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Report

American Society of Transplantation and Cellular Therapy International Affair Committee: Report of the Third Workshop on Global Perspective to Access to Transplantation at the 2022 Tandem Meeting

Shinichiro Okamoto[1], Minako Iida[2], Nada Hamad[3,4,5], Fernando Barroso Duarte[6], Anna Sureda[7], Alok Srivastava[8], Sebastian Galeano[9], Nelson Chao[10], Damiano Rondelli[11], Mary E. Flowers[12,*], on behalf of the Asia-Pacific Blood and Marrow Transplantation Group (APBMT), Australia and New Zealand Transplant and Cellular Therapy (ANZTCT), Brazilian Society of Blood and Marrow Transplantation (SBTMO), European Society for Blood and Marrow Transplantation (EBMT), Indian Society for Blood and Marrow Transplantation (ISBMT), Latin America Bone Marrow Transplantation Group (LABMT)

[1] *Division of Hematology, Department of Medicine, Keio University School of Medicine, Tokyo, Japan*
[2] *Department of Promotion for Blood and Marrow Transplantation, Aichi Medical University School of Medicine, Nagakute, Japan*
[3] *Department of Hematology, St. Vincent's Hospital, Sydney, Australia*
[4] *School of Clinical Medicine, Faculty of Medicine and Health, University of New South Wales, Sydney, Australia*
[5] *School of Medicine, University of Notre Dame Australia, Sydney, Australia*
[6] *Hospital Universitario Walter Cantídio, Universidade Federal do Ceara, Fortaleza, Brazil*
[7] *Clinical Hematology Department, Institut Català d'Oncologia-Hospitalet, Barcelona, Spain*
[8] *Department of Hematology, Christian Medical College, Kilminnal, Ranipet, Tamil Nadu, India*
[9] *Department of Hematology, Hospital Británico, Montevideo, Uruguay*
[10] *Division of Hematologic Malignancies and Cellular Therapy, Duke University, Durham, North Carolina*
[11] *Division of Hematology and Oncology; Blood & Marrow Transplant Section, Department of Medicine, University of Illinois College of Medicine, Chicago, Illinois*
[12] *Clinical Research Division, Fred Hutchinson Cancer Center and Department of Medicine, University of Washington School of Medicine, Seattle, Washington*

INTRODUCTION

In 2019, the American Society of Transplantation and Cellular Therapy (ASTCT) created the International Affair Committee (IAC) to promote international relationships and activities engaging world leaders and trainees contributing to the development of hematopoietic stem cell transplantation (HCT) and cellular therapy. Particularly, the IAC supports ASTCT members engaged in international relationships that value the importance of conjugating scientific advances with real-life opportunities for improving access and enhance research and education collaborations in countries with limited resources. An international Council was formed as an advisory board for educational sessions at Tandem Meetings and elsewhere, with its first meeting held at the 2000 Tandem Meetings. The Council works with ASTCT-IAC members to propose themes and talks for the ASTCT International Workshop at the Annual Tandem Meetings. So far, there have been 3 ASTCT International Workshops. The topic of the first workshop was "Barriers to Transplant" (2020), and that of the second workshop was "Perspective on Post-Transplant Cyclophosphamide GVHD Prophylaxis" (2021).

Here we provide a summary of the Third ASTCT International Workshop, "Global Perspective on Access to Transplantation" (2022), which included representatives of 6 international societies with which ASTCT had agreements: the Asian Pacific Bone Marrow Transplantation Group (APBMT), Australian & New Zealand Transplantation and Cellular Therapy (ANZTCT), Brazilian Society of Bone Marrow Transplantation (SBTMO), European Society of Bone Marrow Transplantation (EBMT), Indian Society of Bone Marrow Transplantation (ISBMT), and Latin American Society of Bone Marrow Transplantation (LABMT).

To address the "Global Perspective on Access to Transplantation" theme of the Workshop, presenters were asked to prepare a short presentation that addressed the following questions:

- Describe a major issue you have confronted and resolved and how you did it.
- What is going on in your society? Are member numbers rising or falling?
- What are issues with training and workforce development and how are you addressing them?
- Is there a standardization to your process? If yes, what do you use for it?

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*Correspondence and reprint requests: Mary E. Flowers, Clinical Research Division, Fred Hutchinson Cancer Center, 1354 Aloha St, Seattle, WA 98109
E-mail address: mflowers@fhcrc.org (M.E. Flowers).

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ACCESS TO TRANSPLANTATION: ASIA-PACIFIC (AP) PERSPECTIVE

Shinichiro Okamoto, MD, PhD and Minako Iida, MD, PhD, on behalf of the Asia-Pacific Blood and Marrow Transplantation Group

As of April 2022, 22 countries/regions participate in the Asia-Pacific Blood and Marrow Transplantation Group (APBMT), and hematopoietic cell transplantation are actively performed in all of these countries and regions except 1 (Cambodia). Since 2006, the APBMT Data Center has been continuously performing a survey on the activity of all forms of HCT [1,2]. The survey collects data on the types of HCT, donor and stem cell sources, and the diseases for which HCT are indicated. The survey data have been used to analyze the latest trends in HCT throughout the AP region to promote HCT in both emerging and developed countries/regions and encourage collaboration on various international studies.

The annual numbers of both allogeneic and autologous HCTs performed in all participating countries/region have continued to increase, and the number of allogenic and autologous HCTs reached approximately 18,000 and 10,000, respectively, in 2019. The degree of annual increase in the number of autologous HCT and allogeneic HCT using unrelated donor or cord blood unit remained unchanged since 2006. Notably, however, the annual number of allogeneic HCTs began to increase steeply around 2013. This can be explained by the rapid increase in the use of related donors for haploidentical transplantation [3]. These data indicate that HCT has been actively performed in AP regions.

The survey also demonstrates the significant differences among the countries and regions that participated in this survey [4]. Since 2014, the number of transplant centers has significantly increased in China, India, Sri Lanka, Thailand, and the Philippines, whereas the numbers decreased in Japan and Taiwan and remained unchanged in the remaining countries. Over the past decade, the annual number of HCTs has increased significantly in China, India, Pakistan, Thailand, and Vietnam and increased only modestly or remained unchanged in the remaining countries/regions. Although the number of centers has decreased in Japan over time, the overall number of HCT centers is still high compared to other countries because HCT is routinely performed by hematology departments, and most procedures are covered under the Japanese national health insurance scheme.

Despite the huge disparities in socioeconomic status among countries in the AP region, the use of HCT has increased steadily in all APBMT member countries over the past decade. The total number of transplantations per 10 million population is higher in Australia, Hong Kong, Japan, Korea, and Singapore. However, among the 18 participating countries/regions, the transplantation rate per population varied widely according to the absolute number of HCTs and the national/regional population size. Although it is plausible to speculate that the access to HCT remains limited in the AP region, how many patients are actually in need of HCT and how many of them actually undergo transplantation remain to be elucidated, especially in emerging countries.

To address this issue, the APBMT conducted a simple questionnaire survey among our member countries/regions. First, we asked what percentage of patients in need of HCT can actually receive this treatment. Twenty out of 22 countries and regions replied. The access rate exceeded 75% in only one-quarter of the countries and region, including Japan, Korea, Singapore, Taiwan, and Australia, all countries and regions with an aging population. The access rate was 50% to 75% in Hong Kong, Iran, and China and <50% in the remaining 9 countries. We then asked which factors are impeding the access to HCT in the 18 countries in which the access rate to HCT was <75%, and 14 countries responded. The number one impediment identified was the financial constraints of patients (85%), followed by inadequate government funding (71.4%), inadequate number of HCT centers (71.4%), lack of donors due to the lack of donor registry/cord blood banks (64.3%), and lack of health insurance (57.1%). Some countries also cited inadequate laboratory infrastructure support and public awareness of HCT (35.7% and 28.6%, respectively). Regarding the inadequate infrastructure support, most responders pointed at the lack of drug and other supportive services, followed by trained healthcare personnel and appropriate laboratory facilities (83.3% and 67.7 %, respectively). Regarding the question of how APBMT can help foster HCT in the country and region, most responders requested educational activities such as web seminars, and more training opportunities for physicians, nurses, and other personnel. This survey confirmed that there is an unmet need for HCT, and that access to HCT is limited in more than 50% of APBMT participant countries and regions.

To address this last need, the APBMT has been working with countries and regions in which the access to HCT is still limited. One example is the experience of Saint Vincent Hospital (SVH) in Sydney. This APBMT affiliation included training Sri Lankan visiting physicians/nurses and other staff involved in HCT at SVH for 6 months in 2014. The SVH staff continued to educate and training via the web, resulting in the first successful autologous HCT performed in Sri Lanka in 2016. Another example is the workshop organized by the Philippine Society for Blood and Marrow Transplantation (PSBMT) in 2017 to promote HCT in the Philippines. The participants in this workshop included officials from various government agencies, representatives of HCT transplant societies, and patient advocacy groups. Representatives from the APBMT and Worldwide Network for Blood & Marrow Transplantation also participated. As a result, the PSBMT was able to secure sufficient support to build a transplantation unit and procure much-needed medicines and other supplies necessary to offer HCT for those in need.

In conclusion, there remains an unmet need for HCT in more than 50% of APBMT participant countries and regions, especially in countries with rapidly expanding population. To increase the access to HCT and improve the quality of this treatment in our region, efficient collaboration not only within our region, but also at a global level, is crucial.

ACCESS TO TRANSPLANTATION: AUSTRALIA AND NEW ZEALAND PERSPECTIVE

Nada Hamad, MBBS, FRACP, FRCPA, on behalf of Australia and New Zealand Transplant and Cellular Therapy (ANZTCT)

Department of Hematology, St Vincent's Hospital, Sydney, Australia; School of Clinical Medicine, Faculty of Medicine and Health, University of New South Wales, Sydney, Australia; and School of Medicine, University of Notre Dame, Sydney, Australia

Australia and New Zealand Transplant and Cellular Therapies (ANZTCT) is a society consisting of medical graduates and scientists involved in the clinical or laboratory management of patients undergoing blood or marrow stem cell transplantation and cellular therapy (TCT) or with a research interest in this field. The goals of the society are to:

- Improve the outcome for Australians and New Zealanders undergoing transplantation of TCT through innovation and

improvements in clinical care and advocate for better patient access
- Foster clinical and laboratory research in TCT
- Monitor and facilitate the professional education and training of health workers involved in TCT
- Form collaborative links with other international organizations with similar objectives
- Track TCT activity and outcomes via the Australasian Bone Marrow Transplant Recipient Registry (ABMTRR).

The ABMTRR was established in 1992 operating under the auspices of the ANZTCT and records TCT outcomes from all centers in Australia and New Zealand. The Registry now holds data on more than 43,000 transplants and includes approximately170,000 patient-years of follow-up from 40 centers in Australia and 6 centers in New Zealand.

Both Australia and New Zealand have publicly-funded health care and TCT services, with transplant centers concentrated in metropolitan areas. Although there are regional autologous HCT centers, allogeneic HCT and cellular therapies are delivered predominantly in metropolitan centers. Not all states in Australia have access to autologous and allogeneic HCT and cellular therapy centers, producing geographic and financial access challenges for patients who would have to geographically relocate to access these services, especially for allogeneic HCT and cellular therapies. There are 11 adult and 4 pediatric allogeneic HCT centers in Australia and 3 adult and 1 pediatric centers in New Zealand. Cellular therapy centers have emerged only recently, with 6 adult and 3 pediatric centers in Australia and 1 adult center in New Zealand offering access to clinical trials to adults.

Global annual HCT rates continue to steadily increase. In 2020, 1251 autologous HCTs, 611 allogenic HCTs, and 63 chimeric antigen receptor T cell (CAR T) therapies were performed in Australia and 229 autologous HCT, 114 allogenic HCT, and 4 CAR T therapies were performed in New Zealand [5]. Factors driving this growth include expanded disease indications, greater donor options (expanding unrelated donor registries and use of haploidentical HCT), and accommodation of older and less fit recipients [6]. Disease-related trends include increases in autologous HCT for multiple myeloma and in allogenic HCT for acute myeloid leukemia. Although more than one-half of allogeneic HCTs are from unrelated donors, there has been a consistent increase in the use of haploidentical donors. The stem cell source remains predominantly peripheral blood, with a gradual decline in bone marrow and cord blood use. There has been an increase the use of in both autologous and allogeneic HCT in patients age >60 years, with 46% of HCTs in Australia and 40% of HCTs in New Zealand now performed in that age group.

Data are limited on the rate of HCT in First Nations people. In Australia, 16 HCTs were performed in patients identifying as Aboriginal or of Torres Strait Islander decent; however, 593 patients had an unknown status regarding to this data field. The ABMTRR does not have data on Maori or Pacific Islander decent for New Zealand. No data are collected in the registry on other ethnicities [5]. Both Australia and New Zealand are very ethnically diverse and rely heavily on international unrelated donors (>80%). The Australian Bone Marrow Donor Registry is advocating for growth of the local Australian donor pool, and in New Zealand the Registry recruits exclusively Maori and Pacific Islander donors to focus resources on this underrepresented population in international registries.

The health and outcomes of long-term survivors after HCT are areas of evolving interest. A recent ABMTRR study compared mortality rates in standard Australian and New Zealand healthy populations using relative survival analysis for HCT between 2002 and 2011. A total of 1562 allogeneic HCT recipients and 3822 autologous HCT recipients were included, with a median follow-up of 5.6 years. Long-term survival rates after allogeneic and autologous HCT were very similar to those in a historic cohort from 1992 to 2001 despite changes in practice over time. Recipients of autologous HCT for myeloma demonstrated substantially lower overall survival than recipients of autologous HCT for other indications, with no clear plateau. The survival of patients who were relapse-free at 2 years after allogeneic or autologous HCT was compared with the survival of the general population after adjustments for year of transplantation, sex, age group, and country to account for the differences between the 2 groups [7]. The point estimates of relative survival during each of the 8 years of follow-up after the 2-year landmark ranged from .96 to .99 for allogenic HCT recipients and from .89 to .96 for autologous HCT recipients. Late deaths were due primarily due to non-relapse-related causes after allogeneic HCT, but relapse or disease progression remained prominent for recipients of autologous HCT, particularly these with myeloma. This data will aid future planning to account for the impact of the expected increases in transplantation activity and number of survivors on resource utilization [6].

The ANZTCT has taken a proactive interest in meeting the necessary quality demands as TCT activity increases. The ANZTCT has developed formal memoranda of understanding and joint membership strategies with the American Society for Transplantation and Cellular Therapy, the European Society for Blood and Marrow Transplantation, and Cellular Therapy Transplant Canada. These arrangements are focused on enhancing access to education and research opportunities for Australian and New Zealand TCT service providers.

These collaborations were also very fruitful during the Coronavirus disease 2019 (COVID-19) pandemic, as the exchange of strategies to maintain services and protect patients, including a shift to frozen products [8], was vital to our pandemic response in the TCT community [8–13]. In Australia and New Zealand, there was a successful early public health response and coordinated transplant community activities that made the ongoing safe delivery of TCT possible during the first year of the pandemic. However, there was a 13% reduction in the number of HCTs, consistent across most disease groups and donor types [13]. Haploidentical transplants were the only donor type that increased, although this increase did not compensate for the declines in other transplant types. Patients with hematologic malignancies might have been adversely impacted by postponement or abandonment of a potentially curative therapy. The delay from request to infusion, which was particularly pronounced for unrelated donor HCTs, appears to have contributed to this reduction [13]. With both Australia and New Zealand now transitioned away from a COVID-19 elimination strategy, ongoing efforts will be necessary to protect vulnerable patients and maintain services.

The ANZTCT is committed to collaborating with governments, patient organizations, industry partners, and centers to promote high-quality TCT clinical practices driven by evidence from the ABMTRR and to promote and support FACT/JACIE accreditation. The ANZTCT advocates for equity of access and outcomes in TCT, especially for emerging therapies, including CAR-T therapies, for all Australian and New Zealand patients through research and stakeholder engagement.

ACCESS TO TRANSPLANTATION: BRAZIL'S PERSPECTIVE

Fernando Barroso Duarte, MD, PhD, on behalf of the Brazilian Society of Blood and Marrow Transplantation and Cellular Therapy (SBTMO)

Hospital Universitario Walter Cantídio, UFC, Fortaleza, Brazil; President of SBTMO

To put the access to bone marrow transplantation (BMT) in Brazil into context, it is important to provide a historical perspective about the development of BTM in Brazil. The first BMT in Brazil was performed by Dr Ricardo Pasquini and his group in Paraná in 1979 [14]. In 1996, the SBTMO was created, and since then it has been an impactful reference in the areas of BMT and cellular therapy, stimulating scientific production, continuing education, and constant updating of treatment protocols. Currently, the SBTMO has more than 1000 associate members, with growth of 40% over the last 2 years. The SBTMO has developed training and qualification actions for professionals, including update programmers and regional meetings and an education program for young physicians and other multidisciplinary professionals aimed at increasing interest in BMT to help prepare future generation and improve BMT teams in Brazil [15].

The Brazilian Transplant Registry (RBT) of the Brazilian Association of Organ and Tissue Transplants (ABTO) provides quantitative indicators and survival data. In 2021, a total of 3826 BMTs were reported, including 1547 allogeneic BMTs and 2279 autologous BMTs [16]. However, in Brazil, there was no specific and consolidated registry of BMT, and the Brazilian Registry of Bone Marrow Transplantation was created in partnership with the Center for International Blood and Marrow Transplant Research (CIBMTR). Many Brazilian centers do not have electronic information systems, and those that do face difficulties in organizing and standardizing data, making it difficult to analyze important indicators.

Given this reality, many centers in Brazil have adopted globally available registry systems, such as the Center for International Blood and Marrow Transplant Research (CIBMTR), a North American platform created in 2004 [17]. Brazil's relationship with the CIBMTR began with the affiliation of Hospital de Clínicas-Universidade Federal do Paraná (HC-UFPR) and with the BMT Program of the Brazilian National Institute of Cancer in Rio de Janeiro, before the National Marrow Donor Program and the IBMTR combined to form the CIBMTR. Subsequently, other Brazilian centers joined the CIBMTR. For data to be sent to the CIBMTR, approval by the National Research Ethics Commission is required. There are currently 67 centers approved by Comissão Nacional de Ėtica em Pesquisa (CONEP), of which 39 are active, 24 are set up, and 4 are inactive [18].

The Brazilian public health insurance (SUS) provides coverage of BMT to its citizens for indications approved by a governmental health agency. The access to HCT in Brazil has increased in recent years owing to the joint efforts of researchers and institutions; however, access to HCT is still limited considering the large Brazilian population and lack of BMT in certain regions. Recently, to determine the impact of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic on access to HCT in Brazil, a survey was carried out to identify the protocols adopted by all BMT centers, difficulties that each center encountered, and measures that were taken. The questionnaire was published on the website of the SBTMO and completed by health technicians from Brazilian HCT units in May to June 2020 and analyzed in April 2021. The results were published in the *Journal of Bone Marrow Transplantation and Cellular Therapy* and presented at the 2022 meeting of . The study showed that such factors as a better understanding of the disease and access to molecular diagnosis for patients and health professionals facilitated the increase in center operationalization over the months of the study [19].

A constant concern is the standardization of the HCT procedures (pre- and post-) and new cell therapies that have gradually become a reality in Brazil. Considering this issue, in 2021, SBTMO published the consensus guidelines for HCT in the *Journal of Bone Marrow Transplantation and Cellular Therapy* [20].

In the same year, the name of SBTMO was changed to the Brazilian Society of Bone Marrow Transplantation and Cell Therapy, and the Cell Therapy Committee was created. SBTMO has partnered with FACT (Foundation for the Accreditation of Cellular Therapy) to develop a FACT-SBTMO Cell Therapy Accreditation Program in Brazil. This partnership is based on mutual interaction and strengthening of the relationship between SBTMO and FACT at the strategic and work levels, focusing on the standardization and accreditation of cellular therapy in Brazil.

SBTMO projects regarding HCT in Brazil in the coming years include, among other aspects, compiling a more accurate record of the reality of HCT in Brazil, making it possible to devise strategies to improve patient care and performance of the procedure; instituting mandatory data reporting or even differentiated qualification of reporting centers; and developing HCT expansion programs in regions of unmet need, particularly in the north and northeast of Brazil.

SBTMO's involvement with new technologies is also important and necessary to continue the mission of maintaining the quality of the HCT program in our country via strong collaboration and participation in clinical research following ethical principles that aim to provide best care to our patients.

ACCESS TO TRANSPLANTATION: THE EUROPEAN BLOOD AND MARROW TRANSPLANTATION AND CELLULAR THERAPY (EBMT) PERSPECTIVE

Anna Sureda, MD, PhD, Clinical Hematology Department, Institut Català d'Oncologia-Hospitalet, Barcelona, Spain on behalf of the EBMT; President of the EBMT

HCT is an established procedure for many acquired or inherited disorders of the hematopoietic system, both benign and neoplastic, including those of the immune system, and as enzyme replacement in metabolic disorders [21]. The EBMT's activity survey describing the status of HCT has become an instrument for observing trends and monitoring changes in HCT technology in Europe and neighboring countries [22,23]. The survey captures the numbers of HCTs from highly committed participating centers, stratified by indication, donor type, and stem cell source. In the last few years, the survey also has included information on cellular therapies with hematopoietic cells for uses other than to replace the hematopoietic system. The last survey was published by Passweg et al. [24] in 2021, looking at data from 2019. Of the 700 centers, 451 (64%) performed both allogeneic and autologous HCTs, 229 (33%) restricted their activity to autologous HCT, and 18 (3%) performed allogeneic HCT only. In 2019, 48,512 HCTs were reported in 43,581 patients (first transplantation), including 19,798 allogeneic HCTs (41%) and 28,714 autologous HCTs (59%). The main indications for allogeneic HCT were myeloid malignancies (n = 10,518; 98% allogeneic and 2% autologous HCT). For autologous HCT, the main indications were lymphoid malignancies (n = 22,640; 19% allogeneic and 81% autologous HCT). Assessing transplantation rates per 10 million population (TR) allows for comparisons of activity in countries with widely different population numbers. Center density per

10 million population allows the comparison of activity by the number of centers. The TR rates for allogeneic HCT ranged from .2 in Nigeria to 476.1 in Israel (median: HCT, 127; TR, 144). Five countries did not report any allogeneic HCTs (Armenia, Bosnia and Herzegovina, Cyprus, Iceland, and Luxembourg). For autologous HCT, rates ranged from 2.3 in Syria to 625 in Switzerland (median: HCT, 181; TR, 281).

The heterogeneity in TR values motivated us to produce a survey among EBMT centers to better identify barriers to HCT access and education. The survey was sent to centers in countries that reported data in 2019 and met the following criteria: ≤ allogeneic HCT/10 million, ≤300 autologous HCT/10 million, and ≤CAR T cell treatments/10 million. Fifty-eight centers responded. Preliminary results were quite relevant; the most important factor in accessibility to both allogeneic and autologous HCT was patient referral (62% and 57%, respectively), followed by financial and insurance status (22%) and support (19%) in the allogeneic HCT setting and financial/insurance status and family support (28% each) in the autologous HCT setting. Financial/insurance aspects, regulatory issues, and center qualification were the 3 most relevant factors when discussing CAR T cell therapies (55%, 28% and 24%, respectively).

Education is one of the most important pillars for EBMT. The Society offers a range of courses, events, online tools, and collaboration opportunities to EBMT members and others involved in HCT and cellular therapy and related fields. The *EBMT Handbook* has become the manual of choice for doctors and practitioners involved in HCT and cellular therapy. Discussing all types of stem cell and bone marrow transplantation, including haploidentical stem cell and cord blood transplantation, the *Handbook* also covers indications for transplantation, management of early and late complications, as well as the new and rapidly evolving field of cellular therapies. The *EBMT Nurses Textbook* was written by and for nurses with an interest in HCT and is the first book of its kind in the field. It brings together the knowledge of nursing leaders in HCT and nursing care to provide nurses with a comprehensive and informative guide covering all aspects of transplantation nursing, from basic principles to advanced concepts. The JACIE accreditation program also has its own open access book that provides a concise yet comprehensive overview on how to build a quality management program for HCT and cellular therapy. The text reviews all the essential steps and elements necessary for establishing a quality management program and achieving accreditation in HCT and cellular therapy. Specific areas of focus include document development and implementation, audits and validation, performance measurement, writing a quality management plan, the accreditation process, data management, and maintaining a quality management program. The first open access *European CAR-T Handbook*, co-promoted by EBMT and the European Hematology Association (EHA), covers several aspects of CAR T cell treatments, including the underlying biology, indications, management of side effects, access, and manufacturing issues. This book, written by leading experts, provides an unparalleled overview of the CAR T cell technology and its application in clinical care, to enhance readers' knowledge and practical skills.

To better promote education within the EBMT and taking into consideration the impact of the COVID-19 pandemic in our lives, the EBMT has also developed a sophisticated e-learning platform that provides online training as well as serves as a repository for the information currently located on the e-materials and Document Center pages. The EBMT is offering free, live webinars hosted by experts for all EBMT members. Preliminary information obtained from our survey indicated that the most important topics for which education was lacking were prevention and treatment of relapse, JACIE accreditation, and quality of life (43%, 39%, and 25%, respectively) in the allogeneic HCT setting and prevention and treatment of relapse, JACIE accreditation, conditioning regimens, and post-transplantation complications in the autologous HCT setting.

The efforts of the EBMT to reach out to the global community have been crystalized in the development of 2 additional committees. In June 2021, the EBMT Board approved creation of the EBMT Equality, Diversity, and Identity (EDI) Committee. EDI outcomes are now reported annually to the EBMT Board. At the EBMT, we believe that closer attention to EDI issues is critical to providing the very best service to our worldwide patient community. In addition, the EBMT Trainee Committee was established in 2021 on behalf of the young ambassadors of 2020, with the overall aim of addressing the specific needs of trainees working in bone marrow transplantation and cellular therapy, as well as providing advice and support for trainees at all levels. The group is composed of trainees and young investigators with a broad range of experience and interests and provides a platform for trainees to engage with the wider EBMT community.

In summary, it is very clear that access to stem cell transplantation is very heterogenous at a European level and that many factors account for these differences. Education is also a need, and the EBMT is already handling educational activities aimed at the different health care professionals involved in the transplantation process. Certainly, these activities will need to be optimized in the future to better meet the needs of our growing community of members.

ACCESS TO TRANSPLANTATION: INDIA'S PERSPECTIVE

Alok Srivastava, MD, FRACP, FRCPA, FRCP, Christian Medical College, Vellore, India, on behalf of The Indian Society for Blood and Marrow Transplantation (ISBMT)

HCT was initiated in India in 1983 [25], followed by the opening of a second center in 1986 [26,27]. Progress was slow initially, with only 11 HCT centers established over the first 2 decades, but this was offset by robust growth over the last 2 decades, during which more than 100 additional HCT centers became functional. The annual number of HCTs performed was <50 at the end of the first decade of HCT activity in India, increased to ~200 in the second decade, ~1200 in the third decade, and currently stands at ~2500. To date roughly 25,000 HCTs have been performed in India, nearly 75% of them in the last decade, according to data collected by the ISBMT registry [28].

Approximately 60% of all HCTs performed in India are allogenic, and the other 40% are autologous. Over the last decade, approximately one-third of all HCTs, and more than one-half of allogenic HCTs in India are performed in pediatric patients (age <18 years). Multiple myeloma and relapsed lymphomas are the major indications for autologous HCT, and thalassemia major, acute myeloid leukemia, and bone marrow failure syndromes are the most common indications for allogenic HCT.

Alternative donor HCT also has increased over the last decade in India. Matched unrelated donor (MUD) transplants are now used in approximately 10% of a allogeneic HCTs, and over the last 5 years, haploidentical transplants have rapidly increased, now accounting for nearly 40% of allogeneic HCTs in India. Apart from access to international donor registries, the establishment of several Indian donor registries have increased the likelihood of finding suitable donors for MUD HCTs. Larger families provide multiple options for haploidentical donors as well.

Several factors have led to this growth, of which comprehensive training in hematology at university-affiliated programs in India, including training in HCT, beginning in the year 2000 is perhaps the most important. Many more training opportunities exist today. Other contributing factors include the improving Indian economy [29] and resulting enhanced access to health care with a robust local pharmaceutical industry that, along with the multinational pharmaceutical companies, ensure that all necessary drugs and other supportive requirements for HCT are available in India [30]. Unlike many other low- and middle-income countries, all drugs and disposable equipment required for HSCT can be locally sourced within India, including access to specialized laboratory tests that may not be available in every HCT center.

The ISBMT maintains a registry of all HCT activity in India. Although activity data has been systematically and accurately collected for more than 2 decades, obtaining outcome data for this registry in the elaborate international formats has been more challenging. Several centers report to the CIBMTR registry and/or EBMT registry, but the vast majority are unable to cope with their formats. Therefore, we have developed a minimum outcome dataset (Table 1). In this format, it has been possible to collect enough outcome data to identify major complications, survival, and causes of mortality. The ISBMT has an arrangement with an independent data management group in an academic institution to collect, host, and analyze all HCT data reported to the ISBMT. Our efforts are now focused on ensuring completeness of the outcomes data. The ISBMT also organizes annual training programs for data management for its member centers.

To address the need for standards for HCT in India, the ISBMT has prepared a document enumerating the minimum requirements for centers in India, balancing what may be ideal with what is practical at this time in the country. This remains a work in progress as we also work with the APBMT to adapt and adopt the JACIE/FACT approach to accreditation for HSCT centers. Some HCT centers in India also seek direct accreditation from JACIE/FACT.

These advances in HCT services and access in India are very encouraging. However, several gaps remain to be addressed. Whereas the more established older centers have teams of physicians, many of the recently established centers function with a single HCT-trained physician. This situation certainly is not ideal, but it does address a great need in India by making these services more widely available outside of the major cities. As these centers expand their services, the number of transplant physicians also increases. Nearly 90% of the current HCT centers are included in India's private healthcare system. With enhanced funding anticipated within the public healthcare system, this should change in the near future, further improving access to HCT. Even though the cost of HCT in India is <10% of that in the United States, cost remains the major barrier to access to HCT in India. Financial support for HCT from various government schemes is increasing, as is support from employers and insurance providers, making HCT increasingly accessible to patients. The transplantation density in India is still much lower than what is required, a gap that needs to be bridged.

ACCESS TO TRANSPLANTATION: LATIN AMERICA'S PERSPECTIVE

Sebastian Galeano, MD, Department of Hematology, Hospital Británico, Montevideo-Uruguay, on behalf of the Latin America Bone Marrow Transplantation Group (LABMT); past President of LABMT

Latin America is a multicultural and multiethnic region with more than 600 million inhabitants, in which the Romance languages (Spanish, Portuguese, French) are predominantly spoken. It stretches from Mexico to Argentina, including most of the Caribbean islands, and comprises countries with great diversity in terms of territorial extension, population, and socioeconomic parameters. The same diversity is observed in the number, rate, and accessibility of the population to HCT.

The Latin American Bone Marrow Transplantation Group (LABMT) [31] collects data on the number and characteristics of HCTs performed in the region, which together with the data reported by the centers to the CIBMTR on trends and rates throughout the years, allows for comparison of our data with that from other regions of the world [32].

In 2018, a total of 5642 HCTs performed in 5445 patients (2196 [40%] allogeneic HCTs and 3249 [60%] autologous HCTs) were reported by 127 teams in 14 Latin American countries, for a TR of 85 (TR = number of first HCTs per 10 million inhabitants per year). As expected, countries with the largest populations tend to have the highest number of procedures, with Brazil accounting for nearly one-half of the total (2643 HCTs in 2018), followed by Argentina (910 HCTs in 2018). However, the population's accessibility to HCT in each country can be better estimated by the TR, which again shows a wide variation among countries, ranging from 338 in 2018 in Uruguay to 0 in countries in which no transplantation activity was reported [33]. Latin American TRs rank in the middle globally,

Table 1
ISBMT Minimal Outcome Data (MOD)

Age (yr)/sex	
Diagnosis and status at transplantation	Specify AML/ALL: CR1/non-CR1 CML: CP1/beyond CP1 Thalassemia: class I/II/III
Conditioning	Specify
Acute GVHD	Yes/no
Chronic GVHD	Yes/no
Current status	Alive/dead
Status at last follow-up	CR/relapse/rejection
Date of relapse/rejection	mm/dd/yyyy
Date of last contact date/date of death	mm/dd/yyyy
Cause of death	infection/GVHD/progressive disease/other (specify)/unknown

AML indicates acute myeloid leukemia; ALL, acute lymphoblastic leukemia; CML, chronic myeloid leukemia; CR, complete response; CP, chronic phase 1; GVHD, graft-versus-host disease.

as reported by the Worldwide Network for Blood and Marrow Transplantation. Of note, the TRs for the region would need to increase by 6- to 8-fold to reach the rates seen in Europe and North America [34].

What are the main variables contributing to the occurrence of lower-than-expected HCT activity in Latin America based on its population? This issue has been addressed by leading experts in our region [35,36], and although multiple variables can impact the development of transplantation activity in the region, the importance of socioeconomic parameters has been highlighted as a key factor. Moreover, some of the disparities in TR observed between countries, and even the absence of procedures in some countries, can be correlated with the main socioeconomic parameters observed in the different countries, such as per capita gross domestic product, percentage of poverty and extreme poverty, and income inequality as estimated by the Gini coefficient [37].

Health care infrastructure, personnel and transplantation-specific expertise, reimbursement, and drug availability are other factors affecting transplantation volume in Latin America and are highly confounded with socioeconomic parameters [35,36].

What are the main trends in our region? Although the numbers are lower than desirable, the trend is toward a sustained increase in the number of HCTs since the first transplantations were performed in our region in the 1970s. The annual 11% increase observed in the years 2012 to 2018 exceeds the worldwide average. A transient decrease in HCT numbers was seen in some Latin American countries in 2019 and 2020, likely related to the COVID-19 pandemic, but a rapid recovery of numbers was seen in 2021 (LABMT, preliminary unpublished data).

Slightly more autologous HCTs than allogeneic HCTs are performed in Latin America, although the latter are growing at a faster rate, owing mainly to a higher proportion of related haploidentical (haplo) HCTs [33]. Haplo-HCT with post-transplantation cyclophosphamide may be particularly attractive in Latin America for patients lacking an HLA-identical sibling owing mainly to the ready donor availability and simplicity of the procedure. Moreover, the development of MUD HCTs in our region poses additional challenges related to the increased costs associated with graft procurement, the genetic diversity of our population, the lower likelihood of finding a suitable donor for Latin American HCT recipients in international registries, and the fact that most countries do not have a well-established national donor registry [33].

What should we expect for the future and what are the main needs for the development of HCT in Latin America? The observed increase in the number of HCTs performed annually is expected to continue; this must be accompanied by adequate infrastructure, availability of supplies, training of human resources, implementation of quality management systems, and prioritizing countries and areas with lower TRs. This is absolutely necessary to improve the population's access to the procedure, and this growth will only be possible as an integral part of the economic, social and human development that the region should continue to experience.

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