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Fostering next generation transplant physicians

Shinichiro Okamoto[1], Miguel-Angel Perales[2,3], Anna Sureda[4], Amado Karduss Urueta[5]

[1]Division of Hematology, Department of Medicine, Keio University School of Medicine, Tokyo, Japan, [2]Adult Bone Marrow Transplantation Service, Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, USA, [3]Department of Medicine, Weill Cornell Medical College, New York, USA, [4]Clinical Hematology Department, Institut Català d'Oncologia - L'Hospitalet, IDIBELL, Universitat de Barcelona, Barcelona, Spain, [5]Instituto de Cancerologia - Clinica las Americas, Medellin, Colombia

Abstract

As opposed to the rapid expansion of hematopoietic cell transplantation (HCT) and other cellular therapies (CT), we are now facing a global shortage of transplant physicians and other professionals to support the activity of HCT/CT. To overcome this obstacle, a variety of approaches are now being undertaken in four international HCT societies. This article aims to share their current attempts to foster the next generation of transplant physicians and allied professionals needed to secure the continued global growth of HCT/CT.

Key words multidisciplinary team approach, HCT, next generation, transplant physician

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Correspondence: Shinichiro Okamoto, Division of Hematology, Department of Medicine, Keio University School of Medicine, 35 Shinanomachi, Shinjuku, Tokyo, 160-8582, Japan, E-mail: okamoto@a.7.keio.jp

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Introduction

A variety of cellular therapies (CT), including hematopoietic cell transplantation (HCT), are actively performed worldwide to treat a variety of diseases that currently have limited or no therapeutic options. In addition, with the improvement of a variety of supportive therapies, the indication of HCT/CT has continued to expand to elderly patients and those who have comorbidities. On the other hand, the rapid expansion of HCT/CT activity is now facing a global shortage of transplant physicians and other allied professionals to support HCT/CT. To overcome this shortage, global collaboration of HCT/CT societies is eagerly needed. This article focuses on the current approaches to foster the development of transplant physicians and other multidisciplinary team members in Europe, North America, Latin America, and Asia-Pacific regions.

APBMT Perspective

HCT and CT (HCT/CT) exploit the therapeutic potential of hematopoietic cells to treat a variety of hematological disorders. Initially, HCT/CT was used for the treatment of hematological malignancies and disorders; however, the indications of HCT/CT continue to expand toward a variety of diseases including non-hematological disorders. However, the expansion also highlights the global shortage of transplant physicians and cellular therapists adequately trained in this field. This shortage can significantly impact patients' access to those therapies and their quality. A critical number of qualified transplant physicians are needed to ensure the continuing expansion of accessibility to HCT/CT, provide a standardized curriculum and training experience to attract young hematologists/medical oncologists, and promote expertise and quality care to meet the needs of both patients and society. In addition, HCT/CT is a highly complex procedure that requires a dedicated

multidisciplinary team to optimize its safety and efficacy. Workforce shortages are also being reported for other multidisciplinary HCT/CT team members, such as nurses, pharmacists, and medical technologists.

To address this unmet need and attract aspiring hematologists to the field of HCT/CT, national and international task forces aiming to develop a structured academic program in HCT/CT should be created. APBMT (Asia-Pacific Blood and Marrow Transplantation Group) addresses the specific needs of trainees working in a variety of aspects or fields in HCT/CT and provides advice to support them at all levels. APBMT will also consider creating groups composed of trainees and young investigators in all fields of HCT/CT with a broad range of experience and interests and serves to provide a platform for trainees to engage with a variety of activities in APBMT. It is also important to encourage medical students and young hematologists to consider a career in HCT/CT and to provide a platform for them to establish themselves within the APBMT community. Also, transplant physicians must be actively engaged in the medical education process and show the excitement and challenges of a career in HCT/CT.

There are several keys to fostering the next generation of HCT/CT physicians. We must recruit candidates when they are younger, give them practical experience, and support them along the way. In other words, we should help them experience many aspects of HCT/CT, including making important decisions, and support them by giving solid advice. At the same time, we should sometimes take a step back from daily patient care and look at the big picture, showing them the wide and attractive vision we have for HCT/CT in the future. To this end, it is crucial to open the HCT/CT academic society to them by setting up forums with many professionals working in this field and creating special educational courses to become qualified as HCT/CT physicians and other multidisciplinary team members.

It is crucial to teach how to create a team for HCT. HCT is a medical treatment that requires the cooperation of not only medical staff but also human resources from various professions. In other words, HCT/CT is a good medical model for practicing a multidisciplinary team approach, and it is not an exaggeration to say that practicing a high-quality multidisciplinary team approach greatly determines the success of HCT/CT. However, there is not always an accurate understanding of what kind of professionals to add to the team and how to work together in order to provide high-quality care to patients. It is not enough to form a medical team by bringing together various professions superficially. When team members trust each other and work together, the power of a multidisciplinary team approach can be demonstrated.

A multidisciplinary team approach, or team medicine is defined as patient-centered medical care that demonstrates their expertise by collaborating with each other equally. In addition to the patient-oriented element, there are three additional elements in team medicine: specialization-oriented, interprofessional-oriented, and collaboration-oriented. There are still many patients and their families who are unable to make their own decisions about treatment indications and subsequent treatment options, and who still prefer to leave medical care to the doctors. The first step in promoting team-based medical care is to fully understand this social background, and for all members of the team to share an awareness that they should put patients at the center and support them throughout the entirety of HCT/CT.

Multidisciplinary team medicine is not the division of work and responsibilities of doctors, nurses, and other professionals, and they are not involved in assuming the tasks of other professions. In multidisciplinary team medicine, it should be recognized that the patient is an important member positioned at the center of the team, and other team members actively support the patient's participation in medical care by fulfilling their accurate understanding of each transplant situation[1].

In team medicine for allogeneic hematopoietic stem cell transplantation, there are three teams involved in the treatment. The Active care team (Team A) is a team that provides direct medical care to patients, mainly consisting of hematologists (transplant doctors), doctors, nurses, pharmacists, radiologists, nutritionists, physical therapists, and other professionals from other departments. One important role of this team is to provide medical care based on Evidence-Based Medicine (EBM) and to create and disseminate it. The Best support team (Team B) is composed of nurses, an HCT Coordinator (HCTC), welfare workers, social workers, a patient's family members, etc. As opposed to Team A, an objective care team for patients, Team B is a team that supports the patient's needs through subjective care (interactive care). They are active listeners of the patient's story, encourage their self-determination, and care for patients to understand their situation. The Community care team (Team C) consists of basic researchers, epidemiologists, pharmaceutical manufacturers, diagnostic reagent manufacturers, medical device manufacturers, and NPOs/NGOs. It is a team consisting of the business community, government, mass media, etc. Team C is a team that provides indirect support to patients' needs and comprehensive support to Teams A and B. Team C is responsible for the citizens' perspective, such as the efficient and fair use of limited medical resources and to guarantee the social nature of care.

A wide range of factors hinder the success of a multidisciplinary team approach. To create the best multi-

disciplinary team, it is important to ensure that team members (1) understand and share the team's mission (the reason why the team exists), (2) know each other well and endeavor to build a relationship of mutual trust, (3) sufficiently commit to the work of the team as professionals and take responsibility for each other (accountability), (4) ensure continuous human resource development (continuity), and (5) seek results as a team and not as individuals.

There is indeed no evidence on whether team medicine leads to improved patient satisfaction or better transplant outcomes. However, it has been objectively shown that when not only doctors but also nurses are involved in the end-of-life decision and symptom alleviation process in intensive-care units, and when the division of work roles is freely and equally decided between doctors and nurses, this leads to appropriate medical practice and patient satisfaction. In the field of allogeneic hematopoietic stem cell transplantation, it is felt that the active involvement of professionals such as HCTC within the team will deepen the understanding of patient transplantation, ensuring high-quality care and improved patient satisfaction. It is important to make team medicine more widely recognized by society.

ASTCT Perspective

The field of HCT/CT has been rapidly evolving over the past few decades[2, 3]. These therapies have been shown to be curative for patients with hematologic malignancies as well as non-malignant hematologic disorders. Significant progress has been made in patient selection, donor selection, conditioning regimens, graft-versus-host disease (GVHD) prevention and treatment, and other supportive care measures, which have resulted in overall improved outcomes[4, 5]. In 2023, we are able to provide transplant options to older patients and patients with co-morbidities. In addition, we are in an era where we can guarantee a donor for all patients, in large part due to the use of alternative donors, including haploidentical donors, mismatched unrelated donors, and cord blood[5-7].

We have also seen the advent and rapid development of other cell therapies, including immune effector cells such as chimeric antigen receptor (CAR) T cells[8]. CAR T cells are now routinely used in patients with non-Hodgkin lymphoma, multiple myeloma, and acute lymphoblastic leukemia[8-10]. In the next few years, we expect to see expansion of these therapies to other hematologic malignancies, as well as potentially to solid tumors. In this context, it is critical to train the next generation of transplant and cell therapy physicians, who will not only take care of patients but also perform the basic, translational, and clinical research that will ensure we continue to advance the field[11]. Furthermore, we must continue to foster collaborations both nationally and internationally. As an example of how the field is evolving, we will briefly review studies performed at Memorial Sloan Kettering Cancer Center in New York over the past 20 years, with a particular focus on studies led by junior investigators both in HCT and in CAR T cells.

One of the main complications of an allogeneic HCT is GVHD, and there have been significant efforts to improve the calcineurin-based backbone that was the standard of care until recent developments with the use of post-transplant cyclophosphamide[12]. We examined the role of the Endothelial Activation and Stress Index (EASIX), a prognostic tool first developed by Luft and colleagues in allogeneic HCT. We evaluated the EASIX score pre- and post-HCT in patients with lymphoid malignancies undergoing unmodified reduced intensity conditioning (RIC) alloHCT with the same GVHD prophylaxis. We showed that EASIX pre-HCT, at day 30, and at day 100, was significantly associated with higher NRM and lower OS[13]. We also showed that EASIX scores are dynamic and variably concordant with NRM when analyzed longitudinally, and that patterns differ between HCT platforms[14]. MSK is known for its pioneering work in the use of CD34 selection for ex-vivo T cell depletion (TCD) to reduce GVHD. Junior investigators have led a number of studies comparing the results of TCD to unmodified transplants at other centers, showing that the platform affords similar overall survival without increasing relapse, but with significantly less acute and chronic GVHD[15]. As the results of these retrospective studies were not borne out in the prospective phase 3 trial BMT CTN 1301[16], we are now focusing on using established or novel prognostic models to better select patients who may benefit from TCD[17-19], as well as working on strategies to improve outcomes after TCD allo-HCT[20, 21].

With the approval of CAR T cells by the US FDA in 2017, we have treated an increasing number of patients with acute lymphoblastic leukemia, lymphoma, and myeloma. This has also been an opportunity for clinical and translational research using data from real-world experience. We have reported outcomes of patients treated at MSK[22-27], as well as within the context of collaborations with other centers and multicenter consortia[28, 29]. These studies, as well as those reported by other centers, have confirmed data from the registration studies and have provided useful information to help select patients for CAR T therapy and manage toxicities and other outcomes.

The American Society for Transplantation and Cellular Therapy (ASTCT) has several initiatives to help de-

velop the next generation of clinical and research investigators in the field of HCT/CT. These include New Investigator Awards that help support the research of junior investigators, the ASTCT Clinical Research Training Course (CRTC), the ISCT-ASTCT Cell Therapy Training Course (CTTC), developed with the International Society for Cell and Gene Therapy, and the ASTCT Leadership Course. The CRTC was launched in 2006 and is designed to help fellows and junior faculty improve their skills in clinical trial design and bench-to-bedside research. The biennial CTTC targets a similar audience but is focused on training in the development and translation of CT. The Leadership Course is targeted to mid-career ASTCT members and is a year-long program to provide training and develop the next generation of leaders in the field of HCT/CT.

Building on the success of these training courses, ASTCT is planning to launch a new training course in 2024 modeled after the CRTC but focused on junior laboratory investigators. Launched in 2022, the Joint ASTCT and the European Society for Blood and Marrow Transplantation (EBMT) Basic and Translational Scientific Meeting is a 2.5-day conference focused on cutting-edge basic and translational biology in the field. Meeting locations alternate between the US and Europe. Another joint meeting with EBMT is the ASTCT + EBMT International Conference on Relapse after Transplant and Cellular Therapy (HSCT^2). These smaller, more focused meetings complement the annual Tandem Meetings of ASTCT and CIBMTR. ASTCT also hosts virtual training courses for allied health professionals including advanced practice providers, nurses, and pharmacists, as well as webinars and other online educational resources. Finally, many of the practice guidelines are hosted on the ASTCT mobile app, which is available on both platforms. In addition to grants, training courses, and meetings, ASTCT provides many opportunities for training and career development through participation in its various committees and special interest groups.

The ASTCT leadership is also very conscious that the issues our patients and members face transcend borders, and it is committed to fostering collaborations with other national and international organizations focused on HCT/CT. This includes the organization of joint meetings and joint sessions, bilateral agreements with national societies, training opportunities for international physicians, and close collaborations when faced with international emergencies such as the COVID-19 pandemic[30].

EBMT Perspective

HCT is a life-saving medical procedure that can cure a variety of hematological disorders, including leukemia, lymphoma, and severe aplastic anemia. As the demand for HCT continues to grow, it is crucial to nurture the next generation of physicians who will specialize in this complex field. This multifaceted approach to fostering HCT physicians involves education, mentorship, research, and patient-centered care.

Education and training

The journey to becoming an HCT physician begins with a solid foundation in medical education. Medical schools and specialized training programs must incorporate comprehensive HCT curricula to prepare future specialists. This education should cover the entire spectrum of HCT, including the basic science behind hematopoietic stem cells, the principles of transplantation immunology, GVHD management, and the latest advancements in transplant techniques and supportive care.

Moreover, specialized training programs such as fellowships in transplant medicine and hematology/oncology should be made available to medical graduates interested in becoming HCT physicians. These programs provide in-depth, hands-on experience in the field, allowing trainees to develop the necessary skills to manage complex transplant cases and navigate the unique challenges of HCT.

Mentorship and clinical experience

Mentorship plays a pivotal role in shaping future HCT physicians. Experienced transplant physicians and hematologists should actively engage with trainees, offering guidance, sharing their expertise, and fostering a culture of continuous learning. Mentorship programs can be formalized within hospitals and transplant centers to ensure that young doctors receive comprehensive guidance throughout their training. Clinical experience is invaluable for aspiring HCT physicians. It provides the opportunity to directly apply theoretical knowledge to patient care. Trainees should rotate through transplant units, working alongside experienced professionals to observe and participate in the entire transplant process, from patient evaluation and donor selection to transplantation and post-transplant care. This hands-on experience is crucial for developing the clinical skills necessary for managing the complex medical and psychological needs of transplant patients[31, 32].

Research and innovation

Research is a driving force behind the advancement of HCT medicine. Future HCT physicians should be encouraged to participate in research projects, fostering innovation and contributing to the field's knowledge base. Research involvement enables trainees to explore novel treatment approaches, improve patient outcomes,

and stay informed about the latest breakthroughs in transplantation science.

To support research efforts, academic institutions and transplant centers should provide resources, funding, and mentorship for young investigators. This includes access to laboratory facilities for basic science research, collaboration opportunities with experienced researchers, and access to patient databases for clinical studies. By nurturing the research skills of future HCT physicians, we can drive progress in the field and develop more effective and less toxic transplant strategies.

Patient-centered care and communication

HCT is not just a medical procedure; it's a transformative experience for patients and their families. As such, training programs for future HCT physicians must emphasize the importance of patient-centered care, empathy, and effective communication.

Effective communication is a skill that transcends clinical expertise. Future HCT physicians should be trained to communicate complex medical information in a clear and compassionate manner. They should learn how to listen to patients' concerns, provide emotional support, and involve patients and their families in decision-making processes. This holistic approach to patient care ensures that patients feel heard, understood, and supported throughout their transplant journey.

Moreover, future HCT physicians should be equipped to address the unique emotional and psychological challenges faced by transplant recipients and donors. This includes managing the anxiety and uncertainty that often accompany the transplant process, as well as providing counseling and resources for coping with potential complications or long-term side effects.

Ethical considerations and cultural competence

HCT is not only a medical procedure but also an ethically complex endeavor. Trainees should receive education and training in the ethical principles that guide transplantation, including issues related to organ and stem cell donation, allocation, and informed consent. They must learn to navigate the delicate balance between providing the best possible care for patients while respecting their autonomy and wishes.

Cultural competence is another crucial aspect of HCT practice. Transplant physicians must be sensitive to the cultural, religious, and ethical beliefs of their diverse patient population. This includes understanding how different cultural backgrounds may impact a patient's decision to undergo transplantation and how cultural values may influence end-of-life care and organ donation decisions.

Multidisciplinary collaboration

HCT is a highly specialized field that requires collaboration with a range of healthcare professionals, including transplant nurses, pharmacists, social workers, and psychologists. Future HCT physicians should be trained to work effectively within a multidisciplinary team, recognizing the unique contributions of each team member and fostering a collaborative approach to patient care. Incorporating interdisciplinary training into HCT education can help trainees understand the diverse roles within the transplant team and how they collectively contribute to the success of each transplant. It also promotes a patient-centered approach that addresses the physical, emotional, and social needs of transplant recipients.

Continuing medical education and lifelong learning

The field of HCT is continually evolving, with new discoveries and treatment approaches emerging regularly. As such, fostering the next generation of HCT physicians requires a commitment to lifelong learning and continuing medical education. Future HCT physicians must stay up to date with the latest research, guidelines, and clinical practices to provide the best possible care to their patients.

Professional organizations, such as ASTCT[33] and EBMT, offer educational resources, conferences, and networking opportunities for HCT physicians to stay informed and connected with their peers. Encouraging participation in these organizations and their activities can help young doctors remain at the forefront of the field.

Conclusion

Fostering the next generation of HCT physicians is a multifaceted endeavor that requires a comprehensive approach encompassing education, mentorship, research, patient-centered care, ethics, cultural competence, multidisciplinary collaboration, and a commitment to lifelong learning. By investing in the development of these future healthcare professionals, we can ensure the continued success of hematopoietic stem cell transplantation, offering hope and improved outcomes to individuals facing life-threatening hematological disorders. Through education and mentorship, support for research, and a patient-centered approach, we can empower the next generation of HCT physicians to provide exceptional care to those in need.

LABMT Perspective

Latin America has 22 countries and nearly 600 million inhabitants. The median gross domestic product

(GDP) is 16,320 US dollars, almost three times less than in Europe[34]. According to the World Bank, most of its countries are classified as upper-middle-income economies; however, there is a significant disparity among the countries. The GDP of the lowest is 2,800 US dollars, while it is 30,000 US dollars for the highest.

The number of transplants in Latin America has increased in the last few years; however, there is still a low transplant rate of just 77 procedures for every ten million persons, while this indicator is almost 500 in North America. The density of teams is 1.6 for 10 million, almost six times less than in Europe or North America[35].

One of the goals of Latin American Blood and Marrow Transplantation (LABMT) is to increase the number and quality of transplants and the number of teams doing transplants. One of the aspects necessary to achieve this goal is to increase the number of hematologists trained in this complex procedure. Our group has done surveys to evaluate the current state of training in our region and to understand the most critical barriers faced[36]. The last survey was presented in the 2023 EBMT meeting. In summary, there are 31 training programs in 10 countries, and 71% of these are formal programs with structured learning curriculums that last 6 to 12 months. Most programs are in the public health system, only 50% offer a salary, and 22.6% charge a fee to the trainee.

In most of these programs, young hematologists acquire expertise in performing autologous and allogeneic transplants, including uses of different cellular sources such as haplo and non-related donors; however, only one has an active program in CAR T cell therapy. The main barriers identified in the survey preventing access to the training were a lack of funding to support the hematologist in training (48.4%), a lack of support for the teaching staff (25.8%), and a lack of recognition by local authorities (9.7%). Apathy or disinterest in hematopoietic stem cell transplant is not a problem in Latin America, as it was reported for only 10% of the interviewees.

Considering that the main obstacles are the paucity of teaching centers and a lack of financial support, it is necessary to work on increasing the number of training programs and, most importantly, to adequately fund them if we are to give more Latin American hematologists access to training. There are some programs already in place to help mitigate the current shortage of training programs. One is the ASH Latin America Training Program[37], which supports the education of a hematologist for three months in a center in Montevideo, Uruguay. Another example is the Young Transplanter Program imparted by the Brazilian Society of Bone Marrow Transplantation (SBTMO), an online course that gives junior hematologists knowledge of the essential aspects of HCT and CT[38].

With the same aim of increasing opportunities for young hematologists to have access to excellent and reliable educational resources, it is essential to take advantage of the educational online materials offered by accredited universities or societies such as EBMT and ASTCT[39, 40] and stimulate regional and international mobility, preceptorships, and partnerships.

One crucial aspect is to adapt the teaching curriculum to the reality of our region. Besides acquiring knowledge and expertise about all aspects of HCT/CT, transplant physicians must be aware of the particularities of patients and donors from our countries, such as endemic infections, dengue, Zika, yellow fever, chikungunya, Chagas disease, tuberculosis, malaria, etc[41]. Also, the Latin American transplant physician needs to learn how to deal with a lack of access to good-quality public services and water, poor nutritional stage, low educational levels, and financial problems of coverage and reimbursement for the procedure and medication[42].

Finally, increasing the number of new transplant physicians is not enough if there is not a proportional increase in the number of well-trained transplant nurses. It is necessary to work with nurses' associations to increase access to educational resources. With this idea in mind, the LABMT has a nurse committee that offers continuing education to nurses from all Latin American countries[43].

In conclusion, the main difficulties in Latin America in fostering the next generation of transplant physicians are an undersupply of well-structured training centers and a lack of financial support for the trainees. We need to work hard to increase the number of teaching centers and fund them.

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Author Contributions

SO wrote the abstract and introduction as well as the section titled "APBMT Perspective." MAP, AS, and AKU wrote the sections "ASTCT Perspective,"

"EBMT Perspective," and "LABMT Perspective," respectively.

Conflicts of Interest

MAP reports honoraria from Adicet, Allogene, Allovir, Caribou Biosciences, Celgene, Bristol-Myers Squibb, Equilium, Exevir, ImmPACT Bio, Incyte, Karyopharm, Kite/Gilead, Merck, Miltenyi Biotec, MorphoSys, Nektar Therapeutics, Novartis, Omeros, OrcaBio, Syncopation, VectivBio AG, and Vor Biopharma. He serves on DSMBs for Cidara Therapeutics, Medigene, and Sellas Life Sciences, and the scientific advisory board of NexImmune. He has ownership interests in NexImmune, Omeros, and OrcaBio. He has received institutional research support for clinical trials from Allogene, Incyte, Kite/Gilead, Miltenyi Biotec, Nektar Therapeutics, and Novartis. SO, AS, and AKU declare no conflicts of interest. Disclosure forms provided by the authors are available on the website. SO is a member of the Editor of Blood Cell Therapy. He was not involved in the editorial evaluation or the decision to accept this article for publication.

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