The largest study of PCB transplantation from unrelated donors (and comprising most of the PCB transplants carried out worldwide between August 1992 and January 1998) was reported by Rubinstein *et al.*[38] The study includes data on 562 patients who were transplanted for a variety of malignant and non-malignant blood disorders, genetic diseases and inborn errors of metabolism, as well as hereditary immunodeficiency states. Patients were followed for likelihood of engraftment, speed of neutrophil and platelet recovery, GvHD, event-free survival, viral infection and, as appropriate, leukemia relapse. The large number of patients in the study, as well as the integration of preliminary data published earlier on smaller patient groups,[9,36,40] resolved differences in three areas: (1) engraftment dependent on cell dose infused, (2) delayed platelet recovery following PCB transplantation, and (3) CMV-antibody status predictive of GvHD and survival. Three months post-transplantation, the overall rate of transplantation-related events was 46% and these events correlated with the recipient's diagnosis, age, number of leukocytes infused, extent of HLA-disparity, and the location of the center (U.S. versus non-U.S.). The number of leukocytes infused (as nucleated cells/kg recipient body weight) was predictive of the speed of both neutrophil and platelet engraftment. Graft failure was highest in patients with Fanconi anemia, severe aplastic anemia and chronic myelogenous leukemia.

The class of HLA mismatch and the presence or absence of CMV-antibodies before transplantation were not associated with transplantation-related events. In accordance with other studies,[9,36,37,39,40] it is generally accepted that the degree of GvHD seen with PCB transplantation is less severe than with BMT. Thus, 31% of patients showed no acute GvHD, 47% grade I–II and 22% grade III–IV. In contrast, a similarly large study of unrelated BMT reported in 1993 by the NMDP gave the probability of severe GvHD (grade III–IV) to be almost 0.5.[3] In general, GvHD following PCB transplantation was more prominent in patients >12 years old, with a greater degree of HLA-incompatibility, with infection, and in transplant centers outside the U.S. The frequency of acute grade III–IV GvHD in PCB transplantation was lower in patients matched for 6 of 6 HLA antigens than in patients with one or more HLA mismatches, but did not correlate with the degree of HLA mismatch. Of patients who had previously had grade III–IV acute GvHD, 80% developed chronic GvHD; in comparison, only 18% of those patients who did not have severe acute GvHD developed chronic GvHD. The generally reported low incidence of GvHD after PCB transplantation is a major concern in leukemic patients as the absence of GvHD might be associated with the absence of a graft-versus-leukemia (GvL) effect. However, a study carried out by the Eurocord-Cord Blood Transplantation Group on 102 children with acute leukemia[39] in early and advanced stage of disease, good and poor risk, reported no remarkable differences in the overall two year event-free survival (interval from PCB transplantation to relapse or death in complete remission) when compared to the two year disease-free posttransplant outcomes of children receiving an unrelated BMT.[41] The two year event-free survival was 30% after PCB transplantation and 33% after BMT.

Another study of BMT[42] reported 47% and 20% disease-free survival in patients with acute lymphoblastic leukemia in first or second remission, respectively. Considering the significantly lower incidence of GvHD seen with PCB transplantation and the detrimental impact of GvHD on a growing organism, the results on overall survival are encouraging. Apparently, the low incidence and severity of GvHD with PCB transplantation are not necessarily associated with a reduced GvL effect in leukemic patients. In fact, the prompt availability of PCB stem cell preparations may eventually permit transplants at a more favorable disease state, and the better tolerated HLA-disparity could be associated with a greater GvL effect.

With adult BM or cytokine-mobilized PB stem cell transplantation, the time to neutrophil engraftment correlates with $CD34^+$ cell dose.[43–46] In addition, preliminary reports have claimed a correlation between the number of megakaryocytic (Meg)-CFC given and time to platelet engraftment following PB transplants.[47–49] Previously, the New York Blood Center and others reported on the correlation between nucleated cell dose and the success and speed of both neutrophil and platelet engraftment following PCB transplants.[38] In addition, preliminary evidence was found indicating that the number of CFC, measured as the total number of granulocyte/macrophage (GM)-CFC, erythroid burst-forming cells (BFU-E) and mixed-cell CFC, transplanted per kg recipient body weight, correlated even more strongly with engraftment kinetics.[50] The median time to reach an absolute neutrophil count $\geq$500 per μl was 25 days (range 10 days to 4 months) and to reach a platelet count $\geq$50,000 per μl was 71 days (range 16 to 250 days) for patients who engrafted. These times to engraftment are similar to those observed with unrelated BMT,[3] but are much longer than with cytokine-mobilized PB transplants.[43,44,46–49]

A number of questions have arisen about the utility of PCB for transplantation of adults because of the observed cell dose effect and the concern for timely engraftment.[38] Consequently, the goal of improving the rate of engraftment as well as speeding the time to recovery of marrow function has spurred investigation of methods to increase the number of HSC and progenitor