Laboratory Testing: Current Aspects

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This special issue of *Hämostaseologie* addresses current aspects of laboratory diagnostics in thrombosis and hemostasis. While the first two manuscripts take a look at classical diagnostics in the coagulation laboratory, two further manuscripts deal with genetic testing in hemophilias A and B and point-of-care analysis in acute medicine. The issue further contains a review on the diagnosis and treatment of coagulation abnormalities in COVID-19 infection and is completed by a perspective article on the diagnosis of inherited mild (to moderate) bleeding disorders.

In the first manuscript, **Sachs et al.**,[1] in the context of thrombophilia screening, ask whether sufficient evidence from the literature is available for specific hereditary thrombophilia markers. Whereas antithrombin-, protein C- and protein S-deficiency, high levels of factor VIII activity, dysfibrinogenemia, as well as the factor V Leiden and prothrombin G20210A mutation are widely accepted risk factors, numerous of the in total 20 markers reviewed in this article are either of dubious use or of no use at all when it comes to counseling of patients with venous thromboembolism. Notably, there appears to be lack of clinical evidence even for several markers that are currently well established in the market and that can be tested on many coagulation systems.

In the second manuscript of this special issue, **Müller et al.**[2] have addressed a critical area in the coagulation laboratory: reference intervals. Assay-specific reference intervals are determined by manufacturers of CE/IVD-marked assays and often adopted by operating laboratories. However, when the assay is finally established in a laboratory, verification of such transferred reference intervals is still mandatory to confirm applicability on site. The same, of course, applies to reference intervals adopted from other laboratories or from published information such as, for children or pregnant women, where manufacturers usually do not provide appropriate information. The article describes how to transfer and verify such reference intervals. Furthermore, Müller et al also summarize how to establish a reference interval by a direct approach (by collecting and testing blood samples) or by data mining as an indirect approach.

The third manuscript, written by **Pezeshkpoor et al.**, gives insights into the molecular genetic analysis of hemophilias A and B.[3] The outcome of such genetic analysis allows genetic counseling of affected families and helps to find a link between the genotype and the phenotype of patients. Genetic analysis in hemophilia has evolved in the last decades, whereat the application of new techniques improved both throughput and costs. The authors discuss the milestones in genetic analysis of hemophilias and highlight the importance of identification of the causative genetic variants for genetic counseling and, particularly, for the interpretation of the clinical presentation of patients with hemophilia.

We are all aware that there is an ongoing debate about whether or not coagulation assays should be moved closer to the patient. Acute care medicine often requires decisions within minutes, because the time window for applying appropriate treatment can be narrow. In the fourth article by **Caspers et al.**,[4] intensive care physicians, traumatologists, and neurologists discuss advantages and challenges in two different classical clinical scenarios: trauma and the management of stroke. With regard to trauma management, the authors conclude that establishing goal-directed coagulation therapies and hemostatic control in the emergency room comes with survival benefits. However, there is still limited evidence to support the use of viscoelastic point-of-care assays compared with conventional coagulation testing. With regard to stroke, the authors discuss the challenges that come with direct oral anticoagulants (DOACs) and how it may become possible to identify DOAC-treated patients in whom direct interventions are feasible without worsening the overall clinical situation.

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Diagnosis of and clinical decision-making in coagulation abnormalities during COVID-19 infection are subject of the fifth manuscript of this special issue. Indeed, especially during the initial period of the SARS-CoV-2 pandemic, coagulation abnormalities were common in patients with COVID-19 infection and associated with both, high morbidity and mortality. In view of the high risk of thromboembolism in COVID-19, several medical societies published recommendations with respect to diagnosis and anticoagulation in affected patients. The aim of the present manuscript by **Uzun et al**.[5] was to describe common hemostatic findings in COVID-19 and to summarize different recommendations with respect to laboratory findings and corresponding treatment-decisions. While providing an excellent overview on the published information and guidance on this topic, the authors also highlight the need of future studies to provide evidence-based recommendations for diagnostics during acute COVID-19 infection.

Finally, the sixth and last manuscript by **Toenges & Steiner**[6] deals with the diagnosis of inherited mild (to moderate) bleeding disorders (MBD). In this perspective article, the authors address the challenges to define and distinguish a MBD from "normal" but also from severe bleeding disorders. They highlight the importance of use of the Bleeding Assessment Tool (BAT) recommended by the International Society on Thrombosis and Haemostasis (ISTH) and also summarize the laboratory parameters that should be analyzed with respect to determined BAT scores. However, a significant number of patients with MBD remains without a specific diagnosis even after comprehensive and repeated laboratory testing. In their "way ahead", the authors focus on (future) approaches which may further reduce the number of patients diagnosed with such bleedings of unknown cause.

We are confident that the articles in this issue, which address different important aspects and new developments in laboratory testing, are of interest not only to our colleagues in training, but also to old hands.

References

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