To the Editor:

The term "bare lymphocyte syndrome" is applied to a heterogeneous group of patients whose cells lack or show deficiencies in major histocompatibility complex (MHC) class II expression caused by impaired transcription of HLA class II encoding genes. At least three complementation groups responsible for these deficiencies have been identified. However, common to all these patients is the lack or severe deficiency of CD4+ T lymphocytes.

Klein et al recently reported results of allogeneic bone marrow transplantation in 19 patients with bare lymphocyte syndrome. Several patients were cured by this approach. However, all patients with stable long-term engraftment had persistently low CD4 counts. The availability of an animal model of MHC class II deficiency in the form of MHC class II knockout (C2D) mice has allowed us to further...
investigate the requirements of MHC class II expression in donor and recipient necessary for immunoreconstitution. C2D mice, developed from C57BL/6J blastocysts lack MHC class II expression and fail to select CD4+ CD8- T lymphocytes. We performed experiments in which class II knockout or C57BL (normal) mice were conditioned with 1,000 cGy of total body irradiation and transplanted with unpurged marrow (4 to 6 × 10^6 cells/mouse) from class II knockout or normal donors. The analysis of intrathymic T cells showed reconstitution of CD4+ cells (and CD4 intermediates) in normal mice transplanted with either normal or C2D marrow, but showed a lack of CD4+ CD8- CD3+ cells in C2D mice transplanted with normal marrow (Fig 1).

However, of interest was the analysis of spleen cells: both C2D recipients of normal marrow and normal recipients of C2D marrow showed abnormal CD4 reconstitution at least when examined early (up to 21 days) after transplantation (Fig 1). The mechanism for abnormal CD4 development in normal recipients is not clear. The data suggest the possibility of a contribution of donor determinants to T-cell selection in the periphery. Furthermore, there may be differences between the use of nonpurged marrow (present study) and T-cell–depleted marrow as used by Markowitz et al., who showed the presence of normal CD4+ cells in the lymph nodes of normal recipients of class II knockout marrow at 12 weeks posttransplant. The possibility that those cells were of donor origin needs to be considered.

Thus, as speculated by Klein et al., results in controlled animal models support the notion of impaired thymic selection in class II-deficient recipients. It is encouraging from the animal model as well as clinical results that those patients who do show long-term reconstitution are able to mount an immune response. Additional results in murine models suggest that CD4 selection can be fully restored by cotransplanting MHC class II transfect transplanted thymic epithelial cells along with hematopoietic cells.

REFERENCES
Defective CD4+ T-lymphocyte reconstitution in major histocompatibility complex class II-deficient transplant models [letter]

R Huss, GT Nepom and HJ Deeg