

# Virtual Mentor

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## Journal Discussion

### Should Women with Transplanted Organs Be Discouraged from Becoming Pregnant?

Kamalkumar P. Kolappa and David A. Gerber, MD

**Ross LF. Ethical considerations related to pregnancy in transplant patients. *N Engl J Med.* 2006;354(12):1313-1316.**

A woman's pregnancy can be one of the most emotion-laden experiences in her life. Though society's views on the necessity of having children have evolved continuously, there is little question about the impact that a woman's choice to bear children has on her and on her family. The choice to become pregnant gets tested, though, when the woman is an organ transplant recipient because pregnancy may endanger the graft, the mother, and the child. Whether or not women who are transplant recipients should be discouraged from becoming pregnant is a discussion that is a complex kaleidoscope of science, law, and ethics. Even though a consensus on the consequences of pregnancy in transplant patients has yet to be reached, more and more women with transplanted organs are becoming mothers, and greater attention should be given to the issue.

In "Ethical Considerations Related to Pregnancy in Transplant Recipients," Lainie Friedman Ross asserts that women who have received transplants are having children in significant numbers [1]. She notes that since the first documented pregnancy in a transplant recipient in 1958, more than 7,000 such pregnancies have occurred. That transplant recipients are becoming pregnant with greater frequency has been corroborated by other authors who cite increasing rates in patients with liver, heart, lung, bone marrow, and pancreas-kidney transplants [2, 3].

### Clinical Considerations

Ross begins by eloquently framing her ethical discussion with a review of the clinical implications of organ transplantation on pregnancy by examining, in turn, its effect on the allograft, the mother, and the fetus.

Regarding the first of these—effects of pregnancy on the allograft—Ross says that, in renal transplant patients, one of the concerns has been that "...the increased glomerular filtration rate caused by pregnancy might lead to hyperfiltration and consequent glomerulosclerosis" [4]. She then states that, while there is evidence of decreased renal function during pregnancy, this impairment mirrors the natural course of organ dysfunction in all kidney recipients, which would seem to rule out pregnancy as an independent contributor to allograft morbidity. She strengthens this

assertion by citing expert opinion on stability of solid organ transplants during pregnancy: "...consensus is that pregnancy does not compromise the function of a renal or liver allograft when the allograft is stable before pregnancy" [5]. Finally Ross highlights current recommendations based on data from the National Transplantation Pregnancy Registry that organ recipients wait two years after transplantation before considering pregnancy, allowing sufficient time for graft stability, after which pregnancy should be feasible with lower risks of permanent decrease in function of the allograft [6].

Next Ross considers the impact of pregnancy on maternal health outcomes. She notes that having transplanted organs has been correlated with an increased risk for conditions such as ectopic pregnancy, preeclampsia, and infection. There also seems to be a greater need for cesarean delivery, particularly in renal transplant patients [5]. The magnitude of this increased risk is unclear, however, as Ross does not further elaborate on this point.

Ross invests more detail in describing risks to the child, discussing the potential teratogenic effects of transplant immunosuppressive therapy that have been demonstrated in animal models. She acknowledges that some immunosuppressive drugs like muromonab-CD3 (Orthoclone OKT3) and antithymocyte globulin do not have animal research data on fetal effects and that there is, in general, a paucity of data regarding long-term medical complications of immunosuppressive therapy. She summarizes her view about the lack of compelling evidence on the risks of these drugs by saying that, "To date, the frequency of birth defects in infants born to women receiving immunosuppressive agents is not statistically different from that in the general population" [5]. Ross does concede that rates of prematurity and low birth weight are higher in infants born of mothers with transplants. This in itself is cause for concern because both prematurity and low birth weight have been decisively linked to increased risk of cognitive and neurodevelopmental abnormalities.

### **Ethical and Legal Considerations**

The discussion of pregnancy in transplant recipients would be incomplete if only the science were considered. Pregnancy and the creation of life spark diverse reactions throughout society, and Ross concisely reviews the major ethical and legal considerations of pregnancy in transplant recipients.

She begins with the physician's duty to review fertility options and their consequences with women who have transplanted organs. Ross initiates the ethics portion of the discussion by stating that, "A major issue is how and when physicians should address fertility issues with female transplant recipients of childbearing age" [5]. Given that as many as half of all pregnancies are unintended [7] is it safe for physicians to wait until a woman expresses an interest in becoming pregnant before initiating a conversation about the implications of organ transplantation on pregnancy? A related point made by Ross is that, even though some doctors discourage women from becoming pregnant when they have shorter-than-average

life expectancies, "...a child is not ethically wronged by being born to a woman who is a transplant recipient, because there is no guarantee that any parent will be healthy and be able to rear her child until adulthood" [8].

Ross also offers insight concerning the ethics of a second transplant should the first graft fail after pregnancy. Since, in most cases, retransplantation is riskier for the patient, and the second organ is less stable than the primary transplant, should a woman whose first graft may have been compromised by the burden of pregnancy have the chance for a second graft, when some patients on the waiting list have yet to receive a first? Ross compares this situation to that of patients who continue to abuse alcohol while waiting for a liver. Though intuitively it seems inappropriate to equate pregnancy with alcoholism, the underlying tie is the choice of voluntary behaviors that predispose one to an increased risk of graft failure. In the end, Ross rejects this argument because "...it is not understood why some organs fail during pregnancy," and therefore one can incorrectly blame organ failure on pregnancy rather than on another etiology. Ross cites Robert Veatch's argument that organs be allocated so that priority is given to younger patients with more quality-adjusted life years (QALYs) regardless of prior transplantation status rather than older patients awaiting first transplant [9]. Based on this model of allocation, Ross feels that women who lose an organ during pregnancy should be eligible for a second transplant.

Perhaps the most controversial aspect of this discussion is raised when Ross asks, "When a transplant recipient becomes pregnant, who is actually the patient?" [8]. This question fuels debate about many ethical-legal concepts including a competent woman's decision-making rights over her own body and the politics of the maternal-fetal conflict of interest. Should a woman have complete control over the health of her unborn child in addition to the rights over her own body? Is it appropriate for society to intervene if certain behaviors of the mother place the fetus in jeopardy? Though the same questions apply in every case of pregnancy, they take on added significance when known risks are greater than those for pregnancies in which the mother does not have a transplanted organ.

### **Approaching the Ethics of Maternal-Fetal Conflict in Transplant Recipients: Lessons from a Parallel Case**

Though maternal-fetal conflict is often thought of as a matter of maternal choices, including behaviors that can impact fetal health during pregnancy, it can also apply to the decision to become pregnant in situations where parents have genetic or infectious conditions that may be passed to the child.

An insightful and parallel discussion regarding the ethics of a pregnancy in which maternal circumstances can impact fetal health can be found in Howard Minkoff and Nanette Santoro's "Ethical Considerations in the Treatment of Infertility in Women with Human Immunodeficiency Virus Infection" [10]. The authors consider infertility treatment in HIV couples in light of the historically controversial outcomes of vertical transmission of HIV from mother to child and the likelihood that a mother will die before her child reaches majority. The clinical course of HIV has changed

drastically with the advent of modern antiretrovirals. When HIV was initially identified, approximately 25 percent of mothers transmitted HIV to their children, and the prospect for infected children was grim. Minkoff and Santoro believe that a new perspective on assisting these women with pregnancy is warranted by the change of disease status. The authors conclude that the decision to treat infertility in women with HIV depends on principles of autonomy, beneficence, and social justice but that autonomy is the deciding factor because,

...decisions involving infertility are not different from other reproductive choices women make. If, as the courts have recognized, women can be entrusted to strike the sometimes complex balance between their own health interests and those of their fetuses, there is no reason to assume that they are not equally capable of understanding the consequences of childbearing and child rearing in the context of HIV infection [11].

### **Conclusion**

Similarly, Ross concludes with regard to this conflict of interest that, "...physicians should respect the decision that each recipient makes about the risk and benefits [of pregnancy]" [12]. But the potential for conflicting interests continues to inspire varied reactions from expecting mothers and physicians to lawyers and the rest of society. Given the theoretical risks to children from immunosuppressive drugs, the higher rates of prematurity, and the low birth weight in infants, to what extent should women be discouraged from becoming pregnant after having received a transplant? Though there is no compelling evidence that immunosuppressives can be blamed for malformations in developing children, the long-term implications of many of these agents are not clearly defined at this time [13]. Are transplant recipients exposing their potential children to undue risk? Should physicians be satisfied with the National Transplantation Pregnancy Registry's recommendation that women wait at least two years for graft stability before recommending pregnancy, or should they encourage alternative means of having children such as adoption? How aggressive should physicians be with contraception education in this patient population considering the high prevalence of unintended pregnancies in the general population?

Though the legality of transplant recipients becoming pregnant and having children is not yet in dispute, the unanswered societal question weighs the wishes of transplant recipients to have children against the health implications for the child that results from the pregnancy.

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Kamalkumar P. Kolappa is a fourth-year medical student at the University of North Carolina at Chapel Hill. His intended postgraduate training will be in plastic and reconstructive surgery. His clinical and research interests include pediatric craniofacial reconstruction as well as human rights and the ethics of global medicine.

David A. Gerber, MD, is an associate professor of surgery at the University of North Carolina School of Medicine in Chapel Hill. He is director of the liver transplant program at the UNC Hospitals and a member of the scientific studies committee of the American Society of Transplant Surgeons.

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