

## SPECIALTY SPOTLIGHT

## Beyond bone marrow: a new source of stem cells

**Technology:** Peripheral blood stem cell transplantation.

**Use:** The use of escalated doses of chemotherapy in patients with cancer is limited by toxic effects on tissues such as the bone marrow. Irreversible damage to bone marrow and the resultant cytopenias lead to death from infections or bleeding. Reinfusion of primitive hematopoietic progenitor cells (stem cells) after high-dose chemoradiotherapy can "rescue" the patient by homing the stem cells to the bone marrow and restoring a normal hematopoietic system. Stem cells, which normally reside in the bone marrow, may be stimulated (mobilized) with chemotherapy or growth factors to enter the peripheral blood. A cell separator (apheresis machine) enables collection of these stem cells by filtering the venous blood through a central line. Stem cells removed from the blood in this manner can then be frozen for later use.

This transplantation technique of administering high-dose chemotherapy followed by intravenous reinfusion of stem cells (autologous or allogeneic) collected from peripheral blood has gained widespread acceptance in the treatment of many different cancers such as relapsed lymphoma, acute leukemias and chronic myeloid leukemia and of aplastic anemia. It is under investigation for the treatment of solid tumours and various benign disorders such as sickle cell anemia and as a vehicle for gene therapy. In chronic myeloid leukemia and aplastic anemia, allogeneic stem cell transplantation represents the only chance of cure, with 5-year survival rates of up to 70%.<sup>1,2</sup> With the use of high-dose therapy and autologous stem cell rescue, 5-year overall survival rates for relapsed lymphoma have increased from 12% to 46%.<sup>3</sup>

**History:** Traditionally, cells used for "rescue" in transplantation were obtained from bone marrow harvested directly from the iliac crests under gen-

eral anesthesia. Progenitor cells were quantified by colony formation in culture, a relatively slow and inaccurate process. In the 1980s the common stem cell antigen (CD34) found on hematopoietic progenitor cells was recognized.<sup>4</sup> Using monoclonal antibodies to CD34 and flow cytometry detection, stem cells can now be identified and quantified rapidly and accurately. The discovery that chemotherapy and growth factors could mobilize CD34 cells into the blood, which could then be collected through an intravenous line, dramatically changed transplantation standards.<sup>5</sup> Today, in most centres worldwide, peripheral blood has largely replaced bone marrow as the source of stem cells for autologous transplantation, and the procedure is under intensive investigation for allogeneic transplantation.

**Promise:** The process of stem cell mobilization and collection from peripheral blood is relatively simple, safely performed on an outpatient basis and can yield several times more stem cells than can bone marrow.<sup>6</sup> Unlike bone marrow harvesting, stem cell collection from peripheral blood requires no general anesthetic, and blood transfusions after collection are rarely needed. Also, blood counts recover faster in patients receiving peripheral blood stem cells than in those receiving bone marrow. This translates into shorter hospital stays, fewer transfusions and decreased antibiotic use.

**Problems:** Technical complications related to intravenous access, fluid and electrolyte shifts with large volume apheresis and side effects from chemotherapy and growth factor mobilization may arise with this approach. Stem cells collected from peripheral blood may be contaminated with tumour cells that may contribute to relapse after transplantation. However, procedures to select cells of choice or to remove unwanted tumour cells from stem cell collections have not been uniformly ad-

vantageous and therefore not routinely used at present. Because stem cells collected from blood typically contain greater numbers of T cells than bone marrow does, there is also a theoretical concern of increased graft-versus-host disease in allogeneic transplants. Thus far, no increase in incidence has been noted with peripheral blood stem cell use. Ethical and safety issues arise with the use of growth factors for mobilizing stem cells in normal donors. No significant side effects are apparent, but long-term follow-up is required.

**Prospects:** Together with improved supportive care in recent years, the advent of peripheral blood stem cell transplantation has improved the safety profile of transplantation and has led to increased use of this technique worldwide. Peripheral blood stem cell transplantation will undoubtedly be applied to an even wider spectrum of malignant and benign disorders in the future as advances are made in gene therapy and ex vivo manipulation of stem cells. — *Christine I. Chen, Armand Keating, Department of Medical Oncology and Hematology, Princess Margaret Hospital, Toronto, Ont.*

## References

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