Journal of Thrombosis and Haemostasis, **8**: 2063–2065 DOI: 10.1111/j.1538-7836.2010.03975.x

OFFICIAL COMMUNICATION OF THE SSC

ISTH/SSC bleeding assessment tool: a standardized questionnaire and a proposal for a new bleeding score for inherited bleeding disorders

F. RODEGHIERO,* A. TOSETTO,* T. ABSHIRE,† D. M. ARNOLD,‡ B. COLLER,§ P. JAMES,¶ C. NEUNERT** and D. LILLICRAP†† ON BEHALF OF THE ISTH/SSC JOINT VWF AND PERINATAL/PEDIATRIC HEMOSTASIS SUBCOMMITTEES WORKING GROUP[1]

**Department of Cell Therapy and Hematology, San Bortolo Hospital, Vicenza, Italy; †Blood Center of Wisconsin, Milwaukee, WI, USA; ‡Michael G DeGroote School of Medicine, Department of Medicine, McMaster University and Canadian Blood Services, Hamilton, Canada; §Allen and Frances Adler Laboratory of Blood and Vascular Diseases, The Rockefeller University New York, NY, USA; ¶Department of Medicine, Queen's University, Kingston, Canada; **Department of Pediatric Hematology/Oncology, UT Southwestern Medical Center, Dallas, TX, USA; and ††Department of Pathology and Molecular Medicine, Richardson Laboratory Queen's University, Kingston, Canada*

To cite this article: Rodeghiero F, Tosetto A, Abshire T, Arnold DM, Coller B, James P, Neunert C, Lillicrap D, on behalf of the ISTH/SSC Joint VWF and Perinatal/Pediatric Hemostasis Subcommittees Working Group. ISTH/SSC bleeding assessment tool: a standardized questionnaire and a proposal for a new bleeding score for inherited bleeding disorders. *J Thromb Haemost* 2010; **8**: 2063–5.

The clinical appreciation of the presence and severity of bleeding symptoms is a fundamental step in the evaluation of patients referred for a possible bleeding disorder [1]. A distinctive bleeding history is a prerequisite for the *diagnosis* of any bleeding disorder and should guide further laboratory investigations [2]. Retrospective data from cohorts of patients with von Willebrand disease (VWD) suggest that this strategy is a clinically useful approach. Furthermore, these data seem to indicate that the severity of bleeding symptoms correlates with the risk of future bleedings [3,4].

In an attempt to standardize the diagnostic criteria of VWD, a bleeding questionnaire and a bleeding score were developed [3], http://www.isth.org/default/assets/File/Bleeding_Type1_VWD.pdf [accessed 14 July 2010] and subsequently adapted by many different investigators to collect the hemorrhagic history in several published and ongoing studies. The questionnaire has proven to be useful for diagnostic purposes, allowing the establishment of *quantitative* cut-offs discriminating healthy subjects and carriers of VWD [3,5]. These cut-offs are usually based on the cumulative bleeding score (BS), determined by the summative index of the maximum severity score of each bleeding symptom *before* diagnosis [5].

Furthermore, the questionnaire and its associated BS systems have also been used for the *description* of symptoms in selected cohorts of patients [4,6–8]. The combination of a standardized bleeding questionnaire and a well-defined interpretation grid (for the computation of the final BS) has been referred to as a Bleeding Assessment Tool (BAT).

Some limitations of available BATs are however apparent, particularly concerning the overall scoring system:

1 Existing tools are most useful to evaluate subjects referred for bleeding symptoms, as BATs were validated by comparison with normal or never referred subjects. Thus, less symptomatic mild bleeding disorder (MBD), e.g. mild hemophilia, may go undetected.
2 The severity of bleeding symptoms trumps other potentially clinically important features, such as the frequency of symptoms (i.e. the *incidence* of bleeding). Furthermore, existing tools were developed to evaluate MBD such as VWD, and are likely to become 'saturated' in severe bleeding disorders (homo/hemizygous forms).

Critical issues for the establishment of an ISTH/SSC-BAT

The ISTH/SSC Joint Working Group agreed to establish a single BAT to standardize the reporting of bleeding symptoms and that would be useful for both pediatric and adult populations (see Supporting Information). The revised BAT could improve upon the diagnosis of MBD (in continuity with previous questionnaires) and the grading of severity in patients with known inherited bleeding disorders. Several issues are to be addressed in the development of a revised BAT [9].

Validity

Different types of validity need to be considered in the construct and analysis of a BAT. The BAT should be able to

Correspondence: Francesco Rodeghiero, Department of Cell Therapy and Hematology. San Bortolo Hospital, Viale Rodolfi, 37, I-36100 Vicenza, Italy.
Tel.: +39 444 753626; fax: +39 444 920708.
E-mail: rodeghiero@hemato.ven.it

[1]The complete list of contributors can be found in the Supporting Information, Acknowledgments.

measure any change or abnormality which must be considered (content validity) and that is felt to be clinically significant for the disease under investigation (face validity). Therefore, a BAT should include questions regarding all symptoms that may be as a result of a haemorrhagic disorder. For instance, hemoptysis is rarely or never associated with a bleeding disorder, and including questions describing such symptoms is unlikely to add any valuable information.

Reliability

This is a critical issue as any BAT should be able to provide reproducible results. Future studies will be needed to evaluate inter-rater and test-retest reliabilities. We deployed two strategies to a priori improve the reliability of the proposed BAT. First, recall of symptoms from a patient should be enhanced by collecting data that may be unequivocally reported by the subjects. Assessment of the presence and severity of bleeding disorders is a retrospective task for physicians, which necessarily requires asking the patient (and/or his/her relatives) about bleeding symptoms that may have occurred months or years before. This is particularly important in the field of *inherited* bleeding disorders, where the presence of bleeding symptoms spans a lifetime and can be sporadic. Even when more objective data can be collected (e.g. quantification of menstrual blood loss by hematin or by a visual assessment tool [10]), the issue of reliability still remains, as what is measured at the time of observation may not accurately reflect the average presentation of a symptom over a longer period of time. In contrast, *acquired* bleeding disorders (e.g. ITP) are normally not lifelong and come to the physician's attention within days to weeks of the initial bleeding event. In these disorders, a more detailed description of the bleeding symptoms is therefore possible and may be collected in a more detailed questionnaire.

Second, the questionnaire will require some degree of assessor training (typically performed by a physician or other health professional) to ensure reliability and to reduce the timeload. With regard to this, one of the most challenging tasks of any BAT is the identification of 'trivial' bleeding, which is a symptom that falls within the definition of a normal event and that should not be recorded as a bleeding symptom, a task better performed by well-trained personnel. The ISTH/SSC joint working group agreed to classify symptoms as significant whenever they:

1 Cause emotional distress to the patient sufficient to interfere with his/her social life/activities (e.g. spontaneous epistaxis forcing the person to leave a meeting).
2 Require medical attention, either for reassurance or intervention (e.g. iron therapy, resuturing, etc.).

Specific criteria for significant bleedings are reported in the Supporting Information.

Furthermore, to improve the predictive value of BAT as a diagnostic tool, only symptoms reported *before* and *at the time of diagnosis* should be included, so as to exclude the confounding effects of prophylactic treatments given on the basis of a pre-established diagnosis of a specific inherited bleeding disorder.

Proposal for a consensus bleeding score for the diagnosis of bleeding disorders

Two bleeding scores have been proposed, one validated for diagnosis [3] and another mainly for descriptive purposes [4]. The latter, with some modifications, has been adapted for use in children [7]. Whereas in the first BS [3] symptoms are scored from 0 (no symptom) to 3 (most severe), in the subsequently modified systems [4,7] the absence of bleeding after at least two hemostatic challenges was scored −1 and the grading spanned from −1 to 4. In both systems, only the most severe scores ever recorded for each symptom (and, in case, minus scores) are considered in obtaining the final total score. Since data comparing different BSs are unavailable, the ISTH/SSC joint working group agreed to develop a new Diagnostic Bleeding Score to be used mainly for the evaluation of patients referred for a possible bleeding disorder, that is for *diagnostic* purposes (see Table S1). The validity, reliability and predictive power of this new BS will need to be tested prospectively. Notably, although 'negative scores' for surgery, tooth extraction and postpartum bleeding were not icluded in the present BS, they can easily be extracted from the proposed questionnaire to allow comparison previously proposed BS.

We acknowledge that a BS specifically adapted for severe bleeding disorders (homo-emizygous bleeding disorders), including also the frequency of bleeding symptoms, could futher improve the description of the natural history of severe diseases. Achieving this goal will be one of the major future commitments of the ISTH/SSC Joint Working Group. Of note, the present questionnaire already includes two additional questions designed to approximate the 'true' incidence of bleeding. The first addresses the number of interventions per year of life; the second, the age of first occurrence, with the expectation that the earlier the onset, the more severe the disorder.

In conclusion, we recommend to adopt the Consensus ISTH BAT (questionnaire and BS) for any future study addressing description of bleeding symptoms or diagnosis of bleeding disorders. Validation of the questionnaire and bleeding scale for clinical use is urgently needed for clinical application.

Disclosure of Conflict of Interests

The authors state that they have no conflict of interest.

Supporting Information

Additional Supporting Information may be found in the online version of this article:

Data S1. The official communication of the SSC.
Table S1. Bleeding score.

Please note: Wiley-Blackwell are not responsible for the content or functionality of any supporting materials supplied by the authors. Any queries (other than missing material) should be directed to the corresponding author for the article.

References

1 Coller BS, Schneiderman P. Clinical evaluation of hemorrhagic disorders: the bleeding history and differential diagnosis of purpura. In: Hoffman R, Benz E, Shattil J, Furie B, Cohen J, Silberstein LE, McGlave P, eds. *Hematology. Basic Principles and Practice*. Philadelphia: Elsevier Churchill Livingstone,, 2005: 1975–99.

2 Rodeghiero F, Tosetto A, Castaman G. How to estimate bleeding risk in mild bleeding disorders. *J Thromb Haemost* 2007; **5**(Suppl. 1): 157–66.

3 Rodeghiero F, Castaman G, Tosetto A, Batlle J, Baudo F, Cappelletti A, Casana P, De Bosch N, Eikenboom JCJ, Federici AB, Lethagen S, Linari S, Srivastava A. The discriminant power of bleeding history for the diagnosis of type 1 von Willebrand disease: an international, multicenter study. *J Thromb Haemost* 2005; **3**: 2619–26.

4 Tosetto A, Rodeghiero F, Castaman G, Goodeve A, Federici AB, Batlle J, Meyer D, Fressinaud E, Mazurier C, Goudemand J, Eikenboom J, Schneppenheim R, Budde U, Ingerslev J, Vorlova Z, Habart D, Holmberg L, Lethagen S, Pasi J, Hill F, Peake I. A quantitative analysis of bleeding symptoms in type 1 von Willebrand disease: results from a multicenter European study (MCMDM-1 VWD). *J Thromb Haemost* 2006; **4**: 766–73.

5 Tosetto A, Castaman G, Rodeghiero F. Assessing bleeding in von Willebrand disease with bleeding score. *Blood Rev* 2007; **21**: 89–97.

6 Goodeve A, Eikenboom J, Castaman G, Rodeghiero F, Federici AB, Batlle J, Meyer D, Mazurier C, Goudemand J, Schneppenheim R, Budde U, Ingerslev J, Habart D, Vorlova Z, Holmberg L, Lethagen S, Pasi J, Hill F, Hashemi Soteh M, Baronciani L, Hallden C, Guilliatt A, Lester W, Peake I. Phenotype and genotype of a cohort of families historically diagnosed with Type 1 von Willebrand Disease in the European study, molecular and clinical markers for the diagnosis and management of Type 1 von Willebrand Disease (MCMDM-1VWD). *Blood* 2007; **109**: 112–21.

7 Bowman M, Riddel J, Rand ML, Tosetto A, Silva M, James PD. Evaluation of the diagnostic utility for von Willebrand disease of a pediatric bleeding questionnaire. *J Thromb Haemost* 2009; **7**: 1418–21.

8 Biss TT, Blanchette VS, Clark DS, Bowman M, Wakefield CD, Silva M, Lillicrap D, James PD, Rand ML. Quantitation of bleeding symptoms in children with von Willebrand Disease: use of a standardized pediatric bleeding questionnaire. *J Thromb Haemost* 2010; **8**: 950–6.

9 Koreth R, Weinert C, Weisdorf DJ, Key NS. Measurement of bleeding severity: a critical review. *Transfusion* 2004; **44**: 605–17.

10 Higham JM, O'Brien PM, Shaw RW. Assessment of menstrual blood loss using a pictorial chart. *Br J Obstet Gynaecol* 1990; **97**: 734–9.