administered 5 to 10 minutes prior to the removal of LST in a dose that was at least three times the recommended dose. The authors report that no patient had bleeding complications.

My major criticism of this paper has to do with the absence of any discussion about the use of heparin infusion before the withdrawal of LST. The authors discuss the use of sedative medications for patient comfort, and even cite the principle of double effect in this regard. Supratherapeutic doses of heparin are used solely for organ preservation, however, not for the benefit of the patient. This is a major ethical issue in the practice of DCD, and the principle of double effect does not seem to be relevant. The intention in administering the heparin is to preserve the organ for procurement, and the unintended effect is potential bleeding in the donor patient. Unlike the use of sedative narcotic medications, which are intended for the patient's benefit despite possible untoward effects, heparin is administered not for the donor patient's benefit but for organ viability and thus, by extension, the benefit of the recipient patient. At least in theory, and possibly in reality, a large dose of heparin may be harmful to the donor patient. What concerns me is that the article fails even to mention this issue.

The prospect of children as living solid-organ donors is the focus of an article in the August 2008 issue of *Pediatrics* ("Minors as Living Solid-Organ Donors"), by Lainie Ross and Richard Thistlethwaite for the Committee on Bioethics of the American Academy of Pediatrics. This article succinctly presents the background on pediatric donations, discusses risks and benefits for donors as well as recipients, and sets forth the five conditions that must be met for a minor to be a living solid-organ donor. Specifically, the Academy believes that "minors may ethically serve as living organ donors but only in specific, limited circumstances," when all five conditions are met: "Children may serve as solid-organ donors if donor and recipient are both highly likely to benefit; surgical risk for the donor is extremely low; all other deceased and living donor options have been exhausted; the minor freely assents to donate without coercion (established by an independent advocacy team); and emotional and psychological risks to the donor are minimized."

In the August 14, 2008, issue of the *New England Journal of Medicine*, Mark Boucek and colleagues report the first three successful cardiac transplantations in children following donation after cardiac death ("Pediatric Heart Transplantation after Declaration of Cardiocirculatory Death"). The mean age of the recipients was 2.2 months. Two of the recipient children had severe and complex congenital heart disease, and the third had severe cardiomyopathy. All three recipients were alive six months following transplantation.

The donors all had severe neurologic injury resulting from birth asphyxia. Their mean age at donation was 3.7 days. The mean time from the withdrawal of life support to the declaration of death was 18.3 minutes. Vascular cannulations

were performed to prepare for organ procurement prior to the withdrawal of life support, and additional heparin (at least three times the maximal therapeutic dose) was administered after the withdrawal of life support. After cardiac arrest, the first patient was observed for 3 minutes before death was declared and organ procurement began. In the second and third donors, the observation period was shortened to 1.25 minutes before death was declared and organ procurement began. This time was based on the longest reported period of autoresuscitation (60 seconds).

There is no substantive discussion about the ethics of DCD in the article, but three "Perspective" articles in the same issue address some of the ethical underpinnings of this medical procedure. In "The Boundaries of Organ Donation after Circulatory Death," James Bernat emphasizes the requirement that the physicians making the death determination be "strictly separated" from those procuring the organs, and raises some issues with regard to organ procurement procedures. These include the duration of asystole (the cessation of electrical activity in the heart) before death is declared and the use of extracorporeal devices which provide circulation and oxygenation to the donor's body in order for organ procurement to occur under *better* circumstances. He raises the specific question whether such circulation and oxygenation would retroactively negate the death determination, effectively reversing what was said to be irreversible.

In the second Perspective article, "Donating Hearts after Cardiac Death: Reversing the Irreversible," Robert Veatch takes up the issue of "irreversibility" in more depth. He gives the reader a very direct and clear appraisal of the issue when he states, "one cannot say a heart is irreversibly stopped if, in fact, it will be restarted." He goes on to say, "Removing organs from a patient whose heart not only can be restarted, but also has been or will be restarted in another body, is ending a life by organ removal." So, in effect, heart transplantation after DCD cannot be done in a matter consistent with the dead donor rule—that is, a patient must be dead before organ procurement occurs. Veatch goes on to suggest two possible ways to get out of this ethical dilemma. One is to change the law so that vital organs could be procured while a donor was still alive. Veatch sees this as practically and morally implausible. The second is to amend the brain-death definition so that the total loss of the higher-brain functions responsible for consciousness would constitute death. Then the more strict criteria, which include loss of whole-brain function, including brain-stem function, would not be necessary, and the issue of cardiac reversibility would become moot.

Finally, in "The Dead Donor Rule and Organ Transplantation," Robert Truog and Franklin Miller expose the dead donor rule for what it is, stating that "at best, the rule has provided misleading ethical cover that cannot withstand careful scrutiny." They object to "gerrymandering the definition of death to carefully conform with conditions that are most favorable for transplantation" and suggest that, with appropriately obtained consent, it may be more ethical to procure organs from patients who have sustained "devastating, irreversible neurologic injuries that do not meet the technical requirements of brain death." All who strive to uphold respect for persons, including their bodily integrity, and who seek to avoid a utilitarian approach to the human body should find this proposal morally objectionable.

Surrogate Decision Making

An article in the September issue of the *Journal of General Internal Medicine* questions the ethical basis for substituted judgment—that is, when doctors and family members try to make the decision that the patient would have made if he or she were able to make decisions ("Substituted Judgment: The Limitations of Autonomy in Surrogate Decision Making"). Alexia Torke, Caleb Alexander, and John Lantos present evidence derived from three lines of research which suggests that substituted judgment is a flawed approach to surrogate decision making. Limitations of substituted judgment include the fact that patients' preferences regarding life-sustaining therapy change over time, that the concordance between patients' and their designated surrogate decision makers is often weak, and that patients often want input for their decisions from their doctors and family. The authors suggest two alternative decision-making models, one considering the patient's best interests based on community standards, and the other using a narrative approach that takes into account a patient's life story and considers the patient's values, interests, and particular circumstances, focusing on his or her dignity and individuality rather than autonomy.

In "Surrogate Decision Making: Reconciling Ethical Theory and Clinical Practice" (*Annals of Internal Medicine*, July 2008), Jeffrey Berge, Evan DeRenzo, and Jack Schwartz discuss differences between current normative standards for decision making and empirical evidence that suggests that modifications are needed to reconcile ethical principles with clinical practice. Like the previous article, this article highlights the complexity of surrogate decision making, and calls for an approach that accounts for the nuanced and complex circumstances of most clinical situations that require careful ethical decisional analysis. It is refreshing to see this discussion occurring. As a clinician and educator, I notice a tendency in medical students and physician trainees to want to use a formulaic approach to making decisions in clinical situations that involve life-and-death treatments for very ill patients. The circumstances do not often lend themselves to such an approach, however. It is important to appreciate the complexities and dynamic nature of clinical practice, and it is good to read articles like these in the medical literature.

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