



MEDICINE

Reproductive Technologies

In the December 2008 issue of *Human Reproduction*, Belgian investigators sought to determine whether or not pre-implantation genetic screening (PGS) enhanced embryo selection in patients undergoing in vitro fertilization (IVF) who received a single blastocyst transfer (C. Staessen et al., “Preimplantation Genetic Screening Does Not Improve Delivery Rate in Women under the Age of 36 following Single-Embryo Transfer”). They designed a randomized and controlled study looking at delivery rates between couples with a female partner younger than thirty-six years assigned to undergo single blastocyst transfer with and without PGS. After 120 women were enrolled in each group, the study was terminated because an interim analysis showed no difference between the two groups and also because it indicated that, if continued, the study was unlikely to meet the prospectively defined objective. In effect, the study could not support an argument for PGS to improve live-birth delivery rates. Another study that also ended prematurely for the same reason—the unlikelihood that the study would achieve its primary objective of showing superiority of PGS—appeared in the same issue of *Human Reproduction* (T. Hardarson et al., “Preimplantation Genetic Screening in Women of Advanced Maternal Age Caused a Decrease in Clinical Pregnancy Rate: A Randomized Controlled Trial”). The authors concluded that PGS did not improve the clinical pregnancy rate in women with advanced age (thirty-eight years or more). In fact, the group subjected to PGS had a lower pregnancy rate. Additionally, the authors state at the end of their article that routine use of PGS for older women should not be recommended.

Two brief points concerning these articles: First, the clinically sterile and objectified way the nascent human being is treated is striking. Second, the science in this area remains fraught with problems, which is not surprising, given its contradiction of natural law.

In the February 2009 issue of *Human Reproduction*, two articles again illuminate serious problems associated with the unnatural manipulation of human

fertility and reproduction. In the first article, “Mifepristone-Induced Abortion and Placental Complications in Subsequent Pregnancy,” Qian-Xi Zhu and colleagues recruited two cohorts of nulliparous women (women who had never borne a child) early in their pregnancy and followed them until delivery. One cohort had a history of mifepristone-induced abortion, and the other cohort had no history of abortion. Nearly ten thousand women were enrolled in the study, but after dropout for various reasons, the final study included 4,673 women in the mifepristone-induced abortion group and 4,690 in the group of women who had never had an abortion. The groups were not significantly different with regard to socioeconomic factors. Overall the rates of placental complications were the same in the two groups; however, the risk for placental abruption was almost two times greater in the mifepristone group than in the group with no history of abortion, although the difference was not statistically significant. Further subgroup analysis revealed that abortions done later than six weeks’ gestation, curettage following mifepristone-induced abortion, and a longer inter-pregnancy interval all increased risks for placental abruption.

The second report, titled “Assisted Reproductive Technology and Major Structural Birth Defects in the United States,” by Jennita Reefhuis and colleagues, analyzed data from the National Birth Defects Prevention Study to determine whether there was an association between artificial reproductive technology (ART) and major structural birth defects. The use of ART continues to increase, and the number of infants born since ART was introduced, has doubled in the United States from 1996 to 2004. This study involved 9,584 case mothers and 4,792 control mothers. ART was reported in 1.1 percent of all control mothers, and in 4.5 percent of control mothers aged thirty-five years or older. Among singleton births, after adjustments for variables including maternal age and prematurity, ART was found to be significantly associated with septal heart defects, cleft lip, cleft palate, esophageal atresia, anorectal atresia, and hypospadias. These data seem to further expose clinical realities about ART that remind me of how it departs from authentic love between a man and a woman in marriage and detracts from self-giving.

In the January 15, 2009, issue of the *New England Journal of Medicine*, Beth Malizia, Michele Hacker, and Alan Penzias discuss their experience with 6,164 patients undergoing 14,248 IVF cycles, reporting live-birth rates of 86 percent after six cycles in women younger than thirty-five years, and 42 percent in women aged forty years and older (“Cumulative Live-Birth Rates after In Vitro Fertilization”). The study concludes that IVF does not reverse the age-dependent decline in fertility. I advise caution about medicalizing certain realities in human biology, such as treating age-dependent infertility as a disease. Why should we think that such interventions as IVF, which is essentially not treatment (i.e., not targeting a disease), should be effective?

Physician-Assisted Suicide

It is interesting to notice a subtle but significant shift in how this topic is presented in the literature. Two recent articles use the phrase “physician-assisted death” in their titles, not “physician-assisted suicide.” Could the use of “suicide” instead of “death” be significant? Is there a subtle undercurrent moving the medical community in the direction of death? After all, the word “death” has very different connotations than the word “suicide.” Using the search term “physician-assisted death” yields only

one-tenth the number of articles produced by a search on “physician-assisted suicide.” I suspect this ratio will increase in the near future, and that will be unfortunate.¹

In the first article, Constantine A. Manthous discusses the basis for the generally inherent aversion that most have toward the idea of physician-assisted suicide, euthanasia, and practices aimed at shortening the dying process (“Why Not Physician-Assisted Death?” *Critical Care Medicine*, January 16, 2009). He broadly explores religious prohibitions to these practices, briefly discusses western medical prohibitions rooted primarily in ancient Greek philosophy and articulated in the Hippocratic oath, and offers thoughts regarding legal prohibitions, particularly as they concern the U.S. Constitution, state laws, and court decisions. Last, he discusses moral neurocognition, a concept that basically deals with the human brain being hard-wired in a way that creates a moral intuition, foundationally based on a biologic drive for self-preservation. He suggests, however, that our aversion to these practices may not be entirely rational, and because certain terms such as “physician-assisted suicide” and “euthanasia” may trigger “neurologic phenomenon that correlate to moral tenets,” that the discussion might be better advanced by the terminology such as “physician-assisted death for irreversible suffering.”

In the December 11, 2008, issue of the *New England Journal of Medicine*, Robert Steinbrook wrote a perspective article on physician-assisted death focusing on Washington state’s initiative to legalize physician-assisted suicide (“Physician-Assisted Death: From Oregon to Washington State”). Although Oregon’s history with PAS has been relatively limited—for example only forty-five physicians wrote eighty-five prescriptions for lethal doses of medications for this purpose in 2007—Steinbrook notes that if the Washington experience is similar to that of Oregon, more prescriptions and more deaths are likely to occur in Washington, since it has almost twice Oregon’s population. Steinbrook’s attention to terminology is also noteworthy. He recognizes that a term like “physician-assisted suicide” is emotionally charged, and that some proponents prefer the terms “physician aid in dying” and “physician-assisted death.” On March 5, 2009, the physician-assisted suicide law in the state of Washington went into effect.

Just when you might think it cannot get any worse, consider a letter to the editor in the September 2008 issue of *Transplant International* from Oliver Detry et al., titled “Organ Donation after Physician-Assisted Death.” The authors report the case of a forty-four-year-old woman with locked-in syndrome—she was fully conscious and communicated by using eyelid movements—who after four years of being in this state requested physician-assisted suicide in accord with Belgian law. The day before euthanasia, she expressed her desire to donate her organs after death. The report goes on to say that intravenous euthanasia was performed in the presence of the patient’s husband in a room adjacent to an operating room. When the patient’s death was confirmed after ten minutes of absent cardiac activity, she was moved to the operating room, where her liver and both kidneys were harvested

¹Based upon a PubMed search performed March 17, 2009, where using “physician assisted suicide” yielded 1,139 articles (since 1988) and “physician assisted death,” 113 articles (since 1992), www.pubmed.gov.

and transplanted. Disturbing as this report is, what I found more chilling was the authors' observation that the possibility of harvesting organs after euthanasia may increase the number of transplantable organs.

Resource Allocation

The article "Who Should Receive Life Support during a Public Health Emergency? Using Ethical Principles to Improve Allocation Decisions," by Doug White and colleagues, is interesting, well presented, and provocative (*Annals of Internal Medicine*, January 20, 2009). The authors discuss allocation of medical resources, using the specific example of patients with respiratory failure being provided with mechanical ventilation in the wake of a widespread influenza pandemic. They advance the debate by first offering a critique of existing public health guidelines, which attempt to address the issue but which the authors think fail to incorporate morally relevant factors. The authors then discuss principles that could be used to guide allocation decisions. They discuss but dismiss a principle based on the social value of a person; they similarly discuss but dismiss a principle that involves factoring in a so-called instrumental value of a person. This is related to a broad social-value concept but relates specifically to the person's function and what they can do for society. Next they discuss a principle based on "maximizing life-years," which takes into account not only the number of lives saved but also the years saved of individual lives. Last, a principle called "life cycle" attempts to balance or promote equal opportunity for people to live through various life phases. This is also sometimes referred to as the fair-innings principle and tends to favor younger over older individuals. The authors propose an allocation strategy that incorporates multiple principles, and couple it with a severity-of-illness scoring system, specifically a Sequential Organ Failure Assessment (SOFA) score. With this proposed system, they argue that the same allocation criteria are applied to everyone, and that the system is more sensitive to the moral complexity of allocating limited resources in the event of public health emergency.

In the January 31, 2009, issue of the *Lancet*, bioethicists from the National Institutes of Health also discuss the issue of scarce medical resource allocation (G. Persad, A. Wertheimer, and E. J. Emanuel, "Principles for Allocation of Scarce Medical Interventions"). These authors also consider the advantages and disadvantages of various principles, recognize the limitations of a single-principle model, and posit a multi-principle model that generally favors younger persons up to a certain point.² Limitations certainly exist with any of the systems, even if they are multi-principled and morally sensitive. This literature is valuable in bringing to light important considerations in resource allocation.

Another facet of justice in health care resource allocation is the subject of the article "Separate and Unequal," published in the February 9, 2009, issue of the *Archives of Internal Medicine*. In this article Anita B. Varkey and colleagues compare

²An exception is that adolescents are prioritized over infants, since an investment has already been made in the adolescent (e.g., education), whereas infants have not yet received any investment. This complete-lives system also considers prognosis.

primary care clinics serving minority patients in New York and the upper Midwest, in order to determine differences among the practice settings. The article reports data from 388 physicians and 1,701 patients in ninety-six clinics where the proportion of minority patients ranged from 30 to 95 percent. The study confirmed a hypothesis that clinics serving a larger proportion of minority patients face greater challenges accessing medical resources such as supplies, pharmacy service, and specialty care and had limited work space (e.g., fewer examination rooms per physician). They also noted that in these clinics patients were more medically and psychosocially complex and that physicians reported less work control and lower job satisfaction. Reducing disparities in access to health care and outcomes across racial and ethnic categories must remain a priority as we seek social justice.

End of Life

Two recent articles touch on different aspects of end-of-life care. The first is titled “Who Will Speak for Me? Improving End-of-Life Decision-Making for Adolescents with HIV and Their Families” (*Pediatrics*, February 2, 2009). In this article, Maureen Lyon and colleagues evaluate the effectiveness of an intervention aimed at increasing congruence and quality of communication between adolescents with HIV/AIDS and their families or surrogates. The authors randomized forty families into two groups; in one, families participated in family- and adolescent-centered advance care planning interviews over three sessions. In this group, compared to the control families, there was increased congruence between adolescents and their families/surrogates for end-of-life care preferences, fewer decisional conflicts, and better communication.

The second article, “Organ Donation, Patients’ Rights, and Medical Responsibilities at the End of Life,” discusses the 2006 revision of the Uniform Anatomical Gift Act, which attempts to increase the availability of transplantable organs by granting new authority to organ procurement organizations (A. Iltis, M. Rie, A. Wall, *Critical Care Medicine*, January 2009). To evaluate the 2007 amendment of the UAGA, the authors reviewed case law and medical ethics literature regarding consent, end-of-life care, laws and regulations concerning advance directives and medical licensure, and literature on the fiduciary obligations of physicians. Overall, while the UAGA may represent an important goal of public policy, by granting authority over the patient and surrogate to organ procurement organizations concerning matters of end-of-life care, it is at odds with U.S. common law and the ethical standards governing medical practice. The authors call for further revisions to the UAGA to resolve the tension between increasing the availability of organs for transplantation and ensuring ethically sound, truly informed consent, respect for dying patients, and the professional integrity of physicians caring for them. To do otherwise risks making patients an object for use by others.

Clinical Research

The January 2009 supplement of *Critical Care Medicine* was dedicated thematically to improving clinical research in critical care and contained an article concerning the ethics of informed consent in emergency critical care research—research which often, by definition, involves little to no time for the consent process to occur (T. Jansen, E. Kompanje, and J. Bakker, “Deferred Proxy Consent in Emergency

Critical Care Research: Ethically Valid and Practically Feasible”). In this article, Tim Jansen and colleagues mention that consent to participate in research can be obtained by a proxy decision maker, can be deferred to a later time, or can be waived. They argue that deferred proxy consent is the preferred approach when informed patient consent cannot be gained. In making this claim, they discuss two dilemmas: First, is a proxy truly able to give informed consent when the patient for whom he or she is responsible is in the midst of a sudden and unexpected emergency? Second, how should the deferred proxy-consent process be handled after the study procedures have finished but before the proxy can be contacted and consent obtained?

Regarding the first dilemma, the authors note that deferred proxy consent does not always secure patient protection, mostly because surrogate family members may be emotionally distraught, thus potentially limiting their capacity to make clear and informed decisions on behalf of the patient. Regarding the second dilemma, the authors raise the issue of using research data obtained from a patient after the study procedures have been completed but before consent can be obtained from the proxy. The primary example is a case in which the patient has died before consent could be obtained. Should the researchers use the data or not? The authors argue for use of the data in these situations and provide a number of reasons for doing so. They state, for example, that family surrogates usually give consent in these situations, that use of the data does not harm the patient, and that non-use of the data jeopardizes the study (by selection bias or devaluation of the contributions of the other patients in the study, for example) and may harm future patients and society in general. While all of these arguments are reasonable, they are untenable because they objectify the patient. And in doing so they nudge the medical community, and society in general, in a direction away from respect for the individual as a subject and toward use of the individual as an instrument in medical research.

JOHN M. TRAVALINE, M.D., F.A.C.P.
Temple University School of Medicine
Philadelphia, Pennsylvania