

## VIEWPOINT

# Reducing the Underimmunization of Transplant Recipients

**Amy G. Feldman, MD, MSCS**

Adult and Child Consortium for Health Outcomes Research and Delivery Science, Aurora, Colorado; and Section of Gastroenterology, Hepatology and Nutrition, Children's Hospital Colorado, Aurora.

**Chris Feudtner, MD, PhD, MPH**

Department of Medical Ethics, The Children's Hospital of Philadelphia, Pennsylvania; and Department of Pediatrics, Medical Ethics and Health Policy, Perelman School of Medicine, Philadelphia, Pennsylvania.

**Allison Kempe, MD, MPH**

Adult and Child Consortium for Health Outcomes Research and Delivery Science, Aurora, Colorado; and Department of Pediatrics, University of Colorado, Aurora.

**Corresponding**

**Author:** Amy G. Feldman, MD, MSCS, Adult and Child Consortium for Outcomes Research and Delivery Science, University of Colorado School of Medicine, Anschutz Medical Campus & Children's Hospital Colorado, 13199 E Montview Ave, Suite 300, Aurora, CO 80045 ([amy.feldman@childrenscolorado.org](mailto:amy.feldman@childrenscolorado.org)).

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**Vaccine-preventable infections (VPIs)** are a common and serious complication after pediatric liver transplantation; in the first 2 years after transplant, 1 of 6 transplant recipients requires hospitalization for VPI, which is associated with graft injury, morbidity, and sometimes mortality.<sup>1</sup> These hospitalizations can increase the cost of the transplant-associated hospitalization by \$70 000.<sup>1</sup>

Although the increased risk for infection owing to immunosuppression after transplant is partially to blame, a primary factor responsible for this statistic is that transplant candidates receive significantly fewer immunizations than do healthy children. Although children with organ failure receive constant medical surveillance, many are not fully vaccinated at the time of transplant despite the known importance of pretransplant vaccination (before a child becomes immunosuppressed and has attenuated antibody responses) and recommendations of the Infectious Diseases Society of America that "all solid organ transplant candidates receive age-appropriate vaccines based on the CDC [Centers for Disease Control and Prevention] schedule."<sup>2,p37</sup> Compared with the 90% reported immunization rate among children entering kindergarten in the United States,<sup>3</sup> the majority of pediatric transplant recipients are not up to date on immunizations at the time of transplant (even when excluding those receiving transplants for acute organ failure).<sup>4</sup>

Because of the adverse outcomes that VPIs have on pediatric transplant recipients and the US investment of \$200 million dollars every year in pediatric liver transplants, we should do better. The situation is more urgent because of the increase nationally over the past 20 years of nonmedical exemptions for school immunizations.<sup>5</sup> The resurgence of VPIs is of concern to many individuals but especially to transplant recipients.

To address this situation, we must pursue a 2-pronged approach involving policy and enhanced practice methods, taking both a stronger stance on requiring immunizations for pediatric transplant candidates and on improving coordination and tracking of vaccine administration to these patients.

US policy should require complete immunization for nonemergent transplants. Currently, individual transplant centers are left to construct their own immunization policies. Transplant organizations, such as the United Network for Organ Sharing, should develop policies that require complete, appropriate-for-age immunization status at the time of a nonemergent transplant. Promoting a vaccine mandate for the pediatric transplant population would advance several important clinical and ethical goals.

First, complete immunization would ensure the child's best interest by minimizing harms. All transplant

recipients are administered immunosuppressive medications to prevent graft rejection and thus are susceptible to infection. Parental refusal to immunize a child leaves that immunocompromised child unprotected against various undesired outcomes. VPIs have been associated with allograft rejection, encephalitis, meningitis, pneumonitis, and death after transplant.<sup>1,6</sup> When a parent's choice is contrary to the best interests of the child and places the child at risk of significant harm,<sup>7</sup> the state has the authority to intervene to protect the child and has done so to allow children to receive life-saving therapies, such as blood transfusions or chemotherapy. Vaccines are potentially lifesaving for an immunocompromised transplant recipient and should be treated as such.

Second, complete immunization of one pediatric transplant recipient protects other pediatric transplant recipients through herd immunity, whereby vaccination of a significant portion of the population provides some protection for individuals who have not or cannot develop immunity. Herd immunity is particularly important in the transplant population because certain transplant candidates and recipients cannot receive vaccines (for example, live vaccines are not administered before transplant when transplant is anticipated to occur in <30 days and are not administered after transplant unless the child is receiving low levels of immunosuppressive treatment). Therefore, underimmunization of a transplant recipient poses a danger to that recipient, immunocompromised members of the transplant community, and other iatrogenically or natively immunocompromised individuals. Of note, even when a transplant candidate does not mount a protective antibody response to pretransplant immunizations, they are more likely than previously unimmunized children to mount a good response to posttransplant immunizations.<sup>8</sup>

Third, requiring complete immunization promotes a more just allocation of a scarce resource. Despite advances in technology and efforts to increase organ donation awareness, there continues to be a large difference between organ supply and demand. Every day, 22 individuals die while awaiting an organ transplant. If a child develops a VPI, that infection has the potential to result in graft failure or death. Loss of the organ harms not only that child but also everyone who died on the waiting list because no organ was available.

Policies to promote complete immunization must be paired with a better practice system to coordinate the immunization of these at-risk children. In the pretransplant period, subspecialists must partner with infectious diseases physicians and primary care

providers (PCPs) to review immunization records, create individualized vaccine timetables using the CDC's accelerated schedule,<sup>9</sup> and ensure that needed vaccines continue to be administered as a child awaits transplant. This will require a handful of initiatives.

First, we will need to provide additional education for PCPs and parents about immunization practices unique to the transplant population, for example, use of the CDC's minimal age and minimal interval schedule.<sup>9</sup> These efforts would be part of a broader strategy to improve communication among families, PCPs, and subspecialists. We must realize that immunizations are a crucial part of pretransplant care.

Second, as mentioned above, we need novel interventions to help track immunizations in a centralized and easily accessible fashion. Currently, immunization records may exist in various locations, including parent vaccine cards, pharmacy records, office data sets, or state registries. Thus, it is difficult for transplant programs to collect and review immunizations as part of the transplant evaluation process. This system could be improved through the use of existing state or regional immunization information systems or registries, which are currently available in almost all states, if subspecialists were given access. A centralized vaccine registry would allow transplant programs to easily collect, review, and update a child's immunization records before transplant.

Third, we need technology-driven calendar alerts to remind all physicians who may see a patient that immunizations are due. Transplant candidates often receive the majority of their care from subspecialists who may not perform immunizations as part of their usual practice. Every visit with a physician is, however, an opportunity to ensure that immunizations are administered before transplant. Specialists could be given access to a state immunization information system as part of existing forecasting functions, or the system could be created de novo within a medical record system.

Finally, we need further research to understand the best methods to assess and monitor immunity after vaccination in children who may have immunodeficiency. Markers of cell-mediated immunity may be better predictors of immunity than standard antibody titers in children who have immunodeficiency with decreased humoral response. Future prospective studies are needed to follow up transplant recipients over time and correlate vaccine status and markers of immunity with disease protection. This would help inform decisions about re-immunization after transplant.

The time has come to move beyond a fragmented system that underimmunizes pediatric transplant candidates to their detriment. Through the combined approach proposed here, joining strengthened policies with improved practices, some of the most medically fragile children will have the best opportunity to fully benefit from organ transplantation.

#### ARTICLE INFORMATION

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