Perspective

Recognition of Hematopoietic Stem Cell Transplantation and Cellular Therapy Expertise to Promote Care Accessibility: A Formally Credentialed Area of Focused Competence in Canada

Sylvie Lachance1,2,*, Marcio M. Gomes3,4, Nadia M. Bambace1,2, Henrique Bittencourt5,6, Kylie Lepic7,8, Mona Shafey3,9,10, Jolanta Karpinski3, Gregory M.T. Guilcher10,11,12

1 Institut Universitaire d’Hémato-oncologie et Thérapie Cellulaire, Hôpital Maisonneuve-Rosemont, Montréal, Quebec, Canada
2 Department of Medicine, University of Montreal, Montreal, Quebec, Canada
3 Specialties Unit, Royal College of Physicians and Surgeons of Canada, Ottawa, Ontario, Canada
4 Department of Pathology and Laboratory Medicine, University of Ottawa, Ottawa, Ontario, Canada
5 Cell Therapy Program, Hematology-Oncology Division, CHU Sainte-Justine, Montréal, Quebec, Canada
6 Department of Pediatrics, University of Montreal, Montreal, Quebec, Canada
7 Cellular Therapy and Transplant Program, Division of Hematology and Thromboembolism, Juravinski Hospital and Cancer Centre, Hamilton, Ontario, Canada
8 Department of Medicine, McMaster University, Hamilton, Ontario, Canada
9 Hematopoietic Cell Transplant Program, Tom Baker Cancer Centre, Calgary, Alberta, Canada
10 Department of Medicine, University of Calgary, Calgary, Alberta, Canada
11 Division of Nephrology, University of Ottawa, Ottawa, Ontario, Canada
12 Section of Pediatric Oncology/BMT, Departments of Oncology and Pediatrics, Cumming School of Medicine, University of Calgary, Calgary, Alberta, Canada

Article history:
Received 21 February 2021
Accepted 10 June 2021

Key Words:
Hematopoietic stem cell transplantation
Cellular therapy
Curriculum
Training

ABSTRACT
Hematopoietic stem cell transplantation (HSCT) and cellular therapy (CT) exploit the therapeutic potential of manipulated or unmanipulated hematopoietic cells to treat diseases. While initially dedicated to the treatment of hematologic malignancies and disorders, the use of these therapies in several diseases and cancers is currently under investigation. Indications are currently booming. In the midst of this expansion, both the American Society for Transplantation and Cellular Therapy (ASTCT) and the European Society for Blood and Marrow Transplantation (EBMT) have highlighted the global shortage of hematologists adequately trained in this field of high expertise. This shortage in transplant physicians and cellular therapists can significantly impact patients’ access to cell-based therapy. To address this unmet need and attract aspiring hematologists to the field of cellular therapy, as well as to standardize training, anticipating this trend, a Canadian national task force aiming to develop a structured academic program in HSCT and CT was created. Workshops were organized to identify and establish the fundamentals of the practice in HSCT and CT. These workshops followed a rigorous process in developing the competency-based training program established by the Royal College. The program begins with the development of the main tasks associated with the practice of the discipline and the evidence that trainees must provide to demonstrate that they can perform these tasks independently (the competence portfolio). It continues with the development of training requirements that summarize the knowledge, skills, and attitudes required to perform these tasks, followed by specific exposure during training (milestones) essential to demonstrate the acquisition of these skills. HSCT and CT together are now formally recognized as an Area of Focused Competence (AFC) by the Royal College of Physicians and Surgeons of Canada, a national organization that provides oversight of the medical education of specialists in Canada. AFCs are areas of specialty medicine that address a legitimate societal and patient population need previously unmet by the system of primary and subspecialty disciplines. The AFC designation for HSCT and CT provides a standardized curriculum, training experience, and accreditation process to attract young hematologists and promote expertise and quality care to meet the needs of both patients and society. A critical number of highly qualified hematologists will ensure continuing expansion of accessibility to HSCT and CT.

© 2021 The American Society for Transplantation and Cellular Therapy. Published by Elsevier Inc. All rights reserved.

Financial disclosure: See Acknowledgments on page 705.
*Correspondence and reprint requests: Sylvie Lachance, MD, FRCPC, Institut Universitaire d’Hémato-oncologie et Thérapie Cellulaire, Hôpital Maisonneuve-Rosemont, 5415 Boulevard Assomption, Montréal, QC, Canada, H1T 2M4.
E-mail address: silvy.lachance@umontreal.ca (S. Lachance).

https://doi.org/10.1016/j.jtct.2021.06.013
2666-6367/© 2021 The American Society for Transplantation and Cellular Therapy. Published by Elsevier Inc. All rights reserved.
INTRODUCTION

Hematopoietic stem cell transplantation (HSCT) and cellular therapy (CT) are the area of enhanced competence within hematology concerned with the use of hematopoietic stem cells in the treatment of pediatric and adult hematologic diseases and cancers. CT relies on knowledge of the stem cell and its environment, of hematopoietic precursors and progenitors, of the human immune and histocompatibility systems, and of techniques for cell evaluation, collection, manipulation, preservation, and administration for therapeutic purposes. CT is the sole curative approach for many patients with severe and life-threatening hematologic disorders [1,2]. The field is growing in knowledge and complexity, and the number of indications has expanded to include many malignant and nonmalignant disorders [3,4].

The Center for International Blood and Marrow Transplant Research (CIBMTR) reported that more than 9000 individuals received an allogeneic HSCT and more than 14,000 received an autologous HSCT in 2018 [5]. The number of HSCTs is constantly increasing worldwide. Age and donor availability, previously considered minimum eligibility thresholds, are no longer factors limiting access to transplant. Alternative donors and stem cell sources are now available for almost all patients needing transplantation [6]. Disease-free and overall survival are improving with better supportive care, which reduces complications and nonrelapse mortality [7]. The efficacy and cost-effectiveness no longer need to be demonstrated [8-11].

Although the number of and indications for cellular therapy schemes are increasing [12], there remains a global shortage of physicians trained in this field of expertise [13], which could significantly impact the availability of these life-saving therapies. The National Marrow Donor Program Symposium on Hematopoietic Cell Transplantation in 2020 established recommendations regarding system capacity challenges and recognized physician shortage among their top priorities [14]. The working group estimated a shortage of more than 1350 new transplantation physicians in the United States by 2020 [15]. The same is true in Australia, New Zealand [16], and Europe, where disparities between Western and Eastern countries are under scrutiny [17]. This estimated number did not take into consideration the newest indications for CT or the greater utilization of unrelated and alternative donors for HSCT. Other elements of the revolution in HSCT and CT include refinements of HLA typing techniques for optimization of donor selection [18]; the use of haploidentical donors coupled with post-transplantation cyclophosphamide [19]; novel conditioning regimens designed to reduce toxicity, thereby improving outcomes and increasing the number of eligible patients [20]; outpatient transplantation [21]; ex vivo and in vivo graft manipulations to expand [22] or change the constitution of the graft or to decrease graft-versus-host disease reaction [23,24]; gene therapy; and the development and approval of chimeric antigen receptor (CAR) T cell therapy [25,26].

There has been a significant growth in published studies reporting on the indications for and results of CAR T cell therapy in hematologic disorders and solid tumors [25]. In its 2018 activity survey on HSCT and CT, the EBMT reported a 100% increase in activity in CAR T cell therapy over a 1-year period [27]. Cell-based treatments are pushing the boundaries on resources required for personalized medicine and its unequaled expertise in both clinical and laboratory sciences [28].

While shortage in manpower in cellular therapy is widely recognized worldwide, one of the solution to improve recruitment and retention proposed by physician workforce group of the National Marrow Donor Program was to develop a HSCT training curriculum. [29]. Accreditation organizations, health care facilities, physician licensing bodies, and the public all expect that physicians who practice in this discipline will have received formal training in the field [30]. In response to these needs, the Royal College of Physicians and Surgeons of Canada has recognized an Area of Focused Competence (AFC) in HSCT and CT for enhanced training in this field of practice in Canada. This AFC provides structure and standards for training, in addition to formal credentials and the designation of Diplomate to successful candidates.

METHODOLOGY FOR AFC DEVELOPMENT

Royal College of Physicians and Surgeons of Canada

The Royal College was established in 1929 by a Canadian Act of Parliament to oversee postgraduate medical education in Canada [31]. Its main objective is to maintain the highest standards of specialist training and specialist care for Canadians. The scope of work of the Royal College includes support setting for specialty determination, accreditation of postsecondary programs in the environment, of hematopoietic precursors and progenitors, HSCT and CT including recognition of unrelated and alternative donors for HSCT. Other elements of the revolution in HSCT and CT include refinements of system capacity challenges and recognized physician shortage among their top priorities [14]. The working group estimated a shortage of more than 1350 new transplantation physicians in the United States by 2020 [15]. The same is true in Australia, New Zealand [16], and Europe, where disparities between Western and Eastern countries are under scrutiny [17]. This estimated number did not take into consideration the newest indications for CT or the greater utilization of unrelated and alternative donors for HSCT. Our ele

The Royal College has criteria for the recognition of a field of practice as an AFC. This requires demonstration that the field encompasses a distinct body of knowledge and a defined scope of practice, separate from and not necessarily affecting existing and related disciplines. It also requires demonstration that the field serves a recognized health need that is not currently being satisfied by other disciplines and makes a positive contribution to improved medical care and health outcomes. Importantly, the Royal College also asks applicants to demonstrate that there is adequate infrastructure to support the discipline; at least one site capable of mounting a training program in the country; a sufficient cohort of experts to provide a high-quality educational experience, resources for appropriate program infrastructure, and an existing professional organization capable of advancing the field. The HSCT and CT application for AFC recognition was first submitted in 2017 by the Hematopoietic Stem Cell Transplant Program of Maisonneuve-Rosemont Hospital, the University of Montreal, and the Canadian Blood and Marrow Transplant Group (currently Cellular Therapy Transplant Canada) with the endorsement of 15 Canadian academic HSCT programs, adult and pediatric, representing Canada’s 10 provinces, the Canadian Hematology Society, and specialty committees in adult hematology, pediatric hematology, pediatric hematology/oncology, and immunology/allergy of the Royal College. Receiving recognition as an AFC requires (1) evidence of the need for physicians with this set of advanced skills, (2) a body of knowledge beyond the scope of existing disciplines, and (3) adequate infrastructure to sustain the discipline.

According to the Canadian Transplant and Cellular Therapy Registry, approximately 2200 HSCTs are performed annually in the country, split roughly between autologous and allogeneic transplantation. It is believed to be an underestimate, because not all HSCTs are reported. Interestingly, currently 100 physicians/PBMs hold a membership in the Canadian Transplant and Cellular Therapy group and are actively practicing in this field. This represents a mean of approximately 22 HSCTs per transplantation physician full-time equivalent (FTE) per year. In contrast, a study by Majdalani et al. [14] in transplant center committee activity in the United States reported a mean of 6.3 HSCTs per transplantation physician FTE per year. Worldwide, this ratio varies according to country and type of transplantation and can reach up to 10 HSCTs per HSCT physician FTE per year. Although imperfect, these numbers clearly demonstrate the Canadian manpower shortage. Among the 15 HSCT programs that supported this application, 8 already had or were planning to develop an academic training program in HSCT and CT.

With the prerequisites met, the application underwent review by the Royal College Committee on Specialties, which includes a national consultation process, and HSCT/CT was finally recognized as an AFC in 2017.

Developmental Process of the AFC in HSCT and CT

Once the AFC was recognized, a Working Group was created to review the initial 2-year program proposal developed at the University of Montreal,
which became the cornerstone of the training program, and adapt it to meet the standards of the Royal College and ensure national applicability and adoption. The AFC Working Group for HSCT and CT first met in 2018. This group consisted of the Chair (S.L.), Vice-Chair (G.G.), and Working Group members from adult and pediatric HSCT and CT programs across Canada (N. B., H.B., K.L., and M.S.). The Working Group was supported by a clinician educator (M.G.), an AFC administrator (C.S.), and the Associate Director of the Specialties Unit from the Royal College (J.K.). A workshop was held in October 2018 to review, identify, agree on, and establish the core elements of the practice in this discipline. This workshop followed a rigorous process for competency-based education curriculum development established by the Royal College, which begins with the end in mind [32,33]. It starts with elaboration of the major tasks associated with the practice of the discipline and the evidence a trainee needs to provide to demonstrate that they can perform these tasks independently (the Competency Portfolio). It goes on to the development of the competency training requirements, which summarize the knowledge, skills, and aptitudes required to perform these tasks, followed by the specific exposure during training (milestones) essential to demonstrate acquisition of the competencies (Figure 1).

This session was followed by webinars held between 2018 and 2019 to finalize entry routes, competency training requirements, the Competency Portfolio and Standards of Accreditation. Together, these documents define the discipline within the Royal College; they were finalized in 2020.

**Implementing the AFC in HSCT and CT**

**Entry Routes**

Entry is possible from adult Hematology or Pediatric Hematology/Oncology after certification in either of these subspecialties. Eligibility requirements to begin training include Royal College certification in Hematology or Pediatric Hematology/Oncology or equivalent, eligibility for the Royal College certification examination in adult Hematology or Pediatric Hematology/Oncology, or registration in a Royal College-accredited residency program in adult Hematology or Pediatric Hematology/Oncology. Both Canadian and international candidates are eligible for training; the term “equivalent” extends eligibility to graduates of Hematology or Pediatric Hematology/Oncology training from all jurisdictions.

**The Competency Portfolio and Standards of Assessment**

The major tasks of the HSCT and CT scope of practice were determined, as listed in Table 1. The Competency Portfolio describes each of the major tasks of the discipline and outlines the corresponding milestones that the trainee needs to perform independently to become a Diplomate in the discipline. The Standards of Assessment detail the information and documentation required as evidence to support that the trainee has acquired the capabilities associated with each milestone.

**Competency Training Requirements**

To perform the major tasks and meet the corresponding milestones, the trainee must acquire a working knowledge of both the clinical and theoretical basis of the discipline, including its foundations in science and research. A list of required competencies to practice in this field was developed according to the CanMEDS competency framework that includes the roles of medical expert, communicator, collaborator, leader, health advocate, scholar, and professional [34,35]. The required knowledge and skills emphasize the key elements of practice of a physician in this AFC discipline: the determination of eligibility for HSCT/CT, identification of potential donors and graft sources, oversight of cellular product collection, graft assessment and manipulation, donor consent and care, preparation of recipients to receive conditioning and CT, and management of early and late complications of treatment. An in-depth understanding of CT prescriptions, processing, and quality assessment and control is also considered essential. In addition, key leader, scholar, health advocate, and professional roles were identified, which include quality management, participation in academic activities including research and teaching, and oversight of a fully accredited HSCT and CT program in collaboration with a multidisciplinary team.

To become graduates in HSCT and CT, candidates must demonstrate, and their portfolio and training program must confirm, that they have acquired the knowledge and skills necessary for independent practice. The HSCT and CT competencies are detailed at https://www.royalcollege.ca/rcsite/ibd-search-e. Required and recommended training experiences are listed in Table 2.

**Standards of Accreditation**

The Standards of Accreditation detail the requirements for a university to initiate and maintain a training program in the discipline. This includes a description of the resources needed for training, such as access to the appropriate patient population, clinical training environment, and supporting consulting and diagnostic services. It also includes the standards for organization of eligibility for HSCT/CT.

**Table 1**

<table>
<thead>
<tr>
<th>Table 1 Major Tasks of HSCT and CT</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Determination of recipient eligibility for HSCT and CT</td>
</tr>
<tr>
<td>2. Selection of conditioning regimens and cellular product</td>
</tr>
<tr>
<td>3. Donor selection, evaluation, and consent</td>
</tr>
<tr>
<td>4. Collection, evaluation, and processing of CT products</td>
</tr>
<tr>
<td>5. Management of the HSCT and CT procedure and postinfusion care</td>
</tr>
<tr>
<td>6. Management of immunosuppression in CT recipients</td>
</tr>
<tr>
<td>7. Management of HSCT and CT program</td>
</tr>
</tbody>
</table>

**Table 2**

<table>
<thead>
<tr>
<th>Table 2 Required and Recommended Training Experiences</th>
</tr>
</thead>
<tbody>
<tr>
<td>Required Training Experiences</td>
</tr>
<tr>
<td>1. Assess CT candidates to determine suitability.</td>
</tr>
<tr>
<td>2. Assess and consent healthy donors for eligibility for cell donation.</td>
</tr>
<tr>
<td>3. Select donors for cell donation.</td>
</tr>
<tr>
<td>4. Participate in interprofessional rounds where decisions are made regarding the suitability of potential recipients for CT, with prioritization according to disease-related and patient-related risks.</td>
</tr>
<tr>
<td>5. Select the CT product and cell dose.</td>
</tr>
<tr>
<td>6. Perform marrow harvest procedures and assess the quality of the graft for transplantation.</td>
</tr>
<tr>
<td>7. Supervise apheresis collection and assess the quality of the cellular product for infusion.</td>
</tr>
<tr>
<td>8. Select the conditioning regimen and graft-versus-host disease prophylaxis.</td>
</tr>
<tr>
<td>9. Manage the CT recipient during preinfusion and postinfusion care in the hospital and in the ambulatory clinic setting.</td>
</tr>
<tr>
<td>10. Manage CT recipients who are acutely ill.</td>
</tr>
<tr>
<td>11. Review chimerism studies and interpret the results.</td>
</tr>
<tr>
<td>12. Manage the immunosuppression of CT recipients.</td>
</tr>
<tr>
<td>13. Participate in a long-term CT recipient follow-up clinic.</td>
</tr>
<tr>
<td>14. Participate in academic activities related to the AFC training program in HSCT and CT.</td>
</tr>
<tr>
<td>15. Participate in quality assurance activities of the CT program.</td>
</tr>
</tbody>
</table>

**Recommended Training Experiences**

1. Observe HLA typing and antibody identification methodology in the HLA laboratory.
2. Participate in unrelated donor search and probability assessments.
3. Observe cellular therapy processing and quality assessment in the CT laboratory:
   a. Observe CD34 cell count evaluation of a peripheral stem cell graft, a marrow graft, or a cord blood graft.
   b. Observe graft manipulation.
4. Participate in scholarly activities relevant to HSCT and CT.
the program and the infrastructure to support program administration, teaching, and assessment. Training programs must meet the accreditation standards for their trainees to achieve Royal College recognition as a Diplomate.

**Funding**

The training program in HSCT and CT would be funded from province/state budgets intended for postdoctoral training programs at medical faculties. International physicians could be sponsored for their training by their home country or through training grant. It is hoped that the establishment of a well-structured and formal certification in HSCT and CT will strengthen the rationale for funding accredited programs and training positions, as well as increase the interest and number of national and international trainees.

**Practice Eligibility Route to Certification**

The practice eligibility route (PER-AFC) allows physicians who have gained expertise in the discipline through their own training and practice to apply for the AFC designation. Such candidates may have completed their training before establishment of the AFC and are established and competent physicians in the field. These candidates may submit an application to demonstrate that they have met the requirements of the AFC; this includes multi-source feedback attesting to their competence in the major tasks of HSCT and CT. Successful candidates receive the diploma and the AFC designation.

**DISCUSSION**

HSCT and CT exploit the curative potential of manipulated or un manipulated hematopoietic cells to treat diseases. It is a fascinating and rapidly evolving field combining fundamental, clinical, and laboratory-based sciences. CT remains the sole curative modality for many hematologic diseases and cancers. Several obstacles to its use have been removed, resulting in a rapid and marked increase in its application in other diseases and cancers. Although the criteria for recipient eligibility and therapeutic indications have widened, the number of highly trained hematologists required in this demanding scope of practice has not followed suit. This shortage is currently viewed as one of the limiting factors for patient accessibility to cellular-based therapy. The development and implementation of a structured training program in this field aims to provide trainees with state-of-the-art knowledge and competencies essential to their practice while assuring the continuous evaluation and improvement of the curriculum for the sake of patients and for quality control.

The HSCT and CT AFC addresses a previously unmet need for standards for the recognition of training acquisition in this highly specialized and growing discipline. It frames and promotes standardized curriculum that will enable graduates to demonstrate to institutions and the public that formal training in the discipline has been obtained and expertise has been achieved. This critical number of highly qualified hematologists will ensure expanded accessibility of HSCT and CT. These transplant physicians will become the next generation of leaders in clinical care, research, and education in Canada and internationally.

The AFC designation in HSCT and CT by the Royal College of Physicians and Surgeons of Canada provides a standardized curriculum, training experience, and accreditation process to improve the quality of education and patient care and meet both patient and societal needs while ensuring public safety. Hopefully, this model will inspire other medical organizations. Hopefully, this model will inspire other medical organizations.

**ACKNOWLEDGMENTS**

The authors thank Colin Sell from the Royal College of Physicians and Surgeons of Canada for administrative support. They also thank the 15 Canadian HSCT programs that provided support for AFC development and recognition: Leukemia/Bone Marrow Transplant Program, Vancouver General Hospital, Vancouver, British-Columbia; Alberta Blood and Marrow Transplant Program, Tom Baker Cancer Centre, Calgary, Alberta; Saskatchewan Hematology and Blood and Marrow Transplant Program, Saskatchewan; Manitoba Blood and Marrow Transplant Program, Winnipeg, Manitoba; Hamilton Hematopoietic Stem Cell Transplant Program, McMaster University, Hamilton, Ontario; Princess Margaret BMT Program, Toronto, Ontario; Ottawa Hospital Blood and Marrow Transplant Program, Ottawa, Ontario; McGill Hematopoietic Stem Cell Transplant Program, Montreal, Quebec; Hematopoietic Stem Cell Transplant and Cellular Therapy program, Hôpital Maisonneuve-Rosemont, University of Montreal, Montreal, Quebec; Pediatric Blood and Marrow Transplant Program, Sainte-Justine Hospital, University of Montreal, Quebec; Blood and Marrow Transplant Program, Hôtel Dieu de Québec, Québec, Blood and Marrow Transplant Program, Hôpital l’Enfant-Jésus, Québec, Quebec; New Brunswick Stem Cell Transplantation Program, Saint John, New Brunswick; Blood and Marrow Transplant Program, QEII Health Sciences Center, Halifax, Noca Scotia; Memorial Health Sciences Center Blood and Marrow Transplant Program, St John’s, Newfoundland.

**REFERENCES**


