transplantation and now provide treatment options for malignancies, marrow failure syndromes, hereditary immunodeficiency states, inborn errors of metabolism, and certain solid tumors, as well as providing a platform for gene therapy.

Among the various HSC sources for transplantation, PCB offers a number of potential advantages: (1) PCB is a waste product after childbirth and its procurement is relatively easy; (2) the ability to ensure ethnic diversity and rare HLA constellations among donors; (3) low risk of transmissible infectious diseases; (4) no risk to the donor; (5) no contamination by residual tumor cells.

Analysis of the clinical results in the first 44 patients transplanted with sibling PCB established the fact that PCB contains sufficient numbers of stem and progenitor cells to engraft at least small recipients and that such transplants were associated with a very low risk of acute and chronic graft-versus-host-disease (GvHD).[9]

As a result of the early success with PCB, programs for the banking of unrelated donor PCB were initiated both in the U.S. and Europe.[10,11] At present, the Placental Blood Program at the New York Blood Center, established in 1992, is the largest PCB bank in the world with approximately 11,000 units collected, HLA-typed, tested for infectious transmissible diseases and cryopreserved. Such PCB stem cell preparations can be made available rapidly, with some units identified and transplanted within one week after the initial search request. To date, the Placental Blood Program of the New York Blood Center has provided nearly 1000 PCB units for unrelated transplantation (P. Rubinstein, personal communication).

PCB Progenitor Cells: *In Vitro* Properties

PCB, mobilized PB and BM display differences in numbers and phenotypes of stem and progenitor cells as well as differences in their proliferative response to cytokines.[12–28] The different characteristics of PCB, BM and mobilized PB may be due to their different ontogenetic stages or to maturation-related differences in the expression of different surface markers.[29–35] Such differences may influence homing and engraftment potential following transplantation. In contrast to BM and mobilized PB, PCB progenitor cells have: (1) a higher proliferative potential[22,23] reflected by the size of hematopoietic colonies growing in semisolid medium; (2) a higher clonogenic potential measured as the percentage of colony-forming cells (CFC) among nucleated cells or $CD34^+$ cells, and by replating capacity of CFC;[24–26] (3) a greater proportion of cells with a more primitive phenotype represented by the presence of stem cell surface markers such as CD34 and c-kit and the absence of lineage-specific markers such as CD 33, transferrin receptor, CD 41, thy 1 and CD 38;[15,16,19–21] (4) a higher content of mixed-cell CFC with the capacity to give rise to colonies containing up to five types of differentiated cells;[27,28] (5) a higher engraftment potential in the nonobese diabetic severe combined immunodeficient (NOD-SCID) mouse;[29] (6) longer telomeres.[30]

PCB in Clinical Transplantation: Outcomes and Possible Limitations

Over the past several years, a number of studies have established PCB as a viable alternative source of HSC for transplantation in the allogeneic related and unrelated settings.[5,9,36–40] The patients in these studies have been heterogeneous with respect to diagnosis and stage of disease. While the range of diagnoses was similar to large studies of BMT, a substantial number of PCB recipients had advanced or relapsed disease and had no other treatment option or suitably-matched family or unrelated BM donor. Between 1995 and 1999, the International Bone Marrow Transplant Registry/Autologous Blood and Marrow Transplant Registry (IBMTR/ABMTR) reported that, of the first patients transplanted with unrelated PCB for leukemia, only 26% were in early stage and 50% in an intermediate stage of their disease. This was contrasted with a similar group of patients who received unrelated BM transplants where 43% and 35% were in early or intermediate stage, respectively.

For both stem cell sources, the largest percentage of all transplants—49% for PCB and 43% for BM—were carried out for treatment of acute leukemia. The second largest category comprised chronic leukemia for BMT (30%) and congenital disorders for PCB transplants (18%). Most (69%) of the PCB transplants were performed on patients under the age of 10 (and, therefore, with low body weight). The use of PCB transplantation decreased progressively with increasing patient age. In contrast, the use of BMT is evenly distributed throughout all age groups (range 17–26%) (M. Horowitz, personal communication).

Observation endpoints reported following transplantation vary widely from several months to several years so that the interpretation of clinical outcomes is difficult, especially for rare diseases with data collected on only a few patients. The comparison of results from recent PCB transplantation studies to historical results with BMT also needs to take into account that stem cell transplantation techniques have been subject to constant refinement over the past decades and outcomes are heavily influenced by the experience of the transplant center. Taking this fact into consideration, the precise interpretation of patient outcomes following PCB versus BM transplantation can only be achieved in future trials by matched/paired case-control studies.