2001 National Survey of Hospital Coagulation Laboratory Practices:

Tests for von Willebrand Disease (vWD), Thrombosis/Hypercoagulability, and Lupus Anticoagulant (LA)

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Introduction

Hospital clinical laboratories play an important role in healthcare; and as documented in this survey, an estimated 97% of hospital laboratories reported performing coagulation tests. Coagulation tests are known to be vital to the diagnosis, treatment and management of bleeding and hypercoagulability disorders, and the majority of them are performed to screen for coagulation disorders or to monitor therapeutic anticoagulant therapy. In response to the uncertainty surrounding coagulation testing practices, we conducted this survey of hospital coagulation laboratories in the US, and chose hospitals as the testing environment to address a broader spectrum of in-house testing practices not subject to observation in physician office laboratories or other point-of-care testing sites. The purpose of this survey was to evaluate the availability of coagulation tests, assess various pre-analytical, analytical and post-analytical stages of the testing process, and evaluate some testing practices critical to clinical management of patients. This paper presents reported practices relating to testing for von Willebrand disease (vWD), thrombosis/hypercoagulability and lupus anticoagulant (LA). The survey used and a summary of our findings can be found at http://www.phppo.cdc.gov/mlp/coag2001.asp.

Methods

A survey of hospital coagulation laboratory directors, consisting of 43 questions relating to selected pre-analytical, analytical and pos-analytical practices, was undertaken in 2001 in order to assess the variability of coagulation testing in US hospitals. A group of coagulation laboratory experts and survey methodologists assisted the CDC in the development as well as the evaluation of the content and format of this survey. Furthermore, several versions of the survey was pilot tested in 9 hospital coagulation laboratories before its final dissemination. From a sampling frame of institutions listed in the 1999 directory of the American Hospital Association (AHA), we randomly selected 800 hospitals (sampling rate, 14%), and assessed practices in their coagulation laboratories. This sampling frame is not limited to the AHA members and it includes 95% of all hospitals as indicated by the Online Survey, Certification and Reporting database of CLIA-registered hospitals. Participants had the option of responding via Internet, and 20 (3%) did so. Inconsistent responses were excluded from data analysis.

Results and Discussion

Response rate. We received returned surveys from 632 institutions, resulting in a response rate of 79%.

Performance of coagulation tests. Of the 629 responding to this question, 612 (97%) reported performing coagulation testing.

von Willebrand Disease (vWD) Testing

Testing Frequency

vWD Test	Number (Percent) of Hospitals
von Willebrand factor (vWF) antigen assay	36 (6%)
vWF (Ristocetin cofactor) activity	42 (7%)
vWF multimers	11 (2%)

- 46% of the respondents (n = 24) used a single test for diagnosing vWD.
- 19% of the respondents (n = 7) that performed vWF antigen assay reported ABO specific reference interval for rthis assay.

Significantly lower vWF antigen levels have been found in individuals with blood type O compared to individuals with other blood types (*Arterioscl Thromb Vasc Biol*. 2000;20:2024-2028). However, use of ABO adjusted ranges for vWF antigen levels might not be essential for the diagnosis of this disorder; bleeding symptoms may depend on vWF antigen levels regardless of the ABO type (*Br J Haematol*. 2000;108:259-264).

Test Methodology

Testing Methodology	Use by Respondents (%)
vWF antigen assay	
1. Latex immunoassay (LIA)	13 (37%)
2. ELISA	10 (29%)
3. Electrophoresis	6 (17%)
4. Other*	6 (17%)
vWF activity	
1. Platelet aggregometry	31 (76%)
2. ELISA	2 (5%)
3. Collagen binding assays	1 (2%)
4. Other	7 (17%)

*5 respondents used immunoturbidimetric assays and 1 used Laurel rocket immunoassay. No respondent reported using more than 1 methodology for vWF antigen assay.

The electroimmunodiffusion (EID) method, also known as Laurel rocket immunoassay, is associated with the greatest variability in vWF antigen test results, and both the EID and LIA methods show poor sensitivity at low vWF antigen levels compared to ELISA methods (*Thromb Haemost*. 1999;82:1276-1282). Forty percent of the respondents used LIA or EID methods.

Most of the respondents used platelet function tests based on platelet agglutination/aggregation as functional tests for vWF activity. These tests have been shown to have the greatest result variability and poorest sensitivity to low vWF antigen levels while showing better performance in identifying Type 2 vWD (*Thromb Haemost*. 1999;82:1276-1282).

Thrombosis/Hypercoagulability Testing

- 5% of the respondents (n = 32) usually performed an assay for protein S activity (functional test) before antigenic assay.
- If results of the functional test were decreased, 17% (n= 5) performed an antigenic assay to differentiate Type I deficiency from Type II while 20% (n = 6) performed free and total protein S antigen assays.
- 6% of the respondents (n = 35) performed activated protein C (APC) resistance assay.
- If after performing APC resistance assay, results indicated resistance to APC, 61% (n = 20) obtained results for factor V Leiden mutation.

Lupus Anticoagulant (LA) Testing

- 18% of the respondents (n = 110) offered an LA profile.
- If the results of a mixing study for activated partial thromboplastin time (aPTT) did not correct to normal, 17% of the respondents (n = 63) routinely initiated workup to diagnose an LA.

If results of the mixing study for aPTT did nor correct to normal, the respondents indicated routinely performing the following assays to diagnose an LA:

Tests for Diagnosis of LA	Respondents (%) Performing the Test*
Dilute Russel viper venom time	46 (79%)
Hexagonal phase phospholipid assay (Staclot LA)	24 (51%)
Lupus sensitive aPTT	19 (40%)
Platelet neutralization procedure	17 (35%)
Tissue thromboplastin inhibition test	4 (9%)
Kaolin clotting time	2 (5%)

*58% of the respondents (n = 29) used >1 test for LA diagnosis.

Concluding Remarks

Limitations

Various laboratory practices noted in this survey are those that have been reported; and like any other surveys, they may not reflect actual practices. Surveys are subject to framing biases which can be reduced (e.g., by pilot testing) but not totally avoided.

Generalizability

Due to the high response (79%) and sampling (14%) rates, results of this survey appear to be generalizable.

In conclusion, we found that

- <20% of hospital laboratories in our study sample performed testing for vWD, thrombosis/hypercoagulability and LA, and
- there were substantial variability among some laboratory practices for those performing vWD, thrombosis/hypercoagulability and LA testing.