The Gears Keep Turning: Current Progress in Platelet Function Testing

Peter Bugert

Institute of Transfusion Medicine and Immunology, Medical Faculty Mannheim, Heidelberg University; German Red Cross Blood Service Baden-Württemberg – Hessen; Mannheim, Germany

Since measure of the bleeding time was introduced by Duke [1] more than 100 years ago, platelet function testing is one of the major issues in hemostasis. Later more specific assays were developed and include platelet aggregometry first described by Born [2] or flow cytometry for detection of platelet-specific activation markers [3]. By now, the broad spectrum of published assays and protocols is completed by a number of commercial test systems. The present issue of TRANSFUSION MEDICINE AND HEMOTHERAPY encompasses a comprehensive overview of the state of the art in platelet function testing [4].

The fields of application of platelet function testing are: i) basic research; ii) clinical diagnosis; iii) transfusion medicine. The monitoring of parameters indicative for platelet functionality or the platelet activation state in platelet concentrates is one focus in transfusion medicine. Noninvasive technologies represent attractive options and are described for pH monitoring [5] and for relative platelet quantification by dynamic light scattering [6]. The ultrastructural evaluation of platelets by transmission electron microscopy (TEM) is an interesting approach to obtain detailed quality information of the platelet concentrate [7]. Platelet functionality is also reflected by their release of alpha and dense granules. Nucleotides (ADP and ATP) belong to the major substances in dense granules, and the quantitative determination by high-

performance liquid chromatography (HPLC) could represent an important approach in basic platelet research or in clinical diagnosis of platelet function disorders [8]. However, implementation of such methods (TEM and HPLC) in a routine laboratory for clinical hemostaseology or blood banks could be challenging.

A novel platelet activation test in unprocessed blood (pac-t-UB) based on flow cytometry is described in the present issue [9]. Markers for platelet activation (P-selectin and fibrinogen binding) are measured in this standardized assay that could be implemented for monitoring platelet concentrates as well as platelet function in patients. Further interest of platelet monitoring lies in the establishment of novel functional markers in addition to the classical activation markers. The surface expression of tissue factor could represent such a novel marker that reflects the hemostatic potential of stored platelets [10].

Despite the availability of a variety of methods and devices, there is still no test system that could cover all aspects of platelet function which includes adhesion, aggregation, degranulation, and plug formation. Reliability, reproducibility, and robustness as well as feasibility in different laboratory and clinical environments are still the great challenges in platelet function testing. However, progress is made, and the gears keep turning in this direction.

References

- 1 Duke WW: The relation of blood platelets to hemorrhagic disease. *JAMA* 1910;55:1185.
- 2 Born GVR: Aggregation of blood platelets by adenosine diphosphate and its reversal. *Nature* 1962; 194:927–929.
- 3 Shattil SJ, Cunningham M, Hoxie JA: Detection of activated platelets in whole blood using activation-dependent monoclonal antibodies and flow cytometry. *Blood* 1987;70:307.
- 4 Kehrel BE, Brodde MF: State of the art in platelet function testing. *Transfus Med Hemother* 2013; 40:73–86.
- 5 Doescher A, Müller TH: Noninvasive pH monitoring in platelet concentrates. *Transfus Med Hemother* 2013;40:88–92.
- 6 Labrie A, Marshall A, Bedi H, Maurer-Spurej E: Characterization of platelet concentrates using dynamic light scattering. *Transfus Med Hemother* 2013;40:93–100.
- 7 Neumüller J, Meisslitzler-Ruppitsch C, Ellinger A, Pavelka M, Jungbauer C, Renz R, Leitner G, Wagner T: Monitoring of platelet activation in platelet concentrates using electron microscopy. *Transfus Med Hemother* 2013;40:101–107.
- 8 Von Papen M, Gambaryan S, Schütz C, Geiger J: Determination of ATP and ADP from human and mouse platelets by an HPLC assay. *Transfus Med Hemother* 2013;40:109–116.
- 9 Roest M, van Holten TC, Fleurke GJ, Remijn JA: Platelet activation test in unprocessed blood (pac-t-UB) to monitor platelet concentrates and whole blood of thrombocytopenic patients. *Transfus Med Hemother* 2013;40:117–125.
- 10 Vignoli A, Giaccherini C, Marchetti M, Verzeroli C, Gargantini C, Da Prada L, Giussani B, Falanga A: Tissue factor expression on platelet surface during preparation and storage of platelet concentrates. *Transfus Med Hemother* 2013;40:126–132.