Overview in Pediatric Hematopoietic Stem Cell Transplantation

Kleebsabai Sanpakit, MD*

** Department of Pediatrics, Faculty of Medicine, Siriraj Hospital*

Hematopoietic stem cell transplantation (HSCT) has been an established curative therapy for the various hematologic nonmalignant and malignant diseases which respond poorly following conventional treatment, immunological disorders and several inherited disorders as well as some oncologic diseases (Table 1)[1-4]. The concept of this effective treatment for nonmalignant diseases is by allowing the replacement of an abnormal hematopoietic system after myeloablative therapy with a normal one[3]. For the treatment of a variety of malignant diseases, HSCT allows the administration of higher and potentially more effective doses of therapy to eradicate the malignant cells before rescue of the bone marrow function with normal hematopoietic stem cells (HSC) because hematopoietic toxicity is dose-limiting for many types of chemoradiotherapy. Further, allogeneic HSCT offers the donor's immune cells that are capable of killing patient's malignant cells. This so-called graft-versus-tumor (GVT) effect is a powerful form of immunotherapy that can eradicate chemoresistant malignant cells[3,5].

HSCT can be categorized according to the relationship between the donor and recipient and according to their anatomical sources of stem cells. The former can be described as followings:

1. Autologous HSCT which is the transplantation using the patient's own hematopoietic cells to

Table 1. Pediatric diseases that have indications for hematopoietic stem cell transplantation[1-4]

1. Malignant diseases
   - 1.1 Acute lymphoblastic leukemia (ALL): after second remission, in first remission with high risk for relapse (e.g., Philadelphia-positive ALL, refractory ALL)
   - 1.2 Acute nonlymphoblastic leukemia (ANLL): after first remission
   - 1.3 Chronic myeloid leukemia
   - 1.4 Myelodysplastic syndrome (MDS): Juvenile chronic myeloid leukemia, Refractory anemia with excess blast, Refractory anemia with excess blast in transformation
   - 1.5 Monosomy 7 syndrome ANLL/MDS
   - 1.6 Non-Hodgkin's lymphoma: Burkitt's lymphoma stage IV, Large cell lymphoma stage IV, relapsed or refractory disease
   - 1.7 Solid tumors: e.g., Neuroblastoma stage IV, relapsed or refractory soft tissue sarcoma
2. Non-malignant diseases
   - 2.1 Immunodeficiency diseases e.g. Severe combined immunodeficiency syndrome, Wiskott-Aldrich syndrome, Congenital neutropenia, Chronic granulomatous diseases
   - 2.2 Hematopoietic diseases e.g. Severe thalassemia, Severe aplastic anemia, Congenital pure red cell anemia, Pyruvate kinase deficiency, Fanconi's anemia
   - 2.3 Storage diseases e.g. Gaucher's disease, Mucopolysaccharidoses, Metachromatic leukodystrophy
   - 2.4 Others: e.g. Infantile osteopetrosis, Dyskeratosis congenita, Refractory autoimmune cytopenia

Keywords : *Stem cell transplantation, Hematopietic, Pediatric, Overview*

J Med Assoc Thai 2005; 88(8): 1147-52
Full text. e-Journal: *http://www.medassocthai.org/journal*

Correspondence to : Sanpakit K, Department of Pediatrics, Faculty of Medicine, Siriraj Hospital, Bangkok 10700, Thailand. Phone: 0-2419-7000 ext 5971-3, 0-2866-3021, Fax: 0-2866-3021, E-mail: sisap@mahidol.ac.th

restore the hematopoietic function after a high dose of chemoradiotherapy. This process involves collecting the HSC before the preparative regimens, cryopreserving, and later reinfusing their own HSC[3]. However, the most significant limitations of using the autologous HSCT have been the potential for viable tumor cells contamination which could cause disease recurrence following reinfusion of HSC[2,3]. Currently, various techniques to deplete clonogenic tumor cells from the autologous HSC have been developed including treatment of the stem cell inoculums in vitro with chemotherapy, the use of tumor-reactive antibody plus complement, antibody conjugated to other toxins such as ricin or antibody conjugated to immunomagnetic beads. An alternative approach is to purify the autologous stem cell inoculums by the positive selection of stem cells such as using CD34 as a target. This procedure can reduce the tumor cell contamination by several logs[3]. The effectiveness of all these techniques are still being established.

2. Syngeneic HSCT which is the transplant from identical twins. Although identical twins make almost ideal donors, only a few patients have such a donor[3].

3. Allogeneic HSCT which is the transplant from the donor who share the same major human leukocyte antigens (HLA) with the patient. However, there will still be differences in many of the minor antigens which can cause immune-mediated injury to the patient by the donor's T cells. This reaction is called graft-versus-host disease (GVHD)[3,6]. The use of HSC from family members who matched for six major HLA (HLA class I: HLA-A, HLA-B and HLA class II: HLA-DR) with the patient is called HLA-matched-relative HSCT which is the conventional allogeneic donor[2,3]. The HLA genes are tightly linked and tend to be inherited as haplotypes with low recombinant frequencies. Thus, there is a 25% possibility that any one sibling will inherit the same paternal and maternal haplotypes as the patient[2,3]. Because the availability of the HLA matched related donors is limited, the expansion of the donor pool to include mismatched family members and HLA-matched and partially matched unrelated donors is essential[2]. Since the HLA genes are so highly polymorphic, in order to find matched unrelated donors, it has been necessary to develop large donor registries[3]. Currently, the Thai Red Cross is the institution that cryopreserve and supply unrelated HSC for all transplant centers in Thailand. Although the rate of GVHD and graft rejection are more common following matched unrelated HSCT than matched related HSCT due to the disparity in minor non-HLA histocompatibility antigens among unrelated individuals. The advances in donor selection using allele-level matching in HLA class I and II should improve the outcome of unrelated HSCT[3,7,8].

Sources of HSC

1. The bone marrow (BM) which is the source of hematopoiesis. The aspiration procedure is conducted in an operating room under sterile conditions with appropriate general anesthesia. Most BM is harvested from the posterior iliac crests with total volume 10 to 20 ml/kg of recipient weight. These volumes represent realistic target volumes that usually yield sufficient HSC for engraftment[2].

2. The peripheral blood (PB) which has a very low concentration of stem cells but they could increase dramatically following the administration of hematopoietic growth factors such as granulocyte colony stimulating factor (G-CSF) and during recovery from intensive chemotherapy. In general, donors receive G-CSF 10 to 16 mcg/kg/day for 3 to 7 days to mobilize sufficient PBSC for collection by the leukapheresis machine through the venous access. Because of ease of collection and the substantial acceleration of engraftment, PB has been increasingly used as the source of stem cells although access issues may present a significant obstacle with young and small donors[2,9].

3. The umbilical cord blood (UCB) which is a rich source of HSC and can be used to successfully reconstitute hematopoiesis after allogeneic HSCT. UCB has been rapidly established as an alternative source of HSC for allogeneic-related and unrelated HSCT. Because UCB is relatively deficient in T cells and its lymphocytes are naive in nature, the possibility that a greater degree of HLA mismatching at 1 to 2 loci might be tolerable without a higher risk for severe GVHD relative to HSCT from a fully matched unrelated donor. The low HSC yields of most cord blood collections has limited the use of this approach to children and perhaps small adults and results in higher rates of graft failure as well as delayed time to engraftment compared to BM transplantation[2,10]. Experimental approaches such as ex vivo expansion of UCB with a cocktail of hematopoietic growth factors or co-transfusion of UCB and mesenchymal cells may enable successful UCB transplantation in adults[11].

The comparison of advantages and disadvantages of HSC from BM, PB and UCB are shown

Table 2. Advantages and disadvantages of HSC from various sources[2,3]

HSC sources	Advantages	Disadvantages
BM	- Adequate HSC content - Low T cell content	- Collect in operating room under general anesthesia
PB	- Adequate HSC content - Rapid engraftment - Ease of collection	- Need administration of hematopoietic growth factors - High T cell content - Increased incidence of chronic GVHD - Could collect in only adequate weight donor for leukapheresis machine
UCB	- Naive HSC - Very low and immature T cell content - Decreased risk of GVHD	- Limited HSC content due to one time collection only - Slow engraftment - Increased risk of graft failure

in Table 2[2,3]. The broader application of HSCT for pediatric diseases has been limited by a lack of HLA-matched donors. Virtually all children, however have at least one haploidentical parent who could serve as a donor. Recent technological advances could overcome the problems of graft rejection and severe GVHD in this haploidentical setting. Haploidentical HSCT is now a viable option for those patients who do not have an HLA matched related or unrelated donor. The relative merits of a haploidentical family donor versus mismatched unrelated BM or UCB donation needs to be assessed in prospective, randomized clinical trials[12].

It has become increasingly clear that allogeneic immunologic effects play key roles in recipient hematopoietic ablation and subsequent tumor cells elimination via allogeneic GVT effect[2,3]. Later studies showed evidence of GVT effect with the observation that relapse rates are lowest in patients with chronic GVHD, higher in patients with no GVHD, and highest in recipients of T cell-depleted allogeneic marrow or syngeneic marrow[3,13]. The subsequent demonstration that effective eradication of host immunohematopoietic stem cells for maintaining graft tolerance and GVT effects can be mediated by donor lymphocytes infusion (DLI) in the process of adoptive allogeneic cell therapy following HSCT[14] strengthened interest in the use of nonmyeloablative conditioning regimens[3]. The primary goal of this approach is to make the recipient tolerant of subsequent DLI with the use of as little cytotoxic conditioning therapy as possible. Hematopoietic SCT after reduced-intensity conditioning, so called mini-transplantation, decreases treatment-related toxicity and mortality while preserving the immune-mediated GVT effect, thereby allowing transplantation in patients who are ineligible for conventional allografting because of underlying poor medical conditions. In the treatment of cancer, the effectiveness of this type of HSCT would thus be due to primarily an immunologic effect on the malignant cells rather than to a direct cytotoxic effect of high-dose chemotherapy[14].

In patients with malignant disease, the mortality caused by GVHD may be counterbalanced by a GVT effect that reduces the incidence of relapse[15]. But with nonmalignant diseases, GVHD is not counterbalanced by any positive effect on disease outcome. Therefore, regimen-related toxicity and the possibility of severe GVHD are major barriers to allogeneic HSCT in these diseases. These concerns are greater with a matched unrelated donor and are substantial with a haploidentical donor[16]. The most reliable way to prevent acute and chronic GVHD is to completely remove T-lymphocytes (CD3+) from the graft by positive selection of CD34+ or negative selection of CD3+ cells. However, the incidence of graft failure increases with the extent of in vitro T-cell depletion, and low T-cell numbers in the graft are predictive of graft failure[16,17]. One way to prevent graft failure despite extensive T-cell depletion, especially in the case of HLA-mismatched HSCT, is to transplant large numbers of CD34+ HSC, so called megadose concept[16,18]. The strategy of this approach is to enhance engraftment by transplant megadose of CD34+ stem cells while maximally reducing residual T-cell contamination of the graft to prevent GVHD[16].

Prior to transplantation, a preparative or conditioning regimen is administered in order to provide the empty hematopoietic space for the infused HSC (myeloablation), to eradicate the patient's disease and, in the case of allogeneic HSCT, to provide sufficient host immunosuppression to prevent graft rejection. The appropriate regimen for any particular patient is determined according to the disease, the source of stem

cells, the type of HSCT and the patient's condition[2,3]. In the treatment of malignancies, preparative regimens are also based on the presumed sensitivity of the particular malignancy being treated. In the setting of major ABO blood group incompatibility, red cell depletion from HSC is indicated before HSC infusion[2]. The duration and severity of neutropenia and immune deficiency after HSC infusion varies widely depending on the conditioning regimen, graft manipulation, choice of graft type (donor and HSC source), development of GVHD and residual thymic activity[2,19]. During this period, supportive care is critical. Patients are at risk for serious infections from various organisms. Accordingly, infections prophylaxis as well as aggressive management of fever in these neutropenic, immunosuppressed hosts is extremely important. Patients require attentive management of transfusions with attention to any ABO differences in the allogeneic HSCT and to adequate irradiation of blood product to prevent transfusion associated GVHD from cellular constituents in the blood product[2,19]. Peripheral blood counts usually begin to increase within one to two weeks of HSCT. Platelets and erythrocyte recover slightly after granulocytes. The use of myeloid growth factor accelerates the engraftment rate. In the allogeneic setting, engraftment can be documented using several cytogenetic techniques, including identification of sex chromosome if donor and recipient are not sex matched, and techniques based on restriction fragment length polymorphism or variable nucleotide tandem repeat[3]. Moreover, in patients with ABO blood group differences from the donor, identification of donor-type red cell antigens also could represent engraftment[1]. The most commonly used regimens for GVHD prophylaxis are cyclosporine A plus methotrexate or cyclosporine A plus methylprednisolone beginning immediately after marrow infusion for 6 months[1]. Although the immediate toxicities that may follow a high-dose conditioning regimen vary according to the specific agents used, but nausea, vomiting, alopecia and oral mucositis do usually occur. So nutritional and psychological support are important[1,3]. Other complications that might occur post HSCT such as veno-occlusive disease of the liver, idiopathic interstitial pneumonia. Occasionally, late complications of HSCT occur such as decreased growth velocity, delayed development of secondary sex characteristics, and infertility[3]. Following HSCT, protective immunity to diseases preventable by routine vaccination is lost over time. Adoptive transfer of immunity from donors to recipients after allogeneic HSCT is not sufficient to prevent this decline. Systemic reimmunization is necessary at appropriate time intervals following transplantation to re-establish immunity. Response to vaccination depends upon the type of transplant, the source of HSC, the immune status of the patient, and the vaccine being used[20]. Live vaccines are generally contraindicated during the first two years post HSCT or as long as the patient is in the immunocompromised state such as chronic GVHD.

In conclusion, HSCT has become an essential component of the treatment of a variety of diseases during the past several decades. The applicability of HSCT has broadened, thereby increasing dramatically the number of transplant recipients worldwide. The HSCT procedure has considerable risk and many patients cannot benefit from the treatment because they lack an appropriate donor. The factors that improve outcome and make HSCT more commonly available treatment modality have been the improved understanding of the critical role of histocompatibility in allogeneic HSCT; the pathophysiology and prophylaxis of GVHD; the identification, collection and expansion of HSC in BM, PB and/or UCB that are capable of sustaining long-lived human hematopoietic reconstitution; the special ex vivo treatment of HSC before infusion and cryopreservation; the identification of essential elements of supportive care during the period of profound hematopoietic ablation and greatest immune compromise; the advances in establishing and maintaining long-term vascular access; and the improved management and prophylaxis of toxicities due to chemoradiotherapy in preparative regimens. The future prospect of HSCT technology is likely to provide leads for research aimed at improving the safety of HSCT.

References

1. Lanzkowsky P. Bone marrow transplantation. In: Lanzkowsky P, ed. Manual of pediatric Hematology and Oncology. 3rd ed. San Diego: Academic press, 2000: 643-68.
2. Guinan EC, Krance RA, Lehmann LE. Stem cell transplantation in pediatric oncology. In: Pizzo PA, Poplack DG, eds. Principles and practice of pediatric oncology. 4th ed. Philadelphia: Lippincott Williams & Wilkins, 2002: 429-51.
3. Appelbaum FR. The current status of hematopoietic cell transplantation. Annu Rev Med 2003; 54: 491-512.
4. Passweg JR. Haematopoietic stem cell transplan-

tation for immune thrombocytopenia and other refractory autoimmune cytopenias. Best Prac Res Clin Hematol 2004; 17: 305-15.
5. Childs RW, Berrett J. Nonmyeloablative allogeneic immunotherapy for solid tumors. Annu Rev Med 2004; 55: 459-75.
6. Vogelsang GB, Lee L, Bensen-Kennedy DM. Pathogenesis and treatment of graft-versus-host disease after bone marrow transplant. Annu Rev Med 2003; 54: 29-52.
7. Davies SM, Kollman C, Anasetti C. Engraftment and survival after unrelated-donor bone marrow transplantation: a report from the National Marrow Donor Program. Blood 2000; 96: 4096-102.
8. Petersdorf EW, Hansen JA, Martin PJ. Major-histocompatibility-complex class I alleles and antigens in hematopoietic cell transplantation. N Engl J Med 2001; 354: 1794-800.
9. Miniero R, Busca A, Bonetti F. Allogeneic transplantation of peripheral blood progenitor cells in children: experience of two pediatric centers. Bone Marrow Transplant 1998; 22(Suppl 5): 33-6.
10. Benito AI, Diaz MA, Gonzalez-Vicent M, Sevilla J, Madero L. Hematopoietic stem cell transplantation using umbilical cord blood progenitors: review of current clinical results. Bone Marrow Transplant 2004; 33: 675-90.
11. Cohen Y, Nagler A. Umbilical cord blood transplantation-how, when and for whom? Blood Reviews 2004; 18: 167-79.
12. Veys P. The role of haploidentical stem cell transplantation in the management of children with haematological disorders. Br J Hematol 2003; 123: 193-206.
13. Horowitz MM, Gale RR, Sondel PM. Graft-versus-leukemia reactions after bone marrow transplantation. Blood 1990; 75: 555-62.
14. Slavin S, Nagler A, Naparstek E. Nonmyeloablative stem cell transplantation and cell therapy as an alternative to conventional bone marrow transplantation with lethal cytoreduction for the treatment of malignant and nonmalignant hematologic diseases. Blood 1998; 91: 756-63.
15. Lee SJ, Klein JP, Barrett AJ. Severity of chronic graft-vs-host disease: association with treatment-related mortality and relapse. Blood 2002; 100: 406-14.
16. Lang P, Klingebiel T, Baden P. Transplant of highly purified peripheral-blood CD34+ progenitor cells from related and unrelated donors in children with nonmalignant diseases. Bone Marrow Transplant 2004; 33: 25-32.
17. Urbano-Ispizua A, Rozman C, Pimentel P. The number of donor CD3(+) cells is the most important factor for graft failure after allogeneic transplantation of CD34(+) selected cells from peripheral blood from HLA-identical siblings. Blood 2001; 97: 383-7.
18. Reisner Y, Martelli MF. Tolerance induction by "megadose" transplants of CD34+ stem cells: a new option for leukemia patients without an HLA-matched donor. Curr Opin Immunol 2000; 12: 536-41.
19. Peggs K. Immune reconstitution following haematopoietic stem cell transplantation. Br J Haematol 2004; 124: 407-20.
20 Singhal S, Mehta J. Reimmunization after blood or marrow stem cell transplantation. Bone Marrow Transplant 1999; 23: 637-45.

การปลูกถ่ายเซลล์ต้นกำเนิดเม็ดเลือดในเด็ก

กลีบสไบ สรรพกิจ

การปลูกถ่ายเซลล์ต้นกำเนิดเม็ดเลือดหรือการปลูกถ่ายไขกระดูกเป็นวิธีการรักษาที่เป็นที่ยอมรับแล้วว่าสามารถรักษาโรคหลายโรคในเด็กให้หายขาดได้ทั้งโรคเลือด เช่น โรคโลหิตจางธาลัสซีเมียที่มีอาการรุนแรง โรคไขกระดูกฝ่อชนิดรุนแรง โรคมะเร็งที่ตอบสนองต่อการรักษาด้วยยาเคมีบำบัดไม่ดี เช่น โรคมะเร็งเม็ดเลือดขาวชนิดเฉียบพลันและเรื้อรัง โรคมะเร็งต่อมน้ำเหลืองบางชนิด และมะเร็งของอวัยวะบางชนิด รวมทั้งโรคทางภูมิคุ้มกันบกพร่อง เช่น Severe combined immunodeficiency disease และโรคที่เกิดจากความผิดปกติทางพันธุกรรม เช่น Storage disease บางชนิด เป็นต้น หลักการรักษาคือ การให้ยาเคมีบำบัดขนาดสูงเพื่อไปทำลายเซลล์ที่ผิดปกติต่าง ๆ ในไขกระดูก โดยเซลล์ต้นกำเนิดเม็ดเลือดที่ปกติจะถูกทำลายไปด้วย ทำให้เกิดช่องว่างในโพรงกระดูก แล้วจึงให้เซลล์ต้นกำเนิดใหม่ที่ปกติเข้าไปเพื่อเพิ่มจำนวนและแบ่งตัวในโพรงกระดูกของผู้ป่วย ในส่วนของการรักษาโรคมะเร็งชนิดต่าง ๆ การปลูกถ่ายไขกระดูกทำให้สามารถเพิ่มปริมาณยาเคมีบำบัดหรือการฉายรังสีรักษาได้เต็มที่ เพื่อให้มีประสิทธิภาพในการกำจัดเซลล์มะเร็งที่หลงเหลืออยู่โดยไม่ต้องคำนึงถึงผลข้างเคียงในแง่ของการทำลายเซลล์ต่าง ๆ ในไขกระดูกซึ่งเป็นผลข้างเคียงที่ขึ้นกับขนาดของยาที่ใช้เพราะสามารถให้เซลล์ต้นกำเนิดใหม่เข้ามาทดแทนได้

การปลูกถ่ายเซลล์ต้นกำเนิดเม็ดเลือดแบ่งออกเป็น 3 ชนิด คือ การปลูกถ่ายเซลล์ต้นกำเนิดโดยใช้เซลล์ของผู้ป่วยเองเก็บไว้ก่อนให้ยาเคมีบำบัดขนาดสูง (Autologous HSCT) โดยใช้เซลล์จากฝาแฝดไข่ใบเดียวกัน (Syngeneic HSCT) และโดยใช้เซลล์ของผู้อื่นซึ่งมี Human leukocyte antigen (HLA) ตรงกันกับผู้ป่วย (Allogeneic HSCT) โดยพี่น้องแต่ละคนของผู้ป่วยมีโอกาสที่ HLA จะเข้ากันได้เพียง 25% แหล่งของเซลล์ต้นกำเนิดเม็ดเลือดสามารถเก็บได้จากไขกระดูก จากหลอดเลือดโดยใช้ยากระตุ้นเม็ดเลือดขาวเพื่อให้เซลล์ต้นกำเนิดออกมาในกระแสเลือดแล้วเก็บด้วยเครื่อง leukapheresis และจากสายสะดือ ขั้นตอนในการรักษาจะต้องมีการเตรียมผู้ป่วยด้วยการให้ยาเคมีบำบัดหรือ การฉายรังสีขนาดสูง (Preparative regimens) ก่อนที่จะให้เซลล์ต้นกำเนิดเม็ดเลือดที่ปกติ ภายหลังการรักษาผู้ป่วยจะมีภูมิต้านทานต่ำมากและมีโอกาสติดเชื้อได้ง่าย จึงต้องการการดูแลเป็นพิเศษทั้งในเรื่องของการป้องกันและรักษาการติดเชื้อ และผลแทรกซ้อนต่าง ๆ จาก preparative regimens ที่ให้ รวมถึงปฏิกิริยา Graft versus host disease Venocclusive disease ภาวะทางโภชนาการ และจิตใจของผู้ป่วย ตลอดจนผลแทรกซ้อนในระยะยาวที่อาจเกิดขึ้นตามมาภายหลัง

การพัฒนาวิธีการรักษาด้วยการปลูกถ่ายไขกระดูกเกิดขึ้นอย่างต่อเนื่อง มีการนำเซลล์ต้นกำเนิดเม็ดเลือดจากผู้อื่นที่ไม่ใช่ญาติผู้ป่วย แต่มี HLA เข้ากันได้มาใช้ (Unrelated HSCT) เพื่อเพิ่มโอกาสในการได้ผู้บริจาคเซลล์ต้นกำเนิดเม็ดเลือด การลดขนาดของ preparative regimens ที่ให้ (Nonmyeloablative HSCT) เพื่อลดผลแทรกซ้อนและอัตราการตายจากการรักษา โดยอาศัยปฏิกิริยาทางภูมิคุ้มกันจาก lymphocyte ของผู้บริจาค (Donor lymphocyte infusion) ที่ให้ภายหลังการให้เซลล์ต้นกำเนิดเม็ดเลือดเพื่อรักษาการ engraftment และทำลายเซลล์ผิดปกติที่ยังอาจหลงเหลืออยู่ในผู้ป่วย การลดปริมาณ T-lymphocyte ที่ปนอยู่ในเซลล์ต้นกำเนิดเม็ดเลือด (T cell depleted HSC) และการทำเซลล์ต้นกำเนิดเม็ดเลือดให้บริสุทธิ์โดยการแยก CD34(+) ออกมาใช้ ทำให้สามารถใช้เซลล์ต้นกำเนิดเม็ดเลือดจากบิดามารดาที่มี HLA ตรงกับผู้ป่วยเพียงครึ่งเดียวได้ (Purified CD34+ haploidentical HSCT) นอกจากนี้การพัฒนาเกี่ยวกับเทคนิคต่าง ๆ ในการเก็บรักษา การเพิ่มปริมาณเซลล์ต้นกำเนิดเม็ดเลือด และการดูแลผลแทรกซ้อนต่าง ๆ ที่อาจเกิดขึ้นจากการรักษา ทำให้สามารถใช้การปลูกถ่ายไขกระดูกรักษาโรคต่าง ๆ ได้เพิ่มขึ้น โดยมีแนวโน้มของผลสำเร็จในการรักษาดีขึ้น และผลแทรกซ้อนในการรักษาลดลง