# Barriers to Pretransplant Immunization: A Qualitative Interview Study of Pediatric Solid Organ Transplant Stakeholders

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**Objectives** To describe the experiences and beliefs of pediatric transplant stakeholders regarding factors that contribute to low pretransplant immunization rates.

**Study design** Semistructured interviews were conducted with transplant team members (hepatologists, cardiologists, nephrologists, transplant nurse coordinators, and transplant infectious diseases physicians), primary care physicians, and parents of heart, liver, and kidney transplant recipients at 3 geographically diverse large pediatric transplant centers in the US. Interviews were conducted between July 2017 and February 2020 until thematic saturation was reached within each stakeholder subgroup. Content analysis methodology was used to identify themes.

**Results** Stakeholders participated in 30- to 60-minute interviews (16 transplant subspecialists, 3 transplant infectious diseases physicians, 11 transplant nurse coordinators, 12 primary care physicians, and 40 parents). Five central themes emerged: (1) gaps in knowledge about timing and safety of pretransplant immunizations, (2) lack of communication, coordination, and follow-up between team members regarding immunizations, (3) lack of centralized immunization records, (4) subspecialty clinic functioning as the medical home for transplant candidates but unable to provide all needed immunizations, and (5) differences between organ type in prioritization and completion of pretransplant immunization.

**Conclusions** There are multiple factors that contribute to low immunization rates among pediatric transplant candidates. New tools are needed to overcome these barriers and increase immunization rates in transplant candidates. *(J Pediatr 2020;227:60-8)*.

Vaccine-preventable infections are a common occurrence after pediatric solid organ transplantation. Hospitalizations for vaccine-preventable infections occur in >15% of pediatric solid organ transplant recipients in the first 5 years after transplant at a rate of up to 87 times higher than in the general pediatric population.[1,2] Vaccine-preventable infections result in significant morbidity and mortality for transplant recipients.[1,2] Transplant hospitalizations complicated by vaccine-preventable infections are on average 39 days longer, have higher rejection rates, and are almost $120 000 more expensive than transplant hospitalizations not complicated by vaccine-preventable infections.[1,2]

Despite recommendations and guidelines published by the Infectious Diseases Society of America and the American Society of Transplantation that pediatric solid organ transplant candidates receive "all age-appropriate vaccines based on the Centers for Disease Control's annual schedule for immunocompetent persons," <30% of pediatric liver transplant recipients are up to date on age-appropriate immunizations at the time of transplantation.[3-5] Immunization rates for influenza, polio, measles, *Haemophilus influenzae* B, hepatitis B, varicella, and pneumococcus are all significantly less in pediatric solid organ recipients than in the overall pediatric population.[5] There have been no studies to understand why this high-risk population is so underimmunized. This study aimed to identify factors that contribute to underimmunization of transplant candidates from the perspectives of key stakeholders involved in pediatric transplantation including parents, primary care physicians (PCPs), transplant subspecialists, transplant infectious diseases (ID) physicians, and transplant nurse coordinators.

## Methods

We used the Standards for Reporting Qualitative Research when writing our article to ensure transparency and rigorous reporting of our findings.[6]

| | |
|---|---|
| ID | Infectious diseases |
| IIS | Immunization information system |
| PCP | Primary care physician |

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### Sampling and Recruitment

All English-speaking transplant hepatologists, cardiologists, nephrologists, ID physicians, nurse coordinators, PCPs, and parents of children who received liver, heart, and kidney transplants between January 1, 2011, and August 30, 2019, at the Children's Hospital Colorado, Ann & Robert H. Lurie Children's Hospital of Chicago (Lurie Children's Hospital) and Children's Hospital of Philadelphia were invited to participate in this qualitative study. Health care providers were invited to participate via an email invitation. Parents of transplant recipients were approached in clinic or via a written invitation. Participants received a reimbursement of $10 for the time involved in the interview. Institutional review board approval was obtained from the University of Colorado (all research took place through the University of Colorado; Children's Hospital of Philadelphia and Lurie Children's Hospital only assisted with patient recruitment) and verbal informed consent was obtained by the interviewer at the start of each interview.

### Data Collection

We developed 2 interview guides (**Appendix**; available at www.jpeds.com), one for parents of transplant recipients and one for health care providers based on relevant literature, expert opinion by members of our team, and domains from the Theoretical Domains Framework (eg, knowledge, roles/identity, beliefs, goals, environmental stressors).[3,7-11] Topic areas queried during each interview included (1) knowledge about appropriate timing and use of immunizations for transplant candidates (including the accelerated immunization schedule), (2) beliefs about the safety and importance of immunizations before transplantation, (3) beliefs about roles and responsibilities for immunizations, and (4) perceptions and opinions regarding team communication about immunizations. Semistructured interviews included some preset topics, but also allowed for flexibility in the flow of conversation through the use of probes to ask follow-up open-ended questions regarding barriers to immunization to allow respondents to tell their story in an in-depth meaningful way.[12]

A masters-trained qualitative interviewer conducted telephone (for nonlocal participants) and face-to-face (for local Colorado participants) semistructured interviews in offices or conference venues. Interviews took place from July 2017 through February 2020 and continued until preliminary analyses indicated data saturation was reached within each stakeholder subgroup (ie, when no new data were being obtained through consecutive interviews). Interviews lasted between 30 and 60 minutes and were digitally recorded and professionally transcribed verbatim using Landmark (thelai.com). The interviewer took detailed notes throughout the interview and at the end of each interview completed a field note to describe the context of the interview, emerging themes that arose, areas for clarification, and other comments. Notes, summary sheets, and transcripts were integrated into the analysis.

### Analysis

Using the principles of content analysis methodology, qualitative analysis began with 2 authors independently repeatedly reading the transcribed interviews to achieve immersion.[13,14] Next the team collaboratively inductively created the codebook through an open coding process.[13,15,16] Immersion in the data allowed for prioritizing participants' perspectives and de-emphasize researchers' ideas and beliefs. This process continued until a final set of codes was agreed upon; the final codes were then applied to the remaining transcripts. The code book is available upon request. Coded transcripts were entered into ATLAS.ti version 8 (ATLAS.ti Scientific Software Development GmbH, Berlin, Germany), a software analysis package used for storing, coding, and searching qualitative data. Coded data were analyzed within and across participant types and study site to identify themes or concepts that the participants discussed. The codebook, coded transcripts, and preliminary findings were discussed repeatedly among the entire multidisciplinary research team throughout the analysis process to establish trustworthiness and confirmability that the findings were consistent with the participants' narratives. Questions and their corresponding responses that were more discrete in nature (eg, parent report of patient being up to date for immunizations), were summarized within and across participant type using descriptive statistics.

## Results

### Participants

We interviewed a total of 82 pediatric transplant stakeholders (**Table I**); 16 transplant subspecialty physicians (hepatologists, cardiologists, nephrologists), 3 transplant ID physicians, 11 transplant nurse practitioners, 12 PCPs, and 40 parents of

**Table I. Participant demographic characteristics (n = 82)**

| Characteristics | No. | % |
|---|---|---|
| Stakeholder type | | |
| Transplant subspecialist (hepatologist, cardiologist, nephrologist) | 16 (10 L, 3 H, 3K) | 20 |
| Transplant ID physician | 3 | 4 |
| Transplant nurse coordinator | 11 | 13 |
| Primary care provider | 12 | 15 |
| Parent or guardian | 40 | 49 |
| Transplant center | | |
| Children's Hospital Colorado | 35 | 43 |
| Children's Hospital of Philadelphia | 27 | 33 |
| Ann and Robert H. Lurie Children's Hospital of Chicago | 20 | 24 |
| Sex | | |
| Female | 68 | 83 |
| Male | 14 | 17 |
| Years in practice (n = 42, excluded parents) | | |
| 0-5 | 10 | 24 |
| 6-10 | 6 | 14 |
| 11-20 | 10 | 24 |
| >20 | 16 | 38 |
| Interview venue | | |
| Hospital (office or conference meeting room) | 18 | 22 |
| Telephone | 64 | 78 |

*H*, heart; *K*, kidney; *L*, liver.

transplant recipients. The average duration of each interview was 35 minutes and the majority (n = 64 [78%]) were conducted over the phone. Of the 40 parents, 52% had a child who received a liver transplant, 25% a heart transplant, and 23% a kidney transplant; 35% were transplanted at Children's Hospital Colorado, 35% at Children's Hospital of Philadelphia, and 30% at Lurie Children's Hospital. The median length of time from their child's transplant to the time of interview was 3 years and the mean time was 2.9 years (range, 3 months to 7 years). Of the 40 parents interviewed, 95% believed that their child was up to date on age-appropriate immunizations at the time of transplantation. The majority of parents (68%) recalled receiving information about pretransplant immunizations solely from the transplant team. Immunizations were most often administered at the PCP's clinic. The majority of transplant providers (63%) stated that their knowledge about immunizations in the transplant population came from on-the-job training or mentoring from colleagues, 30% learned from published articles or guidelines, and 7% were educated at national meetings (Table II).

## Themes

Although participants each had unique transplant experiences, 4 common themes arose that were uniform across stakeholder type and across centers: (1) gaps in knowledge about timing and safety of pretransplant immunizations, (2) lack of communication, coordination, and follow-up between team members regarding immunizations, (3) lack of centralized immunization records, and (4) subspecialty clinic functioning as the transplant candidate's medical home but unable to provide all needed immunizations. In addition, we noted a fifth theme that there were differences regarding prioritization of vaccines between kidney, liver, and cardiac stakeholders. Illustrative quotations for each theme are provided in Table III.

**Table II. Interview responses**

| Questions | No. | % |
|---|---|---|
| From whom did you receive information about pretransplant immunizations? (n = 40 parents) | | |
| PCP | 5 | 12.5 |
| Transplant team | 27 | 67.5 |
| ID physician | 1 | 2.5 |
| Both PCP and transplant team | 5 | 12.5 |
| Both transplant team and ID physician | 2 | 5 |
| Do you believe your child was up to date on age-appropriate immunizations at the time of transplant? (n = 40 parents) | | |
| Yes | 38 | 95 |
| No | 1 | 2.5 |
| Unsure | 1 | 2.5 |
| Where did your child receive his/her vaccines while awaiting transplant? (n = 40 parents) | | |
| PCP's office | 30 | 75 |
| Liver/kidney/heart clinic | 2 | 5 |
| Inpatient hospital | 2 | 5 |
| Both PCP's office and liver/kidney/heart clinic | 2 | 5 |
| Both PCP's office and inpatient hospital | 3 | 7.5 |
| Unsure | 1 | 2.5 |
| Where did you learn about immunizations in the transplant population? (n = 30 ID physicians, transplant coordinators, hepatologists, nephrologists, cardiologists) | | |
| Meetings/conferences | 2 | 7 |
| Literature/published guidelines | 9 | 30 |
| Colleagues | 4 | 13 |
| On-the-job training | 15 | 50 |

### Gaps in Knowledge about the Timing and Safety of Pretransplant Immunizations

Across all sites, transplant ID physicians were the only stakeholder type who expressed definitive knowledge about the timing of the accelerated immunization schedule that is outlined by the Infectious Diseases Society of America in their Clinical Practice Guideline for Vaccination of the Immunocompromised host. PCPs, subspecialists, and nurse coordinators frequently stated that they either "had never heard of an accelerated schedule" or "had heard of the schedule but didn't know the specifics and would defer to ID or the pharmacists about the details on how to accelerate vaccines." A few participants stated that they believed that there were "no consensus guidelines on immunization of the transplant candidate." Parents denied specific knowledge about the details of vaccine scheduling and stated that they "relied on the medical team to make an accurate vaccine schedule."

There was also concern about the safety of live vaccines before transplantation raised by PCPs and transplant coordinators. Although PCP's considered immunizations to be in their "scope of care," many expressed concerns about the safety of immunizing a "sick" or "fragile" child. Parents stated that sometimes PCP's deferred vaccines because the child had a runny nose or a low-grade fever in clinic. PCP's also voiced apprehension that if they gave an incorrect immunization they could "mess up the transplant" or "impair future graft function." One coordinator also expressed safety concerns that "the potential risk that a child could develop disease from the vaccine outweighed the benefit of them getting vaccinated."

### Lack of Communication, Coordination, and Follow-up between Team Members Regarding Immunizations

Many stakeholders were concerned about how initial immunization plans were communicated between clinical team members. One ID physician stated, "while we're the ones making the recommendations, they [the PCPs] are the ones assuming the responsibility to give the immunizations. How my recommendations get transmitted to the PCP to implement, I'm not exactly sure." Another ID physician stated, "we make a game plan and then hope all the pieces fall into place. But follow-up is not owned by anyone. We don't have a standard system to close the loop." A PCP noted "we get inundated with piles of subspecialty letters and consult notes every day, often things get lost in the stack and I'm not sure appropriate follow-up always occurs." Parents commented that it was often difficult for them to communicate between their PCP and transplant team. For example, one mother stated, "my PCP and transplant center aren't on the same computer system." Another parent said, "I don't feel like the three of us were ever communicating together."

**Table III. Emergent themes and illustrative quotes for each theme**

**Theme 1: Gaps in knowledge about pretransplant immunizations**

Subtheme: Gaps in Knowledge About Timing

- "I don't know what the accelerated schedule is. To be honest we always defer to our pharmacists or infectious diseases doctors on how we can accelerate the schedule." (C)
- "I don't have the accelerated schedule committed to memory because I am not a pediatrician who does vaccines all the time." (H)
- "I would say there aren't expert recommendations on immunizations for transplant candidates." (H)
- "As transplant ID, our expertise is in understanding vaccines and when they can be given. We have expertise in coming up with a vaccine schedule especially when the child needs exceptions to the general schedule." (ID)
- "I don't know enough about immunizations. I stay in my lane and don't occupy my time with discussions about specific immunizations." (TC)
- "I don't think there are specific guidelines for immunizations pretransplant." (PCP)
- "I don't know if there is anything different about giving inactive vs live vaccines pretransplant." (PCP)
- "I rely on the doctor being accurate about the vaccine schedule because I have no idea about vaccines." (P)

Subtheme: Gaps in Knowledge about Safety

- "There's a lot of misconceptions about vaccinations pretransplant, in terms of efficacy and safety. It freaks people out whether vaccines will be safe and what could happen if you give something too close to transplant." (ID)
- "The safety concern I have is the potential risk that they could develop the disease if we give them a live vaccine." (TC)
- "If I have even the smallest uncertainty, I will not immunize a transplant candidate without approval from the subspecialist, I'm not going to mess the transplant up so I err on the side of caution and don't give them." (PCP)
- "The PCP said we are not going to stress his body out any more than it has already been stressed out. So, we fell behind on vaccines." (P)

**Theme 2: Lack of communication, coordination and follow-up between team members regarding immunizations**

- "I don't directly communicate with pediatricians about immunizations. We ask parents to communicate with their PCPs." (C)
- "I review immunizations records and then make recommendations about what additional vaccines the child needs. But then our expectation is that either the hepatology team will itself give the vaccinations or transmit our plan to the PCP." (ID)
- "We don't have a mechanism set up to follow up on all these patients to make sure that they've been compliant with what we recommended." (ID)
- "The ID team is very focused on the vaccine schedule and getting everybody immunized, but they don't realize the difficulty for the transplant team to ensure that vaccines are given." (TC)
- "There is no formal system to follow up with the family to see if recommendations were executed. We all have a different way of remembering to follow-up on these things. There's no structured way of doing it." (TC)
- "PCPs get clinic notes from various subspecialties. I'm sure they get piles every day. I don't know if appropriate follow up is always arranged. I think we all put a lot of responsibility on the parents to follow through with whatever recommendations are made." (TC)
- "We give recommendations and then we put the onus on the family to do it. When they come back to clinic we'll say did you get that done? But we don't usually require they send us an update vaccine record. So, we just take the family's word for it." (TC)
- "There are a lot of cooks in the kitchen; nobody has defined who will do what." (PCP)
- "They don't necessarily keep each other updated." (P)
- "If I didn't make the appointment for a follow up vaccine- I don't know that anyone would have called to say hey, you missed your shot. It was pretty much up to you as the parent to make sure that it all fell into place." (P)
- "The PCP may assume that something is happening and the liver doctor assumes the same thing is happening and then it doesn't get done. So, you (the parent) have to take responsibility to make sure it gets done." (P)

**Theme 3: Lack of centralized immunization records**

- "We collect records from the state registry, the electronic medical record and the family's records." (H)
- "The state registry is only as good as the people who fill it in." (H)
- "I think some of our families that have moved a lot and haven't kept great records of their immunizations- then it can be more difficult to track things down." (C)
- "In our state we have an immunization system, where any vaccines the child gets at their pediatrician should go into it, however, not all pediatricians participate in that network so the record isn't always complete." (ID)
- "If they see a PCP in our system we can look it up in EPIC. If they are from our state, we can see the statewide immunization record. But if they're in a different state, we have to call the PCP and the parents." (TC)
- "It's kind of shocking to me that there is not a universal registry for immunization which all providers can access." (TC)
- "We have to ask the parents to call us once the vaccines are administered because the immunization registry is often behind and not up to date." (TC)
- "We have patients from out of state but I cannot query any other state- so I'm always in the dark as to did the patients get any recent vaccines." (TC)
- "We don't have a streamlined process in place. We ask the parents if they're up-to-date on immunizations and then try to backtrack to get a copy of those immunization records so that we can review them ourselves." (TC)
- "Our state does not have a state registry so we have to deal straight with the family and the pediatrician to get records. It can be challenging if the family doesn't go regularly to the pediatrician or if they've had multiple pediatricians." (TC)
- "In my state we have a state registry but I have to send all my kids out of state for transplant and I'm not sure the team can access our state registry." (PCP)
- "It was hard because the ID doctor was working in the hospital, and the PCP was on their own different system and they had access to different records. It left a lot on the parent." (P)

**Theme 4: Subspecialty clinic functioning as the medical home but unable to provide needed immunizations**

- "Once they're sick enough they need subspecialty management and they're either being admitted to the hospital or seeing us in clinic once a month- they stop going to their pediatrician." (N)
- "We're making a recommendation but we can't actually carry through with it to give them the immunizations." (H)
- "To go back and forth from the hepatologist's office to your pediatrician is definitely a potential barrier." (H)
- "It would facilitate things if we were able to offer vaccines in transplant clinic." (H)
- "In a perfect world we would have a little side clinic, and after we're done seeing the patient we could check the box the vaccines they need pretransplant and they could get the shots. But currently that doesn't happen- we don't have the infrastructure, the staff to give the vaccines or the stock of those vaccines." (H)
- "The system isn't flexible enough for all the families. Some families have no problem getting all their vaccines through their pediatrician but some families clearly can't do it. We need to be able to offer vaccines wherever it works best for the individual patient." (ID)
- "We have very limited access to vaccination within our clinics so we really only have the feasibility to give our patients the annual flu vaccine and Prevnar." (TC)
- "It's burdensome on the family to come 3 days a week for dialysis and then have to make another appointment on top of that with their PCP." (TC)
- "Families gravitate towards their subspecialty home because they feel more comfortable there, but a lot of preventative stuff falls off which is problematic." (PCP)
- "When you see specialists, especially transplant specialists, they should take over because they know what is going on with the child." (P)

(*continued*)

**Table III. Continued**

| Theme 5: Organ-specific differences |
|---|
| Kidney: |
| "In kidney we have the benefit that patients can be on dialysis to give them time to get their vaccines before we list them." (N) |
| "On the kidney side they're on dialysis and we have easy access to them." (N) |
| "With kidney you always have dialysis, so that gives you more time." (TC) |
| "In kidney vaccines are a nonnegotiable part of the transplant process. I don't think we should transplant kids that aren't immunized unless it's a matter of life and death." (TC) |
| "I can tell you that they would not give your child a kidney if they weren't up to date on everything." (P) |
| Liver |
| "The rapidity of the immunization program depends on how sick the child is and how soon they need a liver transplant." (H) |
| Heart |
| "There are certain patients in the ICU who are very sensitive to every outside kind of stimulation, sometimes just getting a vaccine could potentially affect how they are doing. If they get a fever, they might end up needing to be monitored. So, we might decide there's not time to get vaccines." (C) |
| "Some of our patients get treatments pretransplant like IVIG that would make them ineligible for a vaccine or would make the vaccine not very helpful." (C) |
| "We don't have many options for keeping patients alive while they're waiting for a heart transplant, and we don't want to have to turn down an offer because a patient gets a fever." (TC) |
| "If we have patients listed at a lower status at home and doing well, we will absolutely recommend that they get the vaccines but if they are on mechanical support for critical condition, vaccines are not something that are at the top of the list." (TC) |
| "When these patients are in the intensive care unit, we're not really thinking about the vaccine status, we're just trying to keep their heart going into transplant." (TC) |

*C*, cardiologist; *H*, hepatologist; *IVIG*, intravenous immunoglobulin; *N*, nephrologist; *P*, parent; *TC*, transplant nurse coordinator.

All participants expressed difficulty with tracking when additional vaccines were next due. The initial first round of "catch-up" vaccines recommended during the transplant evaluation were often administered, but then both parents and providers reported having difficulty remembering when to administer the second and third rounds of vaccines. Providers acknowledged that they often rely on the parents to follow-up on long-term recommendations. However, parents expressed feeling burdened by this responsibility. As 1 parent stated, "we already are trying to keep track of medications that needed to be given, and multiple doctor visits, and possible hospitalizations and remembering when my child is next due for vaccines is very difficult." Another stated that it was "an overwhelming task-we were trying to juggle so much."

### Lack of Centralized Immunization Records

Uniformly, participants described acquisition of immunization records from multiple locations as a barrier. One hepatologist stated, "I don't even know all the ways you can look up if immunizations have been given." Transplant physicians and nurse-coordinators described acquisition of records as "tiring," "difficult," and "frustrating," especially in the setting of an out-of-state patient. One PCP stated, "if the family has moved around a lot and they haven't kept great records of their immunizations, it can be difficult to track things down." Many providers stated that they rely on parents to collect and bring immunization records. However, parents noted that "with a very sick child it is hard for a parent to remember every detail, especially about small things like dates vaccines were given."

All providers expressed concerns about state immunization information systems (IIS) now active in 50 states, 5 cities, the District of Columbia, and 8 US Territories. Some providers stated that there was no state IIS where they practice. Others who knew they had a state IIS stated, "the information is only as good as the person who enters it." Providers noted that, even if they used the state IIS, they only had access to records of in-state patients and many transplant recipients do not live in the same state as their transplant center. Subspecialists were unsure if they even had access to the IIS.

### Subspecialty Clinic Functioning as the Medical Home But Unable to Provide Needed Immunizations

Parents and providers described subspecialty clinics serving as the medical home for the patient before transplantation. One nephrologist stated, "it's a burden for families to come here 3 days a week for dialysis and then make separate appointments at the PCP for immunizations." A parent said "the normal checkups and everything with that all went out the window because we were in the hospital so much. The transplant doctor knew what my child needed so we didn't even go see his pediatrician." However, all transplant providers acknowledged that "it's challenging because we can't actually administer all immunizations in our subspecialty clinic. We lack the infrastructure, the staff to give the vaccines, and we aren't stocked with vaccines."

### Organ-Specific Immunization Issues

Prioritization of immunization among all needed pretransplant care varied between heart, liver, and kidney transplant providers. As 1 nephrologist stated, "I think all transplant providers feel that vaccines should be given. But it varies by organ a little because of the urgency of things." Kidney providers discussed dialysis as "a way to give kids time to get their vaccines done." Contrastingly, heart providers described their patients as "sick in the intensive care unit. They are sensitive to every outside kind of stimulation, sometimes just getting a vaccine can make them unstable." As a heart transplant coordinator stated, "we don't have many options for keeping patients alive while they're waiting for a heart transplant. We would not want to have to turn down an offer because a patient gets a fever following vaccines and they need an infectious workup." Additionally, cardiologists noted that "some heart candidates receive treatments

pretransplant like intravenous immunoglobulin. . . that would make immunizations less effective." Liver providers fell somewhere in the middle, describing that "in acute liver failure we don't have time to get children up-to-date on immunizations, but for children with chronic liver disease we require them to be up-to-date before listing."

## Discussion

Vaccine-preventable infections are a common and significant problem after pediatric solid organ transplantation.[1,2] Despite published immunization recommendations for pediatric solid organ transplant candidates to receive all age-appropriate vaccines,[3,17] and the increased risk of infections for all immunosuppressed transplant recipients, vaccine rates among transplant candidates remain suboptimal, with the majority of pediatric transplant recipients not up to date for recommended immunizations at the time of transplantation.[5] In the general pediatric population, studies have suggested that parental concern about vaccine side effects, safety, and pain; lack of knowledge about vaccines and the diseases they prevent; lack of access to health care; lack of insurance coverage; and moral or religious objections may be contributing factors to underimmunization.[18-22] However, there are no studies investigating why transplant candidates who are at high risk for infectious diseases are paradoxically less immunized than their healthy counterparts. This study suggests that there are unique factors related to the medical complexity, fractured well-child care, and joint management by a subspecialist and PCP that contribute to low immunization rates before transplantation.

Healthy children receive the majority of their immunizations at their PCP's office. However, parents of transplant recipients identified difficulty in attending PCP visits during the pretransplant period. Parents stated that in the months leading up to transplant, their child was being seen frequently (sometimes 2-3 times a week) in s subspecialty clinic or had repeated or prolonged hospitalizations for acute medical decompensation, making it difficult to visit the PCP. Despite these frequent visits to the subspecialist or hospital, only 22% of parents interviewed in this study recalled receiving any of their child's immunizations in a subspecialty clinic or during an inpatient hospital stay. In a prior survey study of North American pediatric hepatologists, only 6% of respondents stated that they were able to administer all needed vaccines in hepatology/transplant clinic.[23] Subspecialty providers interviewed in this study described insurance reimbursement, nursing time and training, and difficulties with keeping vaccines stocked for only a small number of patients as barriers to providing immunizations in specialty clinic. All clinical encounters (subspecialty clinic appointments, dialysis visits, the transplant evaluation, and in-patient hospital stays) should be considered an opportunity to administer needed vaccines. Providing immunizations in the emergency department, the dialysis unit, and the in-patient hospital ward has been a successful strategy in increasing immunization rates in other high-risk populations.[24-28] Further research is needed to fully understand and assess the specific barriers and costs involved in making vaccines available in subspecialty clinics and dialysis units. State legislation is needed to mandate third-party payers to reimburse all providers, including subspecialists, for the full costs of purchasing, storing, and administering vaccinations to patients.[29]

Increasing opportunities for immunizations to be delivered outside of the primary care clinic is only 1 part of the solution to improving pretransplant immunization rates. Additionally, a novel tool is needed to provide the entire team caring for the transplant candidate (parents, PCPs, and transplant subspecialists) with education, guidance, and automated reminders about immunizations. A health information technology tool could potentially address and overcome many of the transplant-specific immunization barriers identified in this study including parent/provider misunderstanding about the timing and safety of immunizations before transplantation, challenges in collecting and accessing a child's complete immunization records, difficulty managing communication between multiple care team members, and complexity of tracking when additional immunizations need to be administered as a child awaits transplantation (**Table IV**).[30] Digital health tools (mobile phone, electronic medical record, and web based) have shown initial success in creating population-based immunization registries, implementing vaccine reminder/recall systems, providing education about vaccines for parents and providers, providing automated clinical decision support or "practice alerts," decreasing missed vaccine opportunities, and increasing immunization rates.[20,21,31-47] A transplant-specific cloud-based health information technology tool could be developed to provide (1) education for parents and providers about immunization use in the transplant population, (2) a communication portal to allow tridirectional communication between parents and providers who may not operate on the same electronic medical record system, (3) an easily accessible centralized vaccine record, and (4) automated vaccine reminders triggered based on the Centers for Disease Control and Prevention's accelerated schedule that alert the parent, PCP, and transplant team when a vaccine is due.[30,48]

In this study, we did not identify parental hesitancy as a barrier to pretransplant immunizations. However, in the general pediatrics population, rates of vaccine hesitancy and refusal are rising and are a major hindrance to universal childhood immunization.[49-51] The reason this theme may not have emerged in our study could be due to the fact that the 3 centers involved in this study have strong vaccine policies requiring immunization for nonemergent transplant candidates. In a study of 114 medical directors, surgical directors, and transplant coordinators from 138 pediatric solid organ transplant programs in the US, only 4% of respondents stated that their program had written policies regarding parental refusal of vaccines before transplantation. When given a hypothetical situation about an unimmunized child (based on parental preference) requiring a transplant, 47% of respondents stated they would proceed with transplant despite the child being unimmunized.[52] A national policy

**Table IV. Barriers to pretransplant immunization and potential solutions**

| Barriers | Potential solutions |
|---|---|
| Gaps in knowledge about safety, efficacy and timing of pretransplant immunizations | Educational sheets and videos on a HIT tool for parents and providers about vaccines and vaccine preventable infection in the transplant population |
| Lack of communication, coordination and follow-up between team members regarding immunizations | Communication portal through a HIT tool that enables easy tridirectional communication between parent, PCP and transplant team who may not be on the same electronic medical record |
| | Automated reminders using the CDC accelerated schedule that alert the parent, PCP, and transplant team when vaccines are due |
| Lack of centralized immunization record | A vaccine repository on a cloud-based HIT tool that is easily accessible by parent, PCP, and all members of the transplant team |
| Subspecialty clinic serving as the medical home but unable to provide needed immunizations | Opportunities to receive immunizations in subspecialty/transplant clinic, during the transplant evaluation, during dialysis, during inpatient hospital stays |
| | State mandated third party payer reimbursement to all practitioners, including subspecialists, who provide vaccines |

*CDC*, Centers for Disease Control and Prevention; *HIT*, health information technology.

from the United Network for Organ Sharing requiring complete age-appropriate immunizations for nonemergent transplants would help prioritize vaccination as part of standard pretransplant care. It would also prevent a patient/family from "center shopping" to find a transplant center that does not require pretransplant immunizations. Center immunization rates should be a part of state-mandated quality metrics and centers with high immunization rates should receive pay-for-performance incentives and/or priority points for their candidates on the United Network for Organ Sharing waitlist.[29,53]

Although we did not access immunization records in this study, in a study of all pediatric liver transplants performed in North America over a one year period (excluding those for acute liver failure) <30% of children were up to date at the time of transplantation for standard age-appropriate immunizations recommended by the Centers for Disease Control and Prevention at the time of transplant.[5] This discrepancy between parental report and actual immunization status is consistent with studies in the general pediatric population demonstrating that parents often overestimate their child's immunization status or incorrectly believe their child to be up to date on immunizations when they are not.[54-57]

There are potential limitations to this study. First, our study was conducted at 3 large centers that each perform >10 transplants (per organ type) per year. This factor may limit generalizability as stakeholders at smaller centers may face additional or different barriers. Second, parents were interviewed from 3 months to 7 years after their child was transplanted (to gain a large enough sample size to reach thematic saturation); therefore, there may be recall bias, leading to unintentional omission of some immunization barriers. Finally, although all parents and providers of transplant recipients in the study period were invited to participate, there may be enrollment bias where those stakeholders who chose to participate had a different experience with pretransplant immunizations than those who chose not to enroll. Specifically, all parents who enrolled in our study were English speakers, and therefore the pretransplant immunization experience for non-English speakers may not be represented. In future studies, it will be important to assess whether parental factors (including primary spoken language, education level, and socioeconomic status) impact the immunization barriers a family faces and ultimately whether the child is successfully vaccinated by the time of transplant.

The development of a novel health information technology tool may address many of these barriers by providing education about immunizations in the transplant setting, enhancing communication and breaking down silos between multiple providers and families, centralizing vaccine records, and providing computerized reminders when immunizations are due. In addition, the ability to provide immunizations outside of the PCP office could increase the likelihood that a child enters transplant fully up to date on age-appropriate immunization. Increasing pretransplant immunization rates will likely decrease post-transplant infections, resulting in significantly improved post-transplant outcomes. ■

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## 50 Years Ago in *The Journal of Pediatrics*

### Management of Listeriosis

Gordon RC, Barrett FF, Yow MD. Ampicillin treatment of listeriosis. J Pediatr 1970;77:1067-70.

*Listeria monocytogenes,* an important facultative human pathogen, is the third-leading cause of death from foodborne bacteria in the US.[1] The infection is most likely to affect pregnant women and their newborns, adults aged ≥65 years, and people with immunodeficiency. Listeriosis outbreaks impose significant economic impact on the food industry and public health.

The primary reason for the difficulty in treating listeriosis is that only a few antibiotics exert bactericidal activity. Thus, 50 years ago, Gordon et al successfully treated 3 cases of listeriosis with ampicillin. The antibiotics for treating listeriosis available at that time had poor safety profiles in newborns. Ampicillin had emerged as a new, safer alternative with good clinical response. The authors successfully treated 2 newborns with *Listeria* meningitis and an 86-year-old woman with septicemia secondary to infection with *L monocytogenes*. Antibiotic susceptibility testing suggested that penicillin, ampicillin, cephalothin, and kanamycin were bactericidal for *Listeria,* and that tetracycline and chloramphenicol were bacteriostatic.

*L monocytogenes* is intracellular, and thus antibiotics need to penetrate the host cells by crossing the lipid bilayer of the cell membrane. The first multidrug-resistant *Listeria* isolate was identified in France in 1988. Since then, only occasional cases of antibiotic resistance in listeriosis have been reported. Except for natural in vitro resistance to older quinolones, fosfomycin, and expanded-spectrum cephalosporins, *L monocytogenes* remains widely susceptible to clinically relevant antibiotics. However, there has been an increase in the minimum inhibitory concentration (MIC) of penicillin, indicating the need to modify the drug dosage.[2]

Today, the primary therapy for listeriosis still consists of a combination of ampicillin or amoxicillin plus gentamicin. The aminopenicillin should be given at high doses 4-6 times daily for a prolonged period. Cotrimoxazole is the drug of second choice. Acquired resistance in *L monocytogenes* from humans has had no clinical consequences so far, and it does not affect the first-line treatment. However, transfer of resistance genes from other bacteria and the recently increasing MICs of aminopenicillins underscore the need for active and continuous surveillance of the susceptibility of *Listeria* to antibiotics.

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