Department of Biomedicine



# Global haematology

# Inequalities in the career pathway for paediatric HSCT and cellular therapy physicians

## Paediatric HSCT and cellular therapy: a puzzling path

and Prevention, University of Rome Tor Vergata, Rome, Italy Pioneering advances in the field of paediatric (CG): Department of haematopoietic stem-cell transplantation (HSCT) and Translational Hematology and Oncology Research, Taussig cellular therapy over the past few decades have trans-Cancer Institute, Cleveland formed the lives of countless children across the globe Clinic, Cleveland, Ohio (CG): dealing with otherwise incurable conditions. Currently, Department of Public Health and Pediatrics. University of around 5000 paediatric patients undergo HSCT in the Turin, Turin, Italy (MS); centres belonging to the European Society for Blood and Pediatric Onco-Hematology. Marrow Transplantation (EBMT) registry every year. The Stem Cell Transplantation and Cellular Therapy Division, majority of such procedures are allograft (>4000 per year), Regina Margherita Children's while autologous transplantations reach approximately Hospital, Turin, Italy (MS): 1000 per year. The main indications for allogeneic Pediatric Blood and Marrow Transplantation Division and transplantations are represented by acute leukaemias and Pele Pequeno Principe Research bone marrow failure syndromes, whereas solid tumours Institute, Hospital Pequeno and lymphomas constitute the most common diagnoses Principe, Curitiba, Brazil (RM); for autologous procedures. Importantly, there has been a Hematology, Facultad de Medicina y Hospital substantial increase in the use of allogeneic HSCT for the Universitario Dr José Eleuterio treatment of immune deficiencies, immune dysregulation González, Universidad conditions, and metabolic disorders, which are unique Autónoma de Nuevo León. Monterrey, Mexico (VJ); Chair to the paediatric population. Furthermore, there is a of Hematology, Bone Marrow continuous, steady increase in HSCTs over time, with Transplant Unit, ASST-Spedali an overall increase of 5.5% in 2021 (an increase of 6.9% Civili Brescia, Department of Clinical and Experimental for allogeneic HSCTs and 1.6% for autologous HSCTs) in Sciences University of Brescia, Europe when compared to previous years. Among the Brescia, Italy (VR): Paediatric 690 actively transplanting EBMT centres, 121 perform Haematopoietic Stem Cell Transplant Unit, Hospital transplantations on both adult and paediatric patients, Sant Ioan de Deu Barcelona. whereas 125 are dedicated to the paediatric population Barcelona, Spain (ST); Department of Hematology, Sanjay Gandhi Post Graduate In the past decade, cellular therapy has further expanded Institute of Medical Sciences Raebareli Road, Lucknow, India

the therapeutic options for specific blood disorders. The use of either academic or commercial chimeric antigen receptor T-cell products has revolutionised the landscape of relapsed and refractory B-cell malignancies, including acute lymphocytic leukaemia and large B-cell lymphoma. Additionally, gene therapy has broadened the treatment options for patients with inborn errors of metabolism, as well as haemoglobinopathies. Given the variety and complexity of the paediatric treatment armamentarium, which requires specific knowledge and skills, the necessity for highly trained specialists is becoming the next challenge for health-care systems, academic programmes, and scientific societies around the world.

The pathway to become a paediatric HSCT physician differs vastly between countries, with substantial discrepancies in duration of training, experience, examinations, and generic competencies required. There is little doubt that some of these dissimilarities are inevitable, due to disparities in global health-care systems and resources. Indeed, access to HSCT is a heterogeneous and complex matter across the globe, and the number of transplantations undertaken in each country has a bearing on the potential for specific and dedicated HSCT training. However, even between neighbouring countries with well established health services, the pathway to paediatric transplantation can diverge remarkably, often contributing to significant confusion among trainees in the different settings and highlighting the striking lack of standardisation in HSCT education.

One of the main aims of establishing the EBMT Trainee Committee in January, 2021, was to address the disparity in HSCT and cellular therapy exposure and education among trainees internationally. Since 2021, our membership has grown to include several paediatric trainees from different backgrounds and based in a variety of countries across the globe, providing us with the perfect opportunity to develop collaborative strategies that address the current global issues in the field of paediatric HSCT and cellular therapy education. For example, we noticed heterogeneity within the main medical societies and their respective congresses in representation of specific paediatric content, whether related to clinical practice or research. Thus, the demand for improved implementation of paediatric needs within education, research, and representation was identified as a

The first step in this process is to understand the differences in global career pathways to become an established paediatric HSCT and cellular therapy physician before we consider any issues that might arise and how we could use our global platform to tackle these concerns.

### The current state: a global perspective

We evaluated paediatric career pathways in nine countries based across five world macro-areas (Europe, North America, South America, Africa, and Asia; figure). This evaluation highlighted the striking discrepancies in the training required to become an established paediatric HSCT and cellular therapy attending physician, with

Figure: Examples of paediatric HSCT and cellular therapy career pathways MRCPCH=Membership of the Royal College of Paediatrics and Child Health. MRCP=Membership of the Royal Colleges of Physicians. HSCT=haematopoietic stem-cell transplantation. FNB=Fellowship of National Board. DM=Doctorate of Medicine. DrNB=Doctorate of National Board. \*Paediatricians become full members of the Royal College of Paediatrics and Child Health and achieve the designation MRCPCH once they have passed the four separate postgraduate medical exams required. †DM and DrNB are subspecialty degrees post MD.

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#### IJК

### Medical school

- 5–6 years
- Medical degree

#### Foundation training

- 2 years rotating through different specialties
- · Generally 3-4 month rotations
- Full General Medical Council licence on completion of first year

#### Paediatric specialty training or internal medicine training

- 2–3 years
- Core paediatric or medical training
- MRCPCH exams (MRCP alternative)\*

### Haematology training

- 5 years
- Laboratory medicine, tranfusion, general haematology, haemostasis and thrombosis, haemato-oncology
- At least 2 years will be in adult haematology
- FRCPath exams

#### Italy

### Medical school

- 6 years
- Medical degree
- Full medical licence

## Haematology Residency Program→ haematology specialist

- 4 years
- 3-4 month rotations through different adult services: general haematology, haemostasis and thrombosis, haemato-oncology, HSCT
- · Pediatric haematology not always included

### Paediatric Residency Program → paediatric specialist

- 5 years
- 3.5-4 years of the common trunk rotating every 3-4 months: general pediatrics, neonatology, pediatric subspecialties
- 12–18 months of elective training and rotations in a chosen subspecialty (including paediatric onco-haematology, HSCT)

### Spain

#### Medical school

- 6 years
- Medical degree

### National exam

- Preparation for approx 6 months
- National exam (MIR) to apply for or enter speciality training

### Paediatrics speciality training

- · 4 years (approx 3 years core training plus 1 year subspecialties)
- Annual review of competencies, but no exit exam required.
- Last 6–12 months (depending on centre) can choose subspeciality

### Haematology, oncology, and HSCT training

- No formal subspecialty training pathway
- Grants or fellowships in paediatric haematology, and oncology, with or without HSCT offered in selected centres only, but not standardised
- No official paediatric HSCT training programme (no exams or experience in adults or the laboratory required), but optional route through adult haematology training

### Brazil

### Medical school

- 6 years

### • Medical degree

### Foundation training in paediatrics (residency) · 3 years rotating through different paediatric

Medical residencies national exam (50 000 applicants)

Mandatory paediatrics or internal medicine board exam

- specialties and general paediatrics
- Generally 2 month rotations

Paediatric specialty training

4 months social service

Needs entrance exam

#### Pediatric haematology or oncology specialty training (residency)

- 2 year duration
- Needs entrance exam, need to select between oncology or haematology

### Pediatric HSCT training (residency)

- 1 year duration
- Paediatric HSCT only Needs entrance exam

### Mexico

### Medical school

- 6 years
- 1 year social service · Mandatory National
- **Evaluation Center Exam**
- Medical degree

· Medical degree

## Paediatric specialty training

3–4 years

- - · Exam, interview, and resume for admission
- covering the syllabus to be promoted

### Haematology training

- 2–3 years
- · Laboratory, transfusion medicine, general haematology, haemostasis and thrombosis, haemato-oncology
- Mandatory haematology board exam

### HSCT training (optional, only certain centres)

- 1 year high speciality programme
- regulated by university
- Paediatric haematology or oncology training required

### Colombia

### Medical school

- 6 years
- 3 years
- Need to pass practical and theory test
- End of degree project (thesis) required

### Paediatric haemato-oncology training

- 2–3 years
- · General haematology, haemostasis and thrombosis, haemato-oncology and solid tumours
- Exam, interview, and resume for admision
- Need to pass practical and theory test covering the syllabus to be promoted
- · End of degree project (thesis) required

# Paediatric HSCT training

- Not regulated
- No university programme offered
- Paediatric haematology oroncology training required
- · Minimum 3-6 months of training in paediatric HSCT (generally abroad)

### USA

## Undergraduate degree

• 4 years

### Medical school

Internship training

through all specialities

· 2 years rotating

(3-4 months)

### Paediatric residency

- - · 3 years The American Board of Pediatrics Exam

Community service

1 vear, independent

practice certificate only

obtained after this year

## Paediatric haematology and oncology and HSCT fellowship

- The American Board of Pediatrics Exam
- · Alternative immunology fellowship for 2-3 years

### Paediatric HSCT felloship

• 1–2 years

## South Africa

### Medical school

- 5–6 years
- · Medical degree

# India

• 5.5 years, MBBS dearee • Includes 1 year

rotatory

internship

# Medical school

## Paediatric or internal

- medicine residency 3 years clinical training
- in either specialty · MD on completion

Paediatric training 4 years, two exams and a masters degree to be completed before eligible for registration as a specialist

- Paediatric haematology training • 2-4 years: 1 year will be in the laboratory (flow cytometry,
- transfusion medicine, molecular genetics, morphology)

### Exam at the end of training: lab and clinical

## Haematology (DM or DrNB)† → adult and paediatric HSCT

- 3 years, adult and paediatric haematology
- Pursued after MD internal medicine, paediatrics, or pathology • 3-6 months rotation through transplantation unit and through haematology lab and coagulation services

- Paediatric oncology (DM or DrNB)† → paediatric HSCT • 3 years, includes both liquid and solid malignancies, does not include non-malignant haematology
- · Pursued only after MD paediatrics • 3-6 months rotation through transplantation unit

### Fellowship in haematology or paediatric oncology (FNB) → adult or paediatric HSCT

- 2 years of training, curriculum similar to 3-year course but trainees get an FNB instead of DM or DrNB degree
- A short rotation of 3 months through the HSCT unit, 1-2 months of laboratory training

### Can be persued after MD internal medicine or MD paediatrics

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For more on the EBMT centres see Bone Marrow Transplant 2023; published online March 6. https://doi.org/10.1038/ s41409-023-01943-3

For more on haematopoietic stem-cell transplantation for immune disorders see Front Pediatr 2019; 7: 295 and Immunol Allergy Clin North Am 2015; 35: 695-711

For more on the discrepencies between countries for HSCT physicians see In Focus Lancet Haematol 2022;

For more on paediatric end-oflife care see Children (Basel) 2021;

For more on the barriers that middle-income countries face see Bone Marrow Transplant 2021; 56: 536-43

For the **survey** see https://redcap.core.wits.ac.za/ redcap/surveys/?s=JECWK RCHNLAIP4HX substantial variation in duration of training, examination requirements, dedicated laboratory training, and specific HSCT and cellular therapy fellowships. The duration of post-medical school training to become a haematologist ranged from 4 years in Spain and Italy, 6 years in India, 10 years in the UK, and 11 years in South Africa, with the latter two requiring specific training in laboratory, transfusion, and haemostasis and thrombosis as part of the broader haematology training pathway. This situation is also the case in Mexico, where the programme is slightly shorter due to the lack of mandatory rotational training through many specialities (mainly adults) after medical school as occurs in the UK and South Africa.

The USA, Brazil, and some centres in Mexico offer specific paediatric HSCT and cellular therapy fellowships as part of the training pathway, whereas in other countries training tends to be more varied, and occur as a subspecialty option within a broader paediatric or haematology training programme. By contrast, paediatric HSCT and cellular therapy training in Colombia is not regulated and is usually undertaken abroad after paediatric haemato-oncology training. Notably, in the USA and Mexico, some immunology tracks will lead to paediatric HSCT, whereas in India, paediatric oncology gives the possibility to perform paediatric HSCT only—as opposed to haematology and paediatric haematology or oncology-allowing allografts in both adults and children. Some of these disparities translate to different transplantation team densities in Latin America (1.8 teams per million population) being lower than that in North America (6.2 teams per million population) or Europe (7.6 teams per million population).

The examination requirements also vary markedly between countries, with the UK, South Africa, the USA, Mexico, and Colombia all requiring separate exit or completion of training examinations for the paediatric and haematology or haemato-oncology elements of training. Although Italy has an official academic thesis defense, Spain has no exit exam requirements to complete training, and Brazil requires entrance, rather than exit, exams for the different stages, including foundation training in paediatrics, paediatric haematology or oncology training, and paediatric HSCT and cellular therapy fellowships.

No country has a nationally-recognised paediatric HSCT and cellular therapy curriculum, and experience and training is largely centre-dependent. Paediatric HSCT and cellular therapy physicians in the UK are currently required to rotate through adult haematology as part of their training pathway and exam requirements. Finally, Italy and Spain instead have optional routes to paediatric HSCT through adult haematology training, although there is no formally recognised paediatric HSCT and cellular therapy programme that forms part of this.

### Final remarks and ongoing efforts

Paediatric HSCT and cellular therapy fields require a specific and distinct knowledge base. The spectrum of disorders, as well as the nuances of paediatric physiology across infancy and childhood, make this subspecialty a completely separate branch of haematology, requiring a particular set of skills. The differences between adult and paediatric patient–physician interactions should also not be neglected. Indeed, the central figure of a caregiver in a child's life affects the relationship between the physician and their patient, moderated by the age of the child in question. This dynamic adds another layer of complexity to the dedicated training that paediatricians working in the HSCT space must possess, to work with caregivers (generally parents) coping with their child facing a life-threatening diagnosis, especially when considering end-of-life care.

To further complicate such an intricate situation, one of the most common barriers to dedicated HSCT and cellular therapy curricula is the lack of infrastructure (eg, expensive drugs, total-body irradiation), which middle-income countries face as one of the most difficult challenges to overcome. This situation is exemplified by the absence of paediatric HSCT and cellular therapy training programmes in Colombia, as discussed previously.

Within the Trainee Committee of the EBMT, the need for a better understanding of the global landscape of paediatric HSCT and cellular therapy training has emerged. The first-hand experience and the opportunity to compare and share opinions has provided us with the unique perspective of an international community, eager to collaborate online. Therefore, one of the main goals of our committee is to investigate and analyse the worldwide situation of HSCT and cellular therapy training, including in paediatric settings. To do so, a survey has been created to gather and collate trainees' experiences, and generate evidence about these disparities in education. By leveraging such data, we call for a better organisation of paediatric training pathways and harmonisation of the haematological curricula of individual countries and scientific societies globally.

As a first step to such a commitment, our Committee has helped create separate paediatric pathways during EBMT educational meetings, with specific, structured, and distinct sessions. Our hope is that medical societies will support paediatric trainees in creating a harmonised path for future generations of haematologists undertaking HSCT and cellular therapy training, with the possibility of international exchange and adequate representation.

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