

“Oh, You Have Blood Group O”: Diagnostic Testing Implications of the NHLBI VWD Guidelines for Diagnosis and Management (2007)

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Methods and Background: The National Heart Lung and Blood Institute (NHLBI) von Willebrand disease (VWD) expert panel (Drs. MB Hultin, AH James, M Manco-Johnson, RR Montgomery, ME Rick, TL Ortel, JE Sadler, M Weinstein, BP Yawn and WL Nichols, chair) recently finalized evidenced-based guidelines for VWD diagnosis and management, with pending publication (www.nhlbi.nih.gov/guidelines/vwd). Among the main and ancillary recommendations (≥ 54), several relate to laboratory diagnostic testing, and some are reviewed in this short presentation.

Results and Conclusions: 1) Recommended initial testing for VWD includes 3 tests: plasma von Willebrand factor antigen (VWF:Ag), ristocetin cofactor (VWF:RCo) activity, and factor VIII coagulant activity (FVIII), with optional reflexive or subsequent specialized VWF assays for evaluation of abnormal results, including VWF multimer analysis. 2) VWF and FVIII test results should be reported in IU/dL (and secondarily in %) if the test calibrator plasmas are linked to WHO standards. 3) The recommended “cut-off” level of VWF:RCo +/- VWF:Ag for definite diagnosis of VWD is <30 IU/dL (%), reflecting multiple considerations, however individuals with 30-50 IU/dL VWF may have VWD or risk of bleeding with invasive procedures and may merit treatment to elevate VWF. 4) Although it has previously been recommended to stratify VWF reference ranges with respect to blood group O and non-O, newly recommended is referencing VWF testing results to the population reference range rather than ABO-stratified ranges, since evolving information supports the concept that the major determinant of bleeding symptoms or risk is low VWF. 5) VWF:RCo/VWF:Ag ratios $\leq 0.5-0.7$ are recommended for initial distinction between type 2 VWD variants (2A, 2B, 2M) and type 1 VWD or normal status, but high variability (CV) of VWF assays as well as variability of VWF contributed by conditions of the patient or sample can compromise such distinction and may merit additional and/or repeat testing.