Transplanting One Problem for Another

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Major advances have been made in the field of pediatric solid organ transplant, with significant improvements in long-term survival for children requiring this life-saving intervention.[1] Developments in supportive care, organ allocation, HLA antigen matching, and immunosuppressive regimens have all contributed to this success.[2–4] With more patients surviving longer, however, there has also been an increase in the long-term complications of transplantation.[5] In addition to other organ toxicities, allograft loss, and impaired health-related quality of life,[6,7] a dramatic increase in cancer incidence has been seen in organ transplant recipients.[8,9] The overall increased incidence of malignancy in patients who have received solid organ transplants has been reported to range from a two- to six-fold increase above the general population,[8,10] depending on the cohort and type of transplant. The cumulative incidence has been reported to be as high as 55% in an adult population at 15 years if skin cancers are also included.[11] A large registry study in the United Kingdom, which included both pediatric and adult patients, found standardized incidence ratios of 2.4 over the general population. This increased to a standardized incidence ratio of 16.6 with the inclusion of skin cancers, and the rates of malignancy appeared to be higher for younger transplant recipients.[12] A large registry study of the Organ Procurement and Transplant Network in the United States found a similarly elevated posttransplant malignancy incidence, but focused only on the adult population.[13]

Until now, there has not been a large study to adequately quantify and describe the incidence of cancer in children posttransplant. In this month's issue of *Pediatrics*, in their article entitled "Cancer Risk Among Pediatric Solid Organ Transplant Recipients in the United States," Yanik et al[14] took on this challenge, evaluating the incidence of cancer in the largest pediatric solid organ transplant population to date. By linking the Scientific Registry of Transplant Recipients to 16 US state or regional cancer registries, the authors were able to obtain information from >17 000 transplants in pediatric patients. In line with previous reports,[15,16] they found a predominance of non-Hodgkin's lymphoma and Hodgkin's lymphoma. Remarkably, the rate of cancer incidence in this posttransplant population was dramatically increased, with overall cancer incidence 19 times higher and incidence of non-Hodgkin's lymphoma 212 times higher than in the general population. Moreover, the surprising identification of 3 patients with multiple myeloma, an incredibly rare cancer in pediatric patients, raises concern about the impact of organ transplant and its therapy on hematopoietic cell precursors. One of the more disturbing features of the study is the relatively short period of follow-up; not only was the median follow-up only 4 years, but the oldest transplant recipient at follow-up was only 38 years old. Although this study captures the highest increased incidence found in the first year posttransplant, it remains to be seen what will happen to this population as they continue to age and reach

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DOI: 10.1542/peds.2017-0542

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PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

FINANCIAL DISCLOSURE: The authors have indicated they have no financial relationships relevant to this article to disclose.

FUNDING: No external funding.

POTENTIAL CONFLICT OF INTEREST: The authors have indicated they have no potential conflicts of interest to disclose.

COMPANION PAPER: A companion to this article can be found online at www.pediatrics.org/cgi/doi/10.1542/peds.2016-3893.

To cite: Borst AJ and Wechsler DS. Transplanting One Problem for Another. *Pediatrics.* 2017;139(5): e20170542

the peak of cancer incidence in late adulthood.[17]

The ability to study such a large population confirms the increased cancer incidence in intestinal transplant and Epstein-Barr virus (EBV)–seronegative recipients, which are somewhat unique risk factors for a pediatric population.[18,19] Because of the significant association between EBV infection and risk of many immunodeficiency-related malignancies, many efforts are being made to prevent or promptly address infection. These include vaccine development, preemptive treatment of viremia with rituximab, and even EBV-specific cytotoxic T lymphocytes.[20,21] The profile of malignancies in the posttransplant population is also similar to that seen in other immunodeficiency states,[22] which may allow us to obtain further insight into the interplay between the immune system and cancer.[23]

A more refined understanding of the mechanisms that contribute to the development of cancer in patients whose immune system is altered will become increasingly important in the era of immune-based therapies for malignancy.[19,24] Given the huge economic burden of these oncologic diagnoses on the health care system[25] and quality of life for the transplant recipients and families,[6,26] the observations of Yanik et al encourage further studies to develop improved strategies for preventing these potentially devastating outcomes.

ABBREVIATION

EBV: Epstein-Barr virus

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