Attendance Report

Nordic Red Blood Cell Meeting 2024

WP.3/T3.1: Stakeholder Network Development

Co-funded by the European Union

Introduction:

The Thalassaemia International Federation (TIF) participated in the inaugural Nordic Red Blood Cell Meeting, which took place on September 12-13, 2024, in Copenhagen, Denmark. Ms. Katia Pelides, TIF's Senior Educational Programmes Officer, and Ms. Catherine Skari, TIF's Senior Communications Officer, represented the Federation at this significant event.

The meeting, organised by the Danish Red Blood Cell Centre of the Copenhagen University Hospital - Rigshospitalet, and led by the Centre's Research Director, Dr. Andreas Glenthøj, brought together experts in red blood cell disorders from across the Nordic States, including Denmark, Sweden, Norway, and Finland. Distinguished international speakers from the UK, Canada, and France also contributed their expertise, creating a truly global perspective on the research and treatment of thalassaemia and other haemoglobinopathies.

Throughout the two-day event, participants engaged in productive discussions on the latest advances in haemoglobinopathy research and treatment protocols. The gathering provided an invaluable platform for sharing insights and best practices, fostering collaborations aimed at improving patient care across the region. This is particularly important given the recent increase in migrant populations from areas with high prevalence of haemoglobinopathies and the growing interest in this field among medical professionals.

The Nordic Red Blood Cell Meeting exemplifies the concerted efforts TIF has been promoting in recent years. In 2022, TIF founded the Nordic Haemoglobinopathy Forum (NHF) with the goal of fostering synergies in regions with emerging patient

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communities, united by common needs and perspectives, as well as shared goals and challenges.

In a welcome speech delivered by Ms. Catherine Skari on behalf of Dr. Androulla Eleftheriou, TIF's Executive Director, the Federation expressed both delight and pride in being part of this initiative, which aligns perfectly with its mission. Dr. Eleftheriou reaffirmed TIF's unwavering commitment to expanding and strengthening its Regional Networks, now established and operational in numerous regions worldwide. She also emphasized TIF's dedication to continually bridging regional needs and perspectives with international advocacy efforts, thereby amplifying the impact of collective actions in the field of haemoglobinopathies.

Sessions and Highlights:

Leveraging EU Health Policies for Better Treatment of Haematological Disorders

Ms. Katia Pelides delivered a comprehensive presentation on behalf of TIF, entitled **"EU Health Policies: Their Value for Patients and Healthcare Professionals Related to Haematological Disorders."** The presentation highlighted the importance of both patients and healthcare professionals (HCPs) being well-versed in the health-related policies that the European Union has been actively developing and updating in recent years. Once implemented by EU Member States, these policies are anticipated to provide significant benefits for individuals living with haemoglobinopathies.

An overview of several key policies was provided, including:

- Patient Rights in Cross-Border Healthcare
- The EU Pharmaceutical Package
- Clinical Trials Regulation
- Health Technology Assessment (HTA) Regulation
- Substances of Human Origin (SoHO) Regulation

Ms. Pelides discussed the strengths and weaknesses of these policies, emphasizing the necessity for HCPs to actively engage with them. This involvement can take various forms, such as participating in public consultations, contributing to national debates, and providing input to medical associations.

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She emphasized that policies have a profound impact on every facet of our lives and highlighted the pivotal role that medical practitioners play in shaping these policies. Their active engagement is crucial to ensuring that new regulations benefit patients, making it imperative for the HCP community to be deeply involved in the EU policy-making processes. The presentation underscored the importance of HCPs leveraging their positions to influence policy decisions and foster positive outcomes for patients.

Dr. Sara El Hoss: Advancing Red Blood Cell Research

Dr. Sara El Hoss, Institut des Maladies Génétiques (IMAGINE), Paris, France, and Visiting Researcher at the King's College University London, UK, delivered an enlightening presentation on the elucidation of molecular mechanisms governing both effective and ineffective erythropoiesis (red blood cell differentiation). Her talk concentrated on the pathophysiology of red cell disorders, with a particular emphasis on sickle cell disease and the genetic factors influencing the persistence of fetal haemoglobin.

Furthermore, Dr. El Hoss provided insights into the ongoing research at the Red Cell Hematology Department of King's College Hospital. The department employs a combination of advanced molecular, cellular, genetic, genomic, and bioinformatic techniques. Their objective is to elucidate the molecular pathways involved in erythroid differentiation in both healthy and diseased states, ultimately aiming to develop improved diagnostics and novel treatments for red cell disorders.

Prof. David Rees: The Evolving Landscape of Sickle Cell Disease and Beta Thalassaemia Treatments

Prof. David Rees, Paediatric Haematologist, King's College Hospital, London, UK, provided an in-depth overview of current and novel treatments for sickle cell disease (SCD) and beta thalassaemia, highlighting their efficacy, clinical benefits, and challenges.

Key points from his presentation included:

Sickle Cell Disease (SCD):

- Hydroxyurea demonstrates a convincing reduction in complications across nearly all performed studies.

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- Crizanlizumab and L-glutamine show modest yet variable benefits in reducing pain.
- Voxelotor consistently increases haemoglobin levels, although its clinical benefits remain unclear and require broader investigation.

Beta Thalassaemia:

- Luspatercept results in a moderate increase in haemoglobin levels.
- Hydroxyurea is widely used in some countries.

Furthermore, Prof. Rees highlighted emerging use of stem cell treatments for both conditions. Gene therapy offers potential curative treatments for SCD and beta thalassaemia, with licensed products now available in the UK and Europe. However, ongoing research is necessary to fully understand the long-term efficacy and safety profiles of these treatments.

Dr. Valentine Brousse: Navigating Paediatric Haemoglobinopathies Care

Dr. Valentine Brousse, a Paediatrician specializing in Haemoglobinopathies, Reference Centre for Sickle Cell Disease, Robert Debré University Hospital in Paris, presented an in-depth discussion on paediatric care for haemoglobinopathies. Her presentation emphasized the holistic and multidisciplinary approach necessary for managing these conditions from neonatal diagnosis through adulthood.

Key points included:

1. **Preventing Traumatic Diagnoses**:
   - Dr. Brousse highlighted the importance of preventing the trauma associated with diagnosis, especially for migrant families who may have experienced prior trauma and discrimination, through effective communication.
2. **Management of Infections**:
   - An overview of possible infections such as pneumococcal and parvovirus B19 was provided, along with strategies for adequate management. The unique aspects of infections in children with SCD, due to factors like spleen dysfunction, were emphasized.

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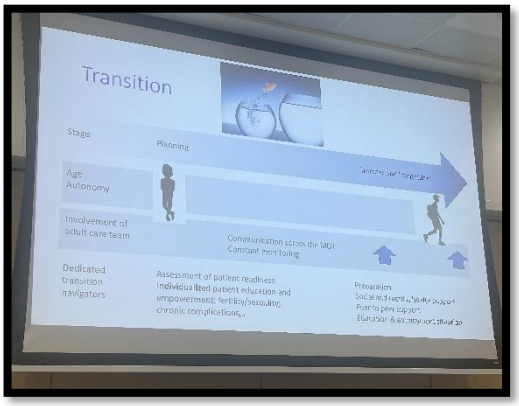

3. **Delayed Haemolytic Transfusion Reaction**:
   - Prevention of delayed haemolytic transfusion reaction in children with SCD was discussed, underscoring the need for careful monitoring and management.
4. **Transition from Paediatric to Adult Care**:
   - Dr. Brousse stressed the importance of a smooth transition from pediatric to adult care, detailing the planning and multidisciplinary approach implemented at Robert Debré University Hospital.
5. **Holistic and Multidisciplinary Approach**:
   - A holistic approach to children's health was advocated, considering not just physical health but also integration into school, psychological well-being, and societal adaptation. This necessitates a multidisciplinary team to address the comprehensive needs of children.
6. **Early Diagnosis and Prophylactic Measures:**
   - Early diagnosis is crucial for starting prophylactic measures and educating families to prevent severe complications. France employs targeted diagnosis based on ethnic background, ensuring careful communication with families.

Dr. Joseph Sharif: Complexities of Sickle Cell Care - Insights on Severe Complications and Hyperhaemolysis

Dr. Joseph Sharif, Consultant Haematologist, Haemoglobinopathy Coordinating Centre, Manchester University NHS Foundation Trust, Manchester, UK, presented a compelling discussion on four cases of sickle cell patients experiencing severe complications, shedding light on the complexities of managing this condition. The cases ranged from a 31-year-old male with fat embolism syndrome to a 17-year-old female with severe haemolysis due to Duffy-positive blood transfusion. These cases highlighted the diverse and often life-threatening complications that can arise in sickle cell patients, emphasizing the need for tailored treatment approaches and careful monitoring.

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The presentation delved into the phenomenon of hyperhaemolysis, a severe haemolytic transfusion reaction with potentially fatal outcomes. A systematic review of 51 cases revealed that most patients were treated with IVIG, with an average recovery time of 18.5 days. The speaker stressed the importance of avoiding further blood transfusions in hyperhaemolysis cases and noted promising results with tocilizumab treatment.

Additionally, data from the UK's National Vigilance Scheme was presented, revealing 670 hemolytic transfusion reactions reported over 15 years, with 144 in sickle cell patients and 74 deaths, underscoring the gravity of transfusion-related complications.

In conclusion, Dr. Sharif emphasized the critical importance of careful transfusion decision-making, weighing risks and benefits for each patient. The need for a multi-disciplinary approach and thorough transfusion history was highlighted as essential for optimal patient care. Key action items included obtaining informed consent for transfusions and reporting all transfusion reactions to the national scheme. The discussion served as a powerful reminder of the high risks associated with transfusions in sickle cell patients and the ongoing need for vigilance and informed decision-making in their care.

Dr. John Brewin: Understanding Neurological Complications in Sickle Cell Disease

In his presentation, entitled ''Neurological complications in sickle cell disease'', Dr. John Brewin, Paediatric Haematology Consultant, King's College Hospital, London, UK, focused on stroke complications in sickle cell disease (SCD), emphasizing that 11% of children with SCD experience strokes, particularly during the first decade of life. Key risk factors identified include prior transient ischemic attacks (TIAs), anaemia, and abnormal transcranial Doppler (TCD) results. The STOP study demonstrated that transfusion programs could reduce the risk of stroke by 92%.

Effective management of stroke in SCD involves annual TCD scans, clinical evaluations, and consideration of hydroxycarbamide treatment. The goal of transfusions is to lower the percentage of haemoglobin S (HbS) below 30%. For secondary prevention, regular transfusions can decrease the risk of recurrent strokes by up to 90%.

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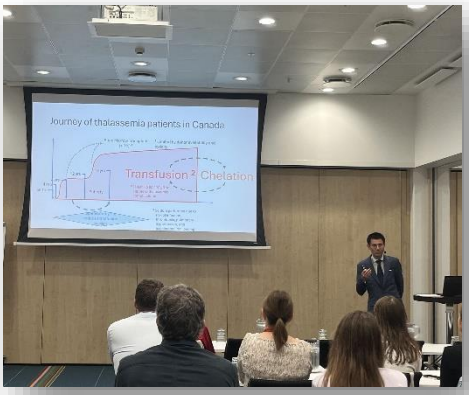
The discussion also highlighted the prevalence of both ischemic and haemorrhagic strokes across all ages in SCD patients, which contributes significantly to morbidity and mortality. A primary prevention program targeting childhood is noted as effective. Acute management strategies require urgent red cell exchange and collaboration with acute care teams to achieve HbS levels below 30%.

However, the risk factors and pathophysiology behind haemorrhagic strokes are not well understood, indicating an urgent need for evidence-based prevention strategies in this area.

Dr. Kevin Kuo: Thalassaemia Care for Children and Adults

Dr. Kevin Kuo, Haematologist, University Health Network, Toronto, Canada, primarily focused on the challenges and management of patients with thalassaemia major, particularly those with transfusion-dependence. He emphasized the complexities associated with chelation therapy, noting specific issues such as gastrointestinal problems caused by lactose in deferasirox and the inconvenience of deferoxamine administration, especially for parents managing their children's treatment.



Additionally, the significant impact of newborn screening was highlighted, which became widespread in Canada during the 2000s and led to an increase in diagnosed cases of thalassaemia. The importance of understanding patient values, preferences, and the psychosocial factors influencing their disease management was also underscored. Dr. Kuo draw attention to the necessity of a comprehensive approach to care that supports patients throughout different life stages and addresses various aspects of their well-being.

Key points from his presentation included:

- The success of managing thalassaemia largely depends on the geographic distribution of patients and demographic factors.
- The increasing population admixture and immigration trends favour the

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adoption of universal newborn screening programs.

- Proper transition care is crucial as it reduces the risk of patients being lost to follow-up, improves adherence to medication, and increases clinic attendance.
- Haemoglobin-H is often underdiagnosed but can have significant health consequences for patients and their offsprings.
- Although therapies like Luspatercept exist and can modestly reduce transfusion needs, they do not significantly address iron overload issues.
- Offering clinical trials to patients is one effective way to elevate the standards of care provided to those with thalassaemia.

Dr. Kate Gardner: Ageing and Survival in Haemoglobinopathies

Dr. Kate Gardner's presentation discussed the evolving challenges and management of ageing in patients with haemoglobinopathies, with a main focus on sickle cell disease (SCD). The presentation highlighted that ageing is an evolving problem, with different age cohorts experiencing varied treatment histories. Older patients over 50, who were not exposed to advanced therapies like hydroxycarbamide and transfusions, might have different health outcomes compared to younger patients under 30.

Dr. Gardner pointed out the significant increase in life expectancy for these patients, transforming the condition from a predominantly childhood illness to one affecting young and older adults. Neurological complications, renal impairment, hepatobiliary complications, both sickle-related and non-sickle-related organ dysfunctions were also discussed. The presentation concluded with a discussion on the use of hydroxycarbamide in older patients, highlighting the importance of continuous research and adaptation of treatment strategies to improve the quality of life and survival of patients with haemoglobinopathies.

Dr. Leena Karnik: Bone Marrow Transplantation in Haemoglobinopathies

Dr. Leena Karnik, a Paediatric Haematologist at St. Mary's Hospital, London, UK, underscored the significance of early curative treatments for haemoglobinopathies, particularly through transplantation. While matched sibling donor transplants remain the standard and non-controversial approach,

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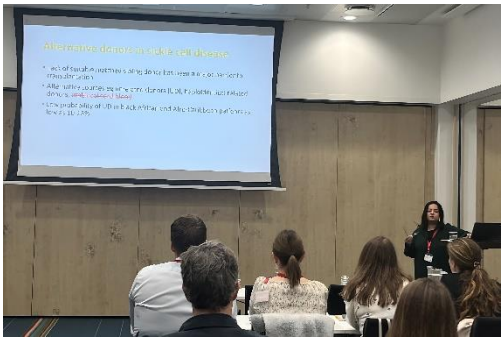
Dr. Karnik highlighted the increasing feasibility of alternative donor sources for patients lacking matched siblings. Data from large cohort studies, including those conducted by the European Society for Blood and Marrow Transplantation (EBMT) and the EBMT Working Party, demonstrate promising outcomes, with an overall survival rate of 96% and a disease-free survival rate of 90%.



The presentation provided an in-depth analysis of specific transplantation conditioning regimens employed in Europe, especially for paediatric patients. Prior to 2015, busulfan-fludarabine-based regimens were commonly used. However, there has since been a transition to treosulfan-fludarabine-based regimens. Despite these advancements, challenges persist for patients without sibling donors, as the diversity of HLA types among African-descended populations reduces the likelihood of finding matched unrelated donors.

Dr. Karnik discussed the limitations associated with using umbilical cord blood alone due to high graft failure and infection rates, suggesting it is not a primary option for transplantation. Instead, haploidentical donor transplants have emerged as a more viable alternative, with refined techniques such as ex vivo T cell depletion demonstrating excellent overall survival rates and minimal acute Graft Versus Host Disease (GVHD). The importance of continuing to refine these methods to ensure successful outcomes and improve the quality of life for patients was emphasized.

Haemoglobinopathy Care in the Nordic States: Examining Practices in Sweden, Norway, Denmark, and Finland

Denmark

Dr. Glenthoj emphasized Denmark's structured approach to haemoglobinopathy care through centralized treatment centers, a robust national screening program, and collaborative multidisciplinary efforts. Despite challenges with novel treatments and demographic changes, Denmark continues to advance its haematology care with an emphasis on quality and patient-centric solutions.

Key points:

- For adults with haemoglobinopathies, treatment is centralized at 2 hospitals: Copenhagen and Aarhus. This centralization aims to ensure high-quality care despite geographical challenges. Paediatric care is slightly more

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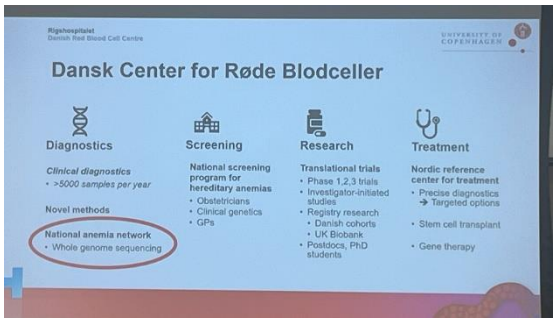
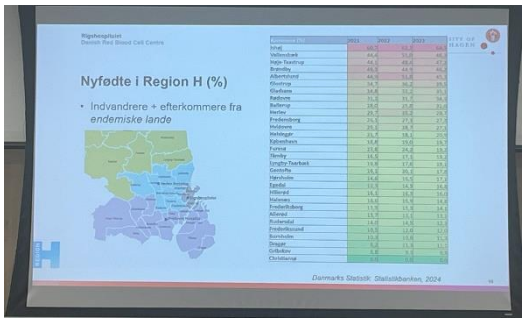
dispersed.

- Denmark has a national screening program for haemoglobinopathies, notably screening pregnant women. The program is poised for expansion to screen all pregnant females regardless of ethnicity, increasing from 5,000 to potentially 30,000 samples annually.
- National Multidisciplinary Team Conferences (MDTs) are held monthly, enabling specialists from across Denmark to discuss complex cases and share knowledge, fostering a collaborative environment to improve patient care.





- Haemoglobinopathies are increasingly prevalent due to demographic changes. For example, in Isføy, 64.3% of pregnant females have ethnic origins linked to haemoglobinopathies.
- Denmark follows standard treatment protocols, including blood transfusions, iron chelation for thalassaemia, and hydroxyurea for sickle cell disease. Novel treatments are not broadly available due to regulatory and economic constraints, limiting their use to clinical trials or named patient basis.
- Denmark actively participates in international clinical trials, aiming to attract more by highlighting organized patient recruitment and adherence to treatment protocols.

Norway

Dr. Nina Schultz, M.D., Department of Haematology, Oslo University Hospital, Norway, highlighted the evolving nature of haematology care in Norway, emphasizing the need for accurate patient data, equal treatment standards, multidisciplinary collaboration, and ongoing education to improve patient outcomes.

Key points:

- Norway's healthcare system is organized into five regions: North, Middle, West, Southeast, and South, with a total of 42 hospitals. The Southeast

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region, encompassing Oslo, has the highest concentration of patients. Ensuring equal treatment regardless of geographic location remains a significant challenge, with disparities likely between Oslo and more remote regions.

- The Norwegian patient registry provides some data, but accuracy is hampered by coding errors and double registrations. Efforts are underway to create a national registry, building on existing local quality registries.
- Southeastern Norway has approximately 75 patients with sickle cell anaemia and 50 with transfusion-dependent thalassaemia. However, there is limited information about patients in other regions.
- Recently, **sickle cell disease has been included in the neonatal screening programs,** potentially identifying more patients early.
- Paediatric patients receive systematic follow-up involving primary care doctors, local hospitals for transfusions or crisis treatment, and annual check-ups at Oslo University Hospital. The adult care model aims to replicate this structure but faces challenges due to a lack of comprehensive patient data.
- National guidelines exist for paediatric care and were last updated in 2020. Adult guidelines are currently in development.
- The Norwegian Interest Group for Red Cell Diseases was established in 2022 to foster multidisciplinary collaboration. The group meets regularly to discuss patient cases, develop national recommendations, and expand its specialty representation.

Sweden

Dr. Christian Kjellander, Haematologist, Department of Laboratory Medicine, Karolinska Institute, Sweden, presented a brief overview regarding the current landscape of haematology care in the country. He emphasized that while there is a solid foundation, especially in paediatric care, there is a pressing need for enhanced screening, more comprehensive registry development, and a more systematic approach to adult patient care to guarantee comprehensive and consistent treatment across Sweden.

Key points:

- Sweden is divided into six regions with primary, secondary, and tertiary referral hospitals. Each tertiary hospital is also a university hospital.

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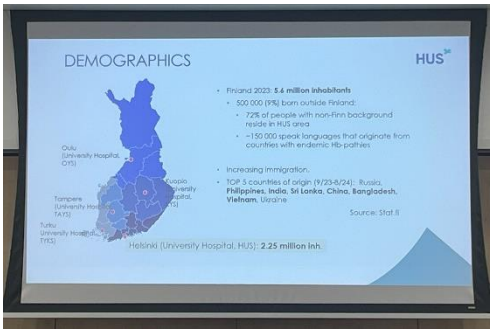
- The country has seen substantial immigration, with around 2 million immigrants as of 2019. Approximately 4% of these immigrants are beta-thalassaemia carriers, and more than 1% are sickle cell carriers, primarily from the Middle East and Asia.
- Administrative codes indicate a rise in patients diagnosed with beta-thalassaemia and sickle cell disease. Between 2008 and 2018, there was a 59% increase in sickle cell disease codes in the Swedish registries.
- Dr. Kjellander led the development of Swedish guidelines for adult sickle cell care, published recently. Most contributing authors were from the Stockholm region, highlighting a strong local interest in haemoglobinopathies.
- Sweden currently lacks a national screening program for haemoglobinopathies. Immigrants are offered healthcare checks, but the utilization of this information is inconsistent, indicating a need for improvement. Efforts to establish patient registries are ongoing, but progress has been slow. The Karolinska Institute has recently been designated as a European reference center, which may bolster these efforts.
- There is a need for better organization and implementation of screening programs and patient registries. Enhancing the utilization of healthcare checks for immigrants and improving the overall system to ensure comprehensive care for haemoglobinopathy patients **are key areas for development**.

Finland

Dr. Ulla Wartiovaara-Kautto, Chief Physician at the Comprehensive Cancer Center, Hematology, HUS - Helsinki University Hospital in Finland, emphasized the country's strong commitment to enhancing patient care and raising public awareness about haemoglobinopathies. However, she noted that political and resource-related challenges continue to hinder the effective delivery of care to patients.

Key points:



- Finland is a vast country with a significant distance of over 1,157 kilometers from south to north. Most of the population, including the majority of immigrants, resides in the southern region.
- Recognizing the need for specialized care, a rare haematological disease clinic was established 10 years ago, which includes

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patients with haemoglobinopathies and bone marrow failures. The clinic currently serves 88 sickle cell disease patients and 46 thalassaemia patients. There has been a noticeable increase in the number of new sickle cell patients, with 14 to 16 new cases in the last six months alone.

- Despite having an efficient blood bank system, Finland faces challenges in obtaining genotyped red blood cells due to a lack of African donors.
- Right-wing political influences have created barriers in classifying haemoglobinopathies as national diseases, which impacts reimbursement systems for drugs.
- Drug availability is limited, with hydroxyurea being the primary medication. The high cost of drugs presents an additional challenge, particularly for immigrants.
- The clinic aims to establish national SOPs and screening programs, although economic and political issues currently pose significant challenges.
- Finland has the capability to conduct clinical trials, with a centralized and well-functioning phase one unit, but faces challenges in attracting trials due to its remote location.

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