

Editorial

Hemostaseology in Pediatrics

Martin Olivieri¹

¹ Paediatric Thrombosis and Haemostasis Unit, Paediatric Haemophilia Center, Dr. von Hauner Children's Hospital, LMU Clinic, Munich, Germany

Hamostaseologie 2022;42:101–102.

It is a great pleasure to serve as guest editor of this “special issue pediatrics.”

“Our children are our future” and sick children need a special, individualized, and comprehensive care. The knowledge of differences between children and adults in physiological and pathophysiological pathways is necessary to guarantee the best treatment for this vulnerable group of patients.

Recent advances in diagnostics, interventional therapies, and new therapeutics licensed for the use in children need to be addressed and discussed critically.¹

The aim of the selection of conceptional reviews in this issue is to point out these particularities in pediatric patients and increase the awareness for new therapeutic modalities and their limitations.

Emicizumab was licensed for prophylaxis of bleeds in patients with hemophilia A (HA) with inhibitors in November 2017 by the U.S. Food and Drug Administration (FDA) and in February 2018 by the European Medicines Agency (EMA), and for HA patients without inhibitors in October 2018 by the FDA and in March 2019 by the EMA.^{2,3} Despite practical guidance recommendations,⁴ clinical trials, and real-world observational studies demonstrating good efficacy and safety for bleeding prevention in HA patients with and without inhibitors, some crucial and critical questions remain still open regarding the use of emicizumab.^{5–7} The first review article entitled “Emicizumab for all Pediatric Patients with Severe Hemophilia A?” by Dr. Wieland⁸ elaborates what is already known about emicizumab and what we would like to know.

Acquired coagulation disorders are rare in children and are associated mainly with severe underlying disorders. Diagnostic and therapeutic approaches are often adapted from adults. Especially acquired von Willebrand syndrome might be an underdiagnosed disorder in childhood aggravating bleeding tendencies in critically ill children. The second

review article “Acquired von Willebrand Disease (AVWD) in Children” by Dr. Sandrock-Lang and Prof. Dr. Zieger addresses diagnostic challenges regarding AVWD and underlying diseases or conditions in which AVWD should be considered and how it is managed.⁹

Due to higher awareness, better diagnostic tests and advances in caring for critically ill children, and those with chronic diseases, the incidence of thrombotic events, especially in hospitalized children, has increased over the past decades.^{10–12} New licensed drugs (direct oral anticoagulants [DOACs])¹³ for therapy of venous thrombosis make it necessary to critically review recent clinical trials and experiences, to introduce these drugs, and to point out their interactions, limitations, and special dosing regimens in childhood. Dr. Halimeh guides us in her review “New Anticoagulants in neonates, children and adolescents” through the use of DOACs in children and their possible pitfalls.¹⁴

V. Schmidt and M. Wildgruber provide in their review “Interventional Treatment Options in Children with Extracranial Vascular Malformations” a detailed overview on clinical presentation of venous, lymphatic, and arteriovenous malformations in children.¹⁵ They evaluated critically the principles of endovascular treatment and their similarities between adult and pediatric practice, highlighting distinct differences regarding the treatment of vascular malformations of children, including dose limitations and procedure-related side effects.

I hope that the articles of this theme issue for pediatrics may contribute to the increase in the awareness about coagulation disorders in the pediatric population and to facilitate respective therapeutic decisions.

I want to thank the authors for writing these interesting and important articles and all the reviewers for their comments to further improve the manuscripts.

Address for correspondence

PD Dr. Martin Olivieri, Paediatric Thrombosis and Haemostasis Unit, Paediatric Haemophilia Center, Dr. von Hauner Children's Hospital, LMU Clinic, Munich, Lindwurmstr. 4, 80337 Munich, Germany (e-mail: martin.olivieri@med.uni-muenchen.de).

© 2022. Thieme. All rights reserved.
Georg Thieme Verlag KG,
Rüdigerstraße 14,
70469 Stuttgart, Germany

DOI <https://doi.org/10.1055/a-1804-2517>.
ISSN 0720-9355.

Conflict of Interest

MO received grants/research support from Bayer, Biotest, Takeda, CSL Behring, Octapharma, Pfizer, Shire, Roche and Swedish Orphan Biovitrium, consultancy and speaker fees from Bayer, Biomarin, Biotest, Grifols, Novo Nordisk, Takeda, CSL.

References

- 1 O'Brien SH, Zia A. Hemostatic and thrombotic disorders in the pediatric patient. *Blood* 2021 [Epub ahead of print]. Doi: 10.1182/blood.2020006477
- 2 Oldenburg J, Mahlangu JN, Kim B, et al. Efficacy of emicizumab prophylaxis in hemophilia A with inhibitors. *N Engl J Med* 2017;377(09):809–818
- 3 Mahlangu J, Oldenburg J, Paz-Priel I, et al. Efficacy of emicizumab prophylaxis in patients who have hemophilia A without inhibitors. *N Engl J Med* 2018;379(09):811–822
- 4 Holstein K, Albisetti M, Bidlingmaier C, et al; 'Ständige Kommission Hämophilie' (Haemophilia board) of the German, Swiss Austrian Society for Thrombosis Haemostasis Research (GTH) Practical guidance of the GTH Haemophilia Board on the use of emicizumab in patients with haemophilia A. *Hamostaseologie* 2020;40(05):561–571
- 5 Mancuso ME, Callaghan MU, Kruse-Jarres R, et al. Efficacy of emicizumab prophylaxis in adolescent/adult patients with hemophilia A previously receiving episodic or prophylactic bypassing agent treatment: updated analyses from the HAVEN 1 study. *Blood* 2017;130(Suppl 1):1071–1071
- 6 Young G, Liesner R, Chang T, Sidonio R, et al. A multicenter, open-label phase 3 study of emicizumab prophylaxis in children with hemophilia A with inhibitors. *Blood*. 2019 Dec 12;134(24):2127–2138. doi: 10.1182/blood.2019001869. PMID: 31697801; PMCID: PMC6908828.
- 7 Wieland Y. Efficacy of emicizumab for all patients with severe hemophilia A. *Hamostaseologie* 2022; 42: 104–115
- 8 Sandrock-Lang K, Zieger B. Acquired von Willebrand disease (AVWD) in children. *Hamostaseologie* 2022; 42: 117–122
- 9 Pipe SW, Shima M, Lehle M, et al. Efficacy, safety, and pharmacokinetics of emicizumab prophylaxis given every 4 weeks in people with haemophilia A (HAVEN 4): a multicentre, open-label, non-randomised phase 3 study. *Lancet Haematol* 2019;6(06): e295–e305
- 10 Setty BA, O'Brien SH, Kerlin BA. Pediatric venous thromboembolism in the United States: a tertiary care complication of chronic diseases. *Pediatr Blood Cancer* 2012;59(02):258–264
- 11 Smitherman AB, Alexander T, Connelly M, et al. The incidence of catheter-associated venous thrombosis in noncritically ill children. *Hosp Pediatr* 2015;5(02):59–66
- 12 Raffini L, Huang YS, Witmer C, Feudtner C. Dramatic increase in venous thromboembolism in children's hospitals in the United States from 2001 to 2007. *Pediatrics* 2009;124(04): 1001–1008
- 13 Male C, Lensing AWA, Palumbo JS, et al; EINSTEIN-Jr Phase 3 Investigators. Rivaroxaban compared with standard anticoagulants for the treatment of acute venous thromboembolism in children: a randomised, controlled, phase 3 trial. *Lancet Haematol* 2020;7(01):e18–e27
- 14 Halimeh S. New anticoagulants in neonates, children and adolescents. *Hamostaseologie* 2022; 42: 124–131
- 15 Schmidt VF, Olivieri M, Häberle B, et al. Interventional treatment options in children with extracranial vascular malformations. *Hamostaseologie* 2022; 42: 133–143