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Editorial

Immune Thrombocytopenia—A Disease or a Group of Disorders? Where Do We Stand in 2019?

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Immune thrombocytopenia (ITP) is an autoimmune disease that is characterized by a significant reduction in the number of circulating platelets and frequently associated with bleeding.[1] Although the pathogenesis of ITP is still not completely elucidated, it is largely recognized that the low platelet count observed in ITP patients is due to multiple alterations of the immune system leading to increased platelet destruction and impaired megakaryocytopoiesis and thrombocytopoiesis.[2] The clinical manifestations and the patients' response to different treatments are very heterogeneous suggesting that ITP is rather a group of disorders sharing common characteristics, namely, loss of immune tolerance toward platelet (and megakaryocyte) antigens[3] and increased bleeding tendency.[4]

In this theme issue of *Hämostaseologie—Progress in Haemostasis*, international experts will provide substantiated discussion on recent evidence with respect to the pathophysiology, diagnosis and treatment of ITP.

In their article, **Marini** and **Bakchoul** present current knowledge on the pathophysiology of ITP.[5] The authors summarize most recent evidence on mechanisms causing platelet destruction in ITP. In addition, elaborate discussion is provided on recent data from translational research. These findings are mainly related to alterations in thrombocytopoiesis that are caused by autoantibodies directed against surface markers on platelets and megakaryocytes. The authors also emphasize that ITP is a complex and multifactorial disease.[6–9]

Kohli and **Chaturvedi** describe the epidemiology and clinical manifestations of ITP.[10] Of particular interest is their discussion on predictors of severe bleeding in ITP patients. Moreover, the authors analyse recent studies and found that lower platelet counts, advanced age and prior haemorrhage are associated with increased risk of severe bleeding. On the other hand, the authors point out the association between ITP and the risk of venous and/or arterial thrombosis. This observation is clinically relevant, particularly with regard to the risk stratification for second-line treatments, including splenectomy and thrombopoietin (TPO) receptor agonists.

Misdiagnosis of ITP may be common, even among experienced hematologists.[11] In his contribution, **Sachs** contradicts the traditional concept of the laboratory investigations of ITP.[12] Based on an extensive literature search, the author suggests that ITP, as other autoimmune disease, should not be considered a diagnosis of exclusion. In fact, detection of a characteristic autoantibody proves the diagnosis of ITP. However, as highlighted in this article, only the direct glycoprotein specific tests have the properties that are required to demonstrate such a characteristic autoantibody.

Management of ITP is challenging and requires intensive communication between patients, physicians and caregivers. After the diagnosis, if ITP is confirmed, the decision to initiate treatment should be based on the platelet count level and other factors that influence the bleeding risk in individual patients. **Mithoowani** and **Arnold** explore common questions about the therapy for ITP.[13] In their article, it becomes evident that the choice of first-line therapy depends primarily on bleeding symptoms and on how quickly a platelet count response is needed. The authors present their approach on fist-line therapy including when to start, which treatment to use, and how to manage bleeding emergencies in ITP.

While first-line therapies are effective in pediatric patients, refractoriness is common among adult ITP patients. **Lambert** covers second-line therapies for ITP and discusses the currently available information on immunomodulatory second-line treatments for ITP.[14] The author points out that adult ITP patients frequently fail first-line therapy and often require second-line therapies such as splenectomy, rituximab or oral immunomodulatory therapy. Specifically, advantages and drawbacks of these treatments are also discussed in this important article.

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For ITP patients who are refractory to immunomodulatory agents, thrombopoietin receptor agonists (TPO-RAs) represent an excellent therapeutic choice. **Neunert** reviews the use of TPO-RAs in ITP.[15] The author underlines that these agents have been shown to increase the platelet count, improve health-related quality of life and reduce bleeding symptoms and concomitant medication need. Neunert also initiates an important discussion on how to identify patients requiring second-line therapy who would benefit most from a TPO-RA rather than intensive immunomodulatory drugs.

One of the most controversial issues in ITP treatment is the eradication of *Helicobacter pylori*. **Vanegas** and **Vishnu** reappraise recent medical literature to determine the effectiveness of platelet response after treatment of *H. pylori* infection and found high variability in the effectiveness between different populations.[16] However, the authors suggest that ITP patients with concomitant *H. pylori* infection may benefit from triple therapy using amoxicillin, clarithromycin and a proton-pump inhibitor.

So, where do we stand in 2019? It can be said that despite the progress that has been achieved recently in understanding the pathophysiology of ITP, the underlying immune mechanisms are still not well elucidated. Consequently, future research should focus on events that lead to the loss of self-tolerance and impaired megakaryocytopoiesis and thrombocytopoiesis in ITP. Identifying these pathomechanisms will help developing innovative agents that are capable of increasing platelet count and restoring tolerance to their surface antigens. However, ITP remains a very complex disorder and heterogeneous in its presentation and response to treatments making an individualized management indispensable. Although the seven articles presented in this edition of *Hämostaseologie—Progress in Haemostasis* focus on different aspects of the disease, they have one issue in common. All authors who have contributed agree that there is an immediate need for further studies to understand the pathogenesis of ITP. Moreover, the ITP experts emphasize the necessity to establish novel therapeutic approaches for ITP.

It gave me a great pleasure to organize and serve as Guest Editor of this theme issue of *Hämostaseologie—Progress in Haemostasis* and to provide you with the editorial introduction to "Immune Thrombocytopenia. Also on behalf of the Editorial Board, I like thank the authors for sharing their expert knowledge in the pathophysiology, diagnosis and treatment of ITP. I trust that you, the readers of *Hämostaseologie - Progress of Haemostasis* will take substantial advantage of this series of reviews and hope that insights provided will be helpful for your daily work.

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Conflicts of Interests

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