In this issue

In this first issue of BTVB, volume 5 of 2026, **Zanon** and colleagues, belonging to numerous Centers of the Italian Haemophilia Association (AICE), present a useful position paper[1] on the bioequivalence of von Willebrand factor (VWF)-containing concentrates. These products are characterized by different manufacturing methods, variable VWF/FVIII ratio and multimers composition and content, which could influence their hemostatic efficacy. The panel of experts discusses in detail the clinical implications for the choice of the products in patients with von Willebrand disease. We are grateful to AICE for their precious contribution which is the first of other articles that BTVB plans to publish this year to celebrate the centennial anniversary of the publication of the cornerstone paper of Dr. von Willebrand.

Doris Barcellona, from the Department of Medical Science and Public Health, University of Cagliari, presents a large and critical review on Cardiovascular risk in hormone replacement therapy (HRT).[2] This therapy effectively alleviates vasomotor symptoms related to menopause, but it can also raise the risk of cardiovascular disease. The Author underlines that oral estrogen-progestin combinations are linked to a higher risk of ischemic heart disease, a dose-dependent effect. She therefore advises using the lowest effective estrogen dose. Progesterone, dydrogesterone, and levonorgestrel should be selected because they do not elevate cardiovascular risk. Transdermal estrogens or estrogen-progestins do not increase the risk of cardiovascular events and are recommended for women at moderate to high risk of stroke and coronary heart disease.

Tiziano Martini, Hemophilia Centre, Immune-Hematology and Transfusion Medicine, University Hospital "Città della Salute e della Scienza", Turin, Italy, discusses findings from a nationwide survey on the diagnostic challenges in current laboratory practice at Italian Hemophilia Centers.[3]. Forty-three RLs participating in the ECAT External Quality Assessment completed an online questionnaire of 51 items across 11 sections. The Author reports that significant heterogeneity exists in reagent selection and application, notably for activated partial thromboplastin time and FVIII/FIX assays, and in von Willebrand disease (VWD) diagnostic workflows and concludes that practices across several reference laboratories do not fully align with national and international recommendations for the diagnosis and monitoring of hemophilia and VWD. Martini recalls an AICE's initiative to establish a working group to improve laboratory diagnostic standards and highlight the need for targeted training and collaboration among clinical, laboratory, and healthcare management stakeholders.

Monisha Harimadhavan *et al*., Department of Clinical Haematology, Mazumdar Shaw Medical Centre, Narayana Health City, Bangalore, India, describe the thrombophilia work-up and clinical outcomes in 226 young/adult Indian patients with unprovoked venous and arterial thrombosis.[4] Antiphospholipid antibody syndrome (APS) was the most frequent abnormality detected, whereas inherited thrombophilia was less common. In venous thrombosis patients, pulmonary involvement was significantly associated with positive thrombophilia results.

Barbara Lunghi and Colleagues, from different Italian Institutions, report, in a retrospective cohort study, on the pharmacokinetics of extended half-life albumin-fused factor IX and heterogeneous *F9* variants in hemophilia B.[5] No information is indeed available about the influence exerted by *F9* variants on extended half-life (EHL)-recombinant factor IX (rFIX) pharmacokinetics. Their preliminary results evidentiate both a moderate role of *F9* variant type in inter-individual EHL-rFIX clearance variability and differences in *F9* genotype-pharmacokinetics non-compartmental analysis parameter association between EHL- and standard half-life-rFIX products.

Armando Tripodi, from the University of Milan, a well-recognized expert in the field of laboratory tests, offers a balanced and informative overview on the role of clinical laboratory in the management of patients treated with DOAC, distinguishing routine dose adjustment from targeted measurement in selected clinical scenarios.[6] Despite the fact that laboratory assessment is often considered unnecessary in patients receiving DOAC, increasing evidence from clinical trials and real-world studies challenges this "one-dose-fits-all" paradigm, showing marked interindividual variability in drug exposure. Importantly, extreme plasma concentrations of DOAC have been associated with an increased risk of thrombotic events or bleeding complications. Tripodi mentions a number of situations in which laboratory testing may meaningfully support clinical decision-making. He concludes that a more nuanced, patient-centered use of laboratory testing may improve the safety and effectiveness of DOAC therapy.

A touching contribution by **Augusto Di Castelnuovo**, from the Research Unit of Epidemiology and Prevention, IRCCS Neuromed, Pozzilli, has been presented in memory of **Mariarosaria Persichillo**, a young Investigator of the Moli-sani project, who passed away last November. She had given a full and enthusiastic contribution both to the Moli-sani Project and to the CV-PREVITAL trial at IRCCS Neuromed.[7] Fifteen years elapsed between these two surveys of cardiovascular (CV) risk factors in the same Italian region. Modifiable CV risk profiles were compared among 2,199 individuals enrolled in the CV-PREVITAL trial (2022-2024) with those of 16,656 participants from the Moli-sani Study (2005-2010), matched for age and absence of prior CV disease. Most individual risk factors were more favorable in CV-PREVITAL compared with Moli-sani participants. Men in CV-PREVITAL had a mean Moli-sani Risk Score several points lower than Moli-sani men; women too showed a 4.5-point reduction. These findings suggest a relevant decline in modifiable CV risk over a 15-year interval, potentially reflecting enhanced prevention awareness, improved therapeutic efficacy, and cumulative effects of long-term public health communication.

In a letter to the Editor, **Tiziano Martini** and colleagues argue that medicine can now offer to newborns a life largely unloaded by the burden of hemophilia.[8] This includes achieving optimal control over joint bleeds and other hemorrhages, preserving joint integrity, and reducing disease impact on social and professional life through the use of extended half-life products or non-replacement therapies. The novel gene therapy, particularly for hemophilia B, now offers the possibility of "forgetting" the disease in daily life for several years.

In another letter to the Editor, **Fabio Candura** *et al.* announce the establishment of the first national registry for congenital hematological disorders in Palestine, an initiative designed to improve the diagnosis and management of patients affected by hemophilia, other inherited coagulation disorders, thalassemia, and related hemoglobinopathies.[9] The registry was developed within the framework of the Haemo-PAL project, coordinated by the National Blood Center (Centro Nazionale Sangue) of the National Institute of Health (Istituto Superiore di

Sanità). This initiative is implemented in partnership with the Palestinian Ministry of Health, despite the severe humanitarian crisis affecting the region.

A commentary by **Sistiana Aiello** and her colleagues at Mario Negri Bergamo Institute, contributes to enlarge the horizon of interests of BTVB to disciplines not strictly related to hemostasis and thrombosis.[10] They comment the results of a randomized controlled trial on low-dose aspirin for preventing intrauterine growth restriction and pre-eclampsia in sickle cell pregnancy in Nigeria (PIPSICKLE). Since TxA2 and PGI2 balance has been repeatedly shown to play a role in the pathogenesis of pre-eclampsia, low-dose aspirin, initiated at the 12th week of gestation in women at risk of pre-eclampsia, has been reported to be associated with prolonged pregnancy duration and increased neonatal birth weight. The PIPSICKLE trial found no significant difference in the composite primary outcome of intrauterine growth restriction, perinatal mortality or miscarriage. However, aspirin was initiated relatively late in most participants. Aiello *et al*. therefore suggest that the negative results of this trial should not discourage further investigations on the use of low dose aspirin in sickle cell disease pregnancy.

Last but not least, a brief but intense interview by **Americo Bonanni**, Head of the Press Office, IRCCS Neuromed, Pozzilli, to Professor **Silvio Garattini** closes this first issue of BTVB 2026.[11] Professor Garattini, 97-year-old, is the founder and the President of the Istituto di Ricerche Farmacologiche Mario Negri in Milan and one of world's most distinguished pharmacologists. In this interview, Garattini reflects on over six decades of biomedical research and its evolving relationship with public health and addresses the critical need for independent research free from industrial influence, and the structural challenges facing the Italian National Health Service. He also offers a candid assessment of the pharmaceutical industry and its priorities, arguing that prevention, multidisciplinarity, and scientific education are the foundations on which future generations must build a more equitable and effective approach to health.

The Editors hope that this issue of BTVB has been of their interest and are looking forward to receive constructive comments on the different contributions presented here over, especially on the form of a Letter to the Editor.

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