Results of a Survey of Hospital Coagulation Laboratories in the United States, 2001

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• ***Context.*—Coagulation and bleeding problems are associated with substantial morbidity and mortality, and inappropriate testing practices may lead to bleeding or thrombotic complications.**

***Objective.*—To evaluate practices reported by hospital coagulation laboratories in the United States and to determine if the number of beds in a hospital was associated with different practices.**

***Design.*—From a sampling frame of institutions listed in the 1999 directory of the American Hospital Association, stratified into hospitals with 200 or more beds ("large hospitals") and those with fewer than 200 beds ("small hospitals"), we randomly selected 425 large hospitals (sampling rate, 25.6%) and 375 small hospitals (sampling rate, 8.8%) and sent a survey to them between June and October 2001. Of these, 321 large hospitals (75.5%) and 311 small hospitals (82.9%) responded.**

***Results.*—An estimated 97.1% of respondents reported performing some coagulation laboratory tests. Of these, 71.6% reported using 3.2% sodium citrate as the specimen anticoagulant to determine prothrombin time (81.3% of large vs 67.7% of small hospitals, $P < .001$). Of the same respondents, 45.3% reported selecting thromboplastins insensitive to heparin in the therapeutic range when measuring prothrombin time (59.4% of large vs 39.8% of small hospitals, $P < .001$), and 58.8% reported having a therapeutic range for heparin (72.9% of large vs 53.2% of small hospitals, $P < .001$). An estimated 96.3% of respondents assayed specimens for activated partial thromboplastin time within 4 hours after phlebotomy, and 89.4% of respondents centrifuged specimens within 1 hour of collection. An estimated 12.1% reported monitoring low-molecular-weight heparin therapy, and to do so, 79% used an assay for activated partial thromboplastin time (58% of large vs 96% of small hospitals, $P = .001$), whereas 38% used an antifactor Xa assay (65% of large vs 18% of small hospitals, $P = .001$).**

***Conclusions.*—Substantial variability in certain laboratory practices was evident. Where significant differences existed between the hospital groups, usually large hospitals adhered to accepted practice guidelines to a greater extent. Some reported practices are not consistent with current recommendations, showing a need to understand the reasons for noncompliance so that better adherence to accepted standards of laboratory practice can be promoted.**

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It is well known that coagulation laboratory tests are performed in almost all hospitals; in our survey of 800 hospitals conducted between June and October of 2001, 97.1% of hospitals reported performing some type of coagulation laboratory test. These tests are known to be vital to the diagnosis, treatment, and management of bleeding and hypercoagulability disorders, and most are performed to screen for coagulation disorders or to monitor therapeutic anticoagulant therapy. Although coagulation testing has been examined within individual laboratories, little is known about various testing practices in a population of hospital laboratories. In response to the uncertainty surrounding coagulation testing practices, we conducted a survey of hospital coagulation laboratories in the United States and chose hospitals as the testing environment to examine a broader spectrum of in-house tests not performed in reference laboratories, in physician office laboratories, or in other point-of-care testing sites. Our purposes were to evaluate the availability of specific coagulation laboratory tests; to assess certain preanalytic, analytic, and postanalytic stages of the laboratory testing process; and to evaluate some testing practices critical to clinical management of patients. We used number of beds as a surrogate measure of hospital size and stratified hospitals into those with 200 or more beds (''large hospitals'') and those with fewer than 200 beds (''small hospitals''). Our rationale for examining large and small hospitals as separate groups was to determine whether they had different practice profiles regarding coagulation laboratory testing practices.

Several surveys addressing specific areas in hospital co-

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The actual survey questionnaire referenced in this article may be downloaded at http://www.phppo.cdc.gov/mlp/pdf/Survey%20Instrument.pdf

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agulation laboratory testing have been conducted,[1–12] but none has dealt with a broad cross-section of this laboratory specialty. Considering that no survey of coagulation laboratory practices can cover all areas, we tailored the present survey to capture 2 types of information. The first dealt with specific coagulation laboratory tests and disorders deemed to have substantial public health significance. The second related to general laboratory testing issues. In conducting this survey, we attempted to gain a better understanding of the state of coagulation testing and the extent of its variability across a stratified (by number of beds) random sample of hospitals in view of the recommendations and guidelines for more uniform, evidence-based coagulation testing practices.[13–28] This article presents reported practices relating to tests for prothrombin time (PT), activated partial thromboplastin time (aPTT), von Willebrand factor (vWF) antigen, vWF activity and vWF multimers, thrombosis/hypercoagulability and lupus anticoagulant, and low-molecular-weight heparin (LMWH). This article also reports on specific quality assurance (QA), test ordering, result reporting, and personnel practices as well as certain clinical service/laboratory characteristics and capacities.

MATERIALS AND METHODS

Study Sample

The target population was US hospitals, and the sampling frame consisted of the 1999 directory of the American Hospital Association, which included 95% of all hospitals, as indicated by the Online Survey, Certification and Reporting database of hospital laboratories registered under the Clinical Laboratory Improvement Amendments of 1988 (CLIA). We stratified hospitals into those with 200 or more beds (large hospitals) and those with fewer than 200 beds (small hospitals). The randomly selected large and small hospitals in the study sample constituted 25.6% (n = 425) of the large and 8.8% (n = 375) of the small hospitals and 13.5% of the 5907 hospitals in the sampling frame. The rationale for the sample sizes we used was based on the criterion of ensuring a maximum confidence interval of ±6% for any estimated proportion within the selection strata.

Questionnaire Development

We began the survey process by formulating a set of questions that underwent numerous revisions to improve clarity, brevity, and formatting. We ended the process by pilot-testing final versions using management personnel of 9 hospital coagulation laboratories. Additionally, we developed an Internet-based questionnaire, located on a secure Web site of the US Centers for Disease Control and Prevention, and offered it to all participants as an alternative means of responding to the questionnaire. This electronic version mirrored the printed questions, answer selections, and formatting. Additionally, it incorporated logical constraints to prevent respondents from entering conflicting or contradictory answers.

Survey Implementation

We collected data between June 2001 and October 2001. One week after the initial mailing, we sent a reminder postcard to each respondent, and we also telephoned nonrespondents within 2 weeks after mailing the postcard. The purpose of the call was to confirm receipt of the survey, to encourage participation, and to secure a commitment to complete and return the survey.

Data Entry and Management

Two different individuals keyed the information from each questionnaire, and the data for each were compared to identify any discrepancies. A data entry supervisor then performed the adjudication process. To further assess the integrity of the data, we examined 10% of the survey booklets after rekeying and adjudicating discrepancies.

Data Exclusion

The paper and electronic data were combined to create the final dataset. We excluded questions with inconsistent responses. Additionally, we excluded all responses with more than one response category checked when instructions specified checking only one. Also excluded were all negative responses to a gate question and positive responses to one or more following subquestions.

Data Presentation and Statistical Analysis

Throughout this report, percentages reported for yes-or-no questions are percentages of affirmative responses, whereas for multiple-choice questions, these are percentages of those responding to one or more selections. We compared responses from large and small hospital laboratories using 2-tailed χ^2 test. All P values $<.05$ were considered to demonstrate statistically significant differences. Because of oversampling of large hospitals and undersampling of small hospitals, we used calculated weights to estimate overall percentages. Percentages of hospitals reported throughout this article relate to these calculated, not actual, percentages. These weights were derived from the number of large and small hospitals in the sampling frame, the proportions that responded performing coagulation laboratory tests, and the proportions responding affirmatively to a gate (and subgate) question(s) for each questionnaire section. Percentages of large and small hospitals, however, relate to the actual proportions of respondents.

RESULTS AND COMMENT

Since the publication of the Institute of Medicine report in 2000,[29] awareness of preventable medical errors has increased, leading to efforts to create systems that will help detect and eliminate them. An area that has a great potential impact on patient safety is coagulation laboratory testing. For instance, outpatients with international normalized ratios (INRs) greater than 6.0 face a significant short-term risk of major hemorrhage.[30] Incorrect coagulation laboratory testing practices and especially those used in monitoring of patients to prevent bleeding or thrombotic events may lead to adverse clinical outcomes. Incorrect aPTT values may result in a risk of subsequent death, thrombosis, bleeding, and overall morbidity.[31] To improve the safety of patients undergoing coagulation laboratory tests, it is necessary first to assess the extent to which hospital laboratories adhere to accepted testing practices. Our results here indicate that many laboratories do not follow certain testing guidelines. Variations in some such practices could have a direct impact on clinical outcomes.

Response Rates

We received 632 completed questionnaires (including 20 surveys submitted electronically) from the 800 sampled hospitals, for a response rate of 79.0% (75.8% of large and 82.9% of small hospitals). This response rate compares well with those obtained in other studies: 50.7% for a survey of aPTT reporting in Canadian medical laboratories,[4] 77.4%[3] and 69.8%[1] for a survey of INR reporting in Canada, and 85.4% for a survey of PT monitoring of anticoagulation therapy in Massachusetts.[2]

Performance of Coagulation Laboratory Tests

As expected, virtually all responding hospitals (97.1%) reported performing some type of coagulation laboratory

Table 1. In-House Performance of Specific Tests

Test*	Large Hospitals, % (No.)	Small Hospitals, % (No.)	Estimated Proportion of Hospitals,%†	*P*
PT	100 (310)	100 (295)	100	>.99
aPTT	99.4 (309)	98.3 (292)	98.6	.23
Bleeding time	89.4 (277)	90.3 (270)	90.0	.70
Fibrinogen	94.9 (295)	59.1 (163)	69.2	<.001
D-dimer	83.2 (252)	45.9 (124)	56.5	<.001
Fibrin(ogen) degradation products	66.9 (200)	35.2 (92)	44.2	<.001
Activated clotting time	57.8 (170)	26.6 (70)	35.5	<.001
Thrombin time	54.5 (159)	19.0 (50)	29.1	<.001
Factor VIII activity	36.5 (105)	2.0 (5)	11.8	<.001
Factor IX activity	32.2 (92)	1.2 (3)	10.0	<.001
Factor VII activity	24.6 (70)	1.2 (3)	7.8	<.001
Platelet aggregation study	24.3 (70)	0.8 (2)	7.5	<.001
Factor V activity	23.5 (67)	0.8 (2)	7.2	<.001
Factor X activity	22.5 (64)	0.8 (2)	7.0	<.001
Factor II activity	19.1 (54)	0.8 (2)	6.0	<.001
Heparin assay (anti-Xa)	16.8 (48)	1.6 (4)	5.9	<.001
vWF (ristocetin cofactor) activity	13.7 (41)	0.3 (1)	4.1	<.001
Bethesda assay-inhibitor titer	14.2 (40)	0	4.0	<.001
Factor VIII antigen	11.7 (33)	0.8 (2)	3.9	<.001
Ristocetin titration of platelet aggregation	12.7 (36)	0.4 (1)	3.9	<.001
Activated protein C resistance	10.6 (32)	1.0 (3)	3.7	<.001
vWF antigen	11.8 (35)	0.4 (1)	3.6	<.001
Euglobulin clot lysis time	8.9 (25)	0.8 (2)	3.1	<.001
Factor V Leiden	9.5 (27)	0	2.7	<.001
Plasminogen (functional) assay	8.2 (23)	0.4 (1)	2.6	<.001
Factor X antigen	6.0 (17)	0	1.7	<.001
Platelet antibody	5.0 (14)	0	1.4	<.001
vWF multimers	1.8 (5)	0	0.5	.03
Plasminogen antigen	0.7 (2)	0	0.2	.18

* PT indicates prothrombin time; aPTT, activated partial thromboplastin time; D-dimer, dimerized plasmin fragment D; and vWF, von Willebrand factor.

† Estimated by weighing reported responses using relative proportions of large and small hospitals in the sampling frame and the proportions that reported performing coagulation testing.

Table 2. Concentration of Sodium Citrate Used

Concentration	Large Hospitals, % (No.)*	Small Hospitals, % (No.)*	Estimated Proportion of Hospitals,%†	*P*
3.2% (109 mmol/L)	81.3 (244)	67.7 (193)	71.6	<.001
3.8% (129 mmol/L)	20.0 (60)	33.7 (96)	29.8	<.001

* Proportions add up to greater than 100% because 8 respondents (4 large and 4 small hospitals) noted that they used both concentrations of sodium citrate.

† Estimated by weighing reported responses using relative proportions of large and small hospitals in the sampling frame and the proportions that reported performing coagulation testing.

tests (97.8% of large hospitals and 96.8% of small hospitals).

In-House Performance of Specific Coagulation Laboratory Tests

We asked participants if they performed any of 29 specific coagulation laboratory tests (Table 1). The 5 most commonly performed coagulation laboratory tests were PT, 100%; aPTT, 98.6%; bleeding time, 90.0%; fibrinogen, 69.2%; and dimerized plasmin fragment D, 56.5%. Except for the hospitals performing tests for PT, aPTT, and bleeding time, and the 2 large hospitals assaying plasminogen antigen, a significantly ($P < .05$) greater proportion of the large hospitals performed each of the 29 surveyed tests in house compared with the small hospitals. Our findings are similar to those obtained from a 1996 random stratified sample of all US laboratories, which documented that the most commonly performed coagulation laboratory test was PT, with an estimated annual test volume of 65.9 million, and that the second most commonly performed coagulation laboratory test was aPTT, with an estimated annual test volume of 45.6 million.[32]

PT Testing Practices

Anticoagulant Concentration.—Most (71.6%) hospitals reported using 3.2% sodium citrate as an anticoagulant. However, 20.0% of large hospital and 33.7% of small hospital respondents reported using 3.8% citrate as the anticoagulant when collecting specimens for PT ($P <.001$; Table 2). A significantly greater proportion of large (80.0%) hospitals exclusively used 3.2% citrate compared with small (66.3%) hospitals ($P < .001$). Use of 3.8% citrate leads to a statistically significant difference in the results of PT assays in the samples less than 80% filled compared with those that are 100% filled.[33] For aPTT assays using 3.8% citrate, a statistically significant difference occurs at less than 90% filled. However, no statistically significant differences were observed in PT results from a 3.2% citrate

Table 3. Format Used to Report Prothrombin Time (PT) Result by US Hospitals and Canadian Medical Laboratories			
Reporting Format for PT*	US, 2001 (n = 626)†	Canada, 1996 (n = 649)[3]	Canada, 1992 (n = 857)[1]
Seconds and INR	80%‡	60%	36%
Seconds, INR, and PT ratio	12%§	. . .	. . .
Not specified	4%	. . .	. . .
INR only	3%	36%	15%
INR and PT ratio	0.5%	1.5%	6%
Seconds only	0%	<1%	36%
PT ratio only	0%	1%	7%

* INR indicates international normalized ratios.

† Reported percentages are the actual proportions and were not estimated by applying weights. This approach could be justified because there were statistically insignificant (P = .33 to .59) differences between large and small hospitals in the way they reported their PT results.

‡ Twenty percent noted that they reported PT results in both seconds and INR, but they failed to indicate whether they also used therapeutic PT ratio.

§ This proportion may be as high as 32% because an additional 20% noted that they reported PT results in seconds and INR while failing to note additionally whether they reported results as therapeutic PT ratio.

tube between filled volumes of 60% and 100% or in aPTT results between filled volumes of 70% and 100%.[33] Based on the 1998 recommendations made by the World Health Organization and NCCLS (scheduled to be renamed Clinical and Laboratory Standards Institute on January 1, 2005), 3.2% citrate is the anticoagulant of choice for coagulation laboratory testing.[19,23] In a 1998 study,[34] the recommendation to use 3.2%, instead of 3.8%, sodium citrate was supported by noting that the concentration of sodium citrate had a significant effect on PT and aPTT assay results. In a 1997 study,[35] underfilling of specimen tubes containing 3.8% sodium citrate prolonged PT and especially aPTT compared with tubes containing 3.2% sodium citrate. Concentration of sodium citrate may have a significant effect on assay results, with 19% of patients receiving intravenous heparin therapy having a greater than 7-second difference when aPTT results were compared.[36] In a survey of aPTT reporting in Canadian medical laboratories, published in 2000,[4] 46% were still using 3.8% citrate. In our survey, an estimated 30% of hospitals noted that they used 3.8% citrate, potentially resulting in prolonged PT and aPTT results and triggering unnecessary anticoagulant therapy.

Reporting of PT Results.—Virtually all (99.9%) hospitals used INR to report PT, whereas 96.9% also reported PT in seconds, and 16.7% reported results as PT therapeutic ratio (Table 3). Although reporting PT results in seconds is useful for managing bleeding patients or those with liver disease, doing so for those on anticoagulant therapy reportedly leads clinicians to inappropriately compare results among hospitals.[3] Reliance on therapeutic PT ratio has been documented to cause errors in anticoagulant therapy.[3,37] Most laboratories reported PT results using INR (Table 3) together with either seconds or seconds and PT ratio. Reporting of PT results in INR has increased over the years from 5% to 57% in 1992 (Canada)[1,2] to 98% to 100% in 1996 (Canada),[3,12] and it stood at 99.9% in the current US survey (Table 3). Reporting of PT results exclusively in INR in Canada increased from 15% of all licensed medical laboratories in 1992 to 36% in 1996. This survey shows that 3% of the US hospital laboratories reported PT results exclusively in INR. Reporting PT results in both seconds and INR increased steadily over the years, from 36% in 1992 (Canada) to 60% in 1996 (Canada); it was 97% in this 2001 US survey. On the other hand, the practice of reporting PT results only in seconds decreased from 36% in 1992 (Canada) to less than 1% in 1996 (Canada) and 2001 (United States) (Table 3). In our study, 17% of the respondents reported providing therapeutic PT ratio. This rate may be compared with a rate of 43% in a survey of anticoagulant therapy monitoring reported in 1996[12] and with rates of 13% and 2.5% in the 1992[1] and 1996[3] surveys of Canadian medical laboratories, respectively.

Reference Interval for PT Assay.—An estimated 89.7% of the respondents (97.3% of large vs 86.6% of small hospitals, $P < .001$) reported conducting in-house evaluations to establish reference intervals for the PT assay. An estimated 58.7% (45.9% of large vs 73.7% of small hospitals, $P < .001$) used less than 40 subjects to establish their PT reference intervals. To *establish* a reference interval, the NCCLS has recommended a minimum of 120 subjects for each reference population or subclass as the smallest number allowing determination of a 90% confidence interval around reference limits.[38] (However, to *verify* a reference interval, a more common practice, the NCCLS recommends a minimum of 20 subjects.) An estimated 4.4% (5.4% of large vs 3.2% of small hospitals, $P = .21$) noted using at least 120 subjects to establish their reference intervals for PT assay. Of the 10.3% not conducting in-house evaluations to establish their reference interval for PT, 55% used manufacturer's inserts, 30% used published values, and 19% used other methods.

Sensitivity of PT Assay to Heparin.—According to consensus guidelines developed at the 1997 conference of the College of American Pathologists (CAP), laboratories should determine sensitivity of their PT assay to heparin and, where possible, select a thromboplastin that is insensitive to heparin in the therapeutic range.[19] An estimated 16.1% (17.9% of large vs 15.4% of small hospitals, $P = .41$) reported determining sensitivity of their PT assays to heparin, and 45.3% (59.4% of large vs 39.8% of small hospitals, $P < .001$) reported selecting a PT-thromboplastin reagent that was insensitive to heparin in the therapeutic range.

International Sensitivity Index of Thromboplastin Lot.—The International Sensitivity Index (ISI) value of the respondents' current thromboplastin lot ranged from 0.89 to 2.63 (average, 1.60; median, 1.81; n = 567). Large hospitals reported a median ISI of 1.56, whereas small hospitals reported a median of 1.89. A total of 40.0% reported ISIs of 1.70 or less for their current thromboplastin lots (50.3% of large vs 36.0% of small hospitals, $P = .001$), whereas a total of 29.3% reported ISIs of 1.20 or less (41.7% of large hospitals vs 24.3% of small hospitals, $P < .001$). Two published studies have reported ISI values of

survey participants. A 1992 report involving 88 acute care hospitals in Massachusetts found ISI values of 1.89 to 2.74.[12] The second report, involving surveys of all licensed Canadian medical laboratories in 1996 and 1992,[3] noted that average ISI value had decreased from 2.07 in 1992 to 1.63 in 1996.[1] Of the respondents to the 1996 survey of Canadian medical laboratories, 35% reported ISI values of 1.20 or less. Optimal ISI has not been rigorously defined by laboratory studies or clinical trials.[19] Sensitive thromboplastin reagents with lower ISI values may offer the potential for improved precision in determining the INR, because INR = (PT ratio)^{ISI}, where PT ratio = patient PT/mean normal PT. However, some studies have suggested that low-ISI reagents may be less precise.[39] No consensus exists as to what the optimal reagent ISI value should be. For instance, the CAP recommends thromboplastins with a manual ISI between 0.90 and 1.70, with a preference toward the lower end of this scale.[19] On the other hand, the American College of Chest Physicians recommends ISI values of 1.20 or less.[40] Therefore, depending on the guideline used, 30% to 40% of hospitals in this survey reported using reagents with recommended ISI values.

Testing Practices for aPTT

Therapeutic Range for Heparin.—It has been recommended that each laboratory establish an individual therapeutic range for heparin specific to its own reagent and instrument system.[41,42] Significant variations between heparin sensitivity of aPTT reagents produced under the same name by the same supplier have been observed.[41] Variations are such that using the recommended aPTT ratio or prolongation of aPTT for monitoring heparin therapy, a hospital would achieve a much different degree of heparinization from year to year. In a 1998–1999 survey of aPTT reporting in Canadian medical laboratories, 66% of institutions had established an individual therapeutic range for aPTT testing.[4] Our survey produced similar results. Of those performing the aPTT assay, an estimated 58.8% reported having an aPTT therapeutic range for heparin when monitoring heparin therapy (72.9% of large vs 53.2% of small hospitals, $P < .001$). Whereas 61.6% reported the aPTT therapeutic range for heparin when monitoring heparin therapy (66.8% of large vs 59.5% of small hospitals, $P = .15$), 10.7% reported including the corresponding heparin concentration with aPTT results (7.0% of large vs 12.2% of small hospitals, $P = .10$).

How the aPTT Therapeutic Range for Heparin Was Determined.—The respondents reported doing the following to determine the aPTT therapeutic range for heparin:

- Using samples from patients on heparin therapy to compare a new reagent lot to an old reagent lot (54.1%; 65.5% of large vs 49.6% of small hospitals, $P = .007$)
- Using heparin-spiked samples to compare a new reagent lot to an old reagent lot (46.1%; 46.8% of large vs 45.9% of small hospitals, $P = .88$)
- Performing anti-Xa assay (26.5%; 47.2% of large vs 18.3% of small hospitals, $P < .001$)
- Using heparin-spiked samples to compare a new heparin lot to an old heparin lot (18.1%; 11.5% of large vs 20.8% of small hospitals, $P = .04$)
- Using samples from patients on heparin therapy to compare a new heparin lot to an old heparin lot (13.0%; 11.4% of large vs 13.6% of small hospitals, $P = .60$)
- Performing protamine sulfate titration (6.8%; 10.6% of large vs 5.2% of small hospitals, $P = .13$)

Reagent sensitivity in ex vivo samples has been reported to be substantially different from reagent sensitivity in in vitro samples.[40] Specific therapeutic ranges may be necessary. Samples prepared by adding heparin to normal plasma in vitro can be misleading and should not be used. In vitro sensitivity curves using different reagents vary at therapeutic heparin levels.[43] In contrast, aPTT reagents reportedly did not differ in ex vivo studies, showing that in vitro curves demonstrated poor performance. In one study,[44] 60% of patients did not adequately compare by aPTT estimation of plasma heparin levels. The aPTT therapeutic range for heparin should be determined by comparing ex vivo specimens (1) with an appropriately validated heparin assay (preferably), or (2) with a previously calibrated aPTT specimen using a method to control for reagent drift.[25] Equivalence should be determined by using ex vivo plasma samples obtained from patients treated with unfractionated heparin rather than spiked in vitro heparinized plasma samples.[40,44] An estimated 46% of all respondents reported using heparin-spiked samples to determine their new reagent's aPTT therapeutic range for heparin, whereas 54% used ex vivo specimens from heparinized patients for the same purpose. These may be compared with the rates of 67% and 33% for heparin-spiked and ex vivo specimens, respectively, obtained in the 1998–1999 Canadian survey.[4] As part of a 1995 CAP comprehensive coagulation survey, 23% of laboratories reported using in vitro heparin spiking to establish an aPTT therapeutic range for heparin.[45] In the 1998–1999 survey of Canadian medical laboratories, 90% used an anti-Xa assay, and 10% used protamine sulfate titration.[4] In this survey, 65% of the respondents assaying for heparin did so using an anti-Xa assay, 15% used protamine sulfate titration, and 19% used other methods. The Canadian survey, however, did not provide an option for other methods.[4]

When the aPTT Therapeutic Range for Heparin Was Reconfirmed.—The respondents reported reconfirming the aPTT therapeutic range for heparin under the following circumstances:

- When new instrumentation was used (75.8%; 83.1% of large vs 72.9% of small hospitals)
- When new reagent lots were used (71.9%; 79.8% of large vs 68.8% of small hospitals)
- When new reagents were used (45.6%; 57.3% of large vs 41.0% of small hospitals)
- After a specified time (19.7%; 23.9% of large vs 18.1% of small hospitals)
- None of the above (10.4%; 5.2% of large vs 12.5% of small hospitals)

The responses from large and small hospitals were significantly different ($P = .046$). Current consensus maintains that therapeutic ranges should be recalculated after the introduction of a new reagent or a new lot of the same reagent or a change in instrument.[4,25,46]

Specimen Management for aPTT Assay.—We asked participants if they managed their specimens in the following ways: assaying them within 4 hours after phlebotomy, centrifuging them within 1 hour of collection, and keeping them at room temperature or at 4°C before testing (Table 4). A significantly ($P = .007$) greater proportion of

Table 4. Specimen Management for Activated Partial Thromboplastin Time (aPTT) Assay				
Practices Used for aPTT Assay Specimen Management	Large hospitals, % (No.)	Small Hospitals, % (No.)	Estimated Proportion of Hospitals,%*	*P*
Specimens assayed within 4 hours after phlebotomy	95.5 (276)	96.6 (259)	96.3	.49
Specimens centrifuged within 1 hour of collection	83.9 (229)	91.5 (238)	89.4	.007
Specimens kept at room temperature prior to testing	84.2 (223)	79.7 (196)	81.0	.19
Specimens kept at 4°C prior to testing	20.3 (47)	24.1 (54)	23.0	.33

* Estimated by weighing reported responses using relative proportions of large and small hospitals in the sampling frame, the proportions that reported performing coagulation testing, and the proportions of the latter that reported performing the aPTT assay.

the small hospital respondents (91.5%) reported centrifuging specimens within 1 hour of collection compared with the large hospital respondents (83.9%). According to the NCCLS guideline, specimens for aPTT assay are stable for up to 8 hours at room temperature, except for patients receiving unfractionated heparin therapy.[23] Heparinized samples, when stored uncentrifuged at room temperature, demonstrate a clinically significant shortening of aPTT, and individual samples demonstrate a more than 50% decrease in ex vivo heparin levels at 4 hours.[41] According to the approved NCCLS guideline, samples can be assayed up to 4 hours after phlebotomy if they are centrifuged within 1 hour of collection.[23] In agreement with this, an estimated 96.3% of hospitals stated that they assayed specimens within 4 hours after phlebotomy, and 89.4% of hospitals noted that they centrifuged specimens within 1 hour of collection. In the 1998–1999 survey of Canadian medical laboratories, 90% of responding laboratories reported analyzing specimens within 4 hours of specimen collection.[4]

Practices Relating to Assays for von Willebrand Disease

An estimated 3.6% of the respondents (11.8% of large vs 0.4% of small hospitals, $P < .001$) reported performing von Willebrand factor (vWF) antigen assay, whereas an estimated 4.1% of the respondents (13.7% of large vs 0.3% of small hospitals, $P < .001$) reported performing vWF activity (ristocetin cofactor activity) assay. Of the respondents performing vWF antigen assay, 19% reported an ABO-specific reference interval for vWF antigen assay. Significantly lower vWF antigen levels have been found in individuals with blood type O compared with individuals with other blood types.[47] 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.[48]

An estimated 1.2% of the respondents (3.4% of large vs 0.3% of small hospitals, $P < .001$) reported providing results for vWF multimers assay. Hospitals reported obtaining vWF multimers results under the following conditions:

- Only when ordered by a clinician (84%)
- When ristocetin cofactor was decreased (34%)
- When ristocetin cofactor was disproportionately decreased relative to vWF antigen (26%)
- When antigen and activity were both low (23%)
- Only if ristocetin-induced platelet aggregation indicated type II B von Willebrand Disease (11%)

Practices Relating to Thrombosis/Hypercoagulability Workup

An estimated 3.1% of the respondents (10.1% of large vs 0.3% of small hospitals, $P < .001$) reported usually performing an assay for protein S activity (functional test) before performing an antigenic assay. If results of the functional test were lower than normal, 16% performed an antigenic assay to differentiate type I deficiency from type II, whereas 19% performed free and total protein S antigen assays. An estimated 3.7% of the respondents (10.6% of large vs 1.0% of small hospitals, $P < .001$) reported performing an activated protein C (APC) resistance assay. If the latter test result indicated resistance to APC, 61% obtained results for factor V Leiden mutation.

Homozygosity or heterozygosity for factor V Leiden in the absence of symptoms does not necessarily indicate that preventive treatment is required.[49] Furthermore, there is no established intervention to reduce thrombotic risk as a consequence of finding a factor V Leiden mutation. Depending on the APC resistance functional assay used and the cutoff values for defining an abnormal result, factor V Leiden mutation may account for 85% to 95% of patients with APC resistance.[50] Factor V Leiden mutation is reported to produce a relative risk of venous thrombosis of 7-fold in the heterozygous state and 80-fold in the homozygous state. However, even in the homozygous state, this mutation does not appear to cause disease early in life, as seen with protein S and protein C homozygosity. Activated protein C resistance with normal factor V genotype is a risk factor for venous thrombosis,[51] but APC resistance appears to have no major effect on life expectancy.[52] Consequently, long-term anticoagulation in carriers of factor V Leiden, on the basis of the carrier state alone, has been controversial; it is interesting to note that an estimated 61% of the respondents performing APC resistance assays also obtained results for factor V Leiden mutation if results indicated resistance.

Practices Relating to Diagnosis of Lupus Anticoagulant

An estimated 12.9% of the respondents (30.3% of large vs 6.1% of small hospitals, $P < .001$) reported offering a lupus anticoagulant profile.

Respondents chose from among the following possible responses for what they would do if a PT result was prolonged, in reference to when respondents performed a mixing study:

- Their laboratory did not offer mixing studies for PT (47.5%; 12.3% of large vs 61.4% of small hospitals).
- They did so only if there was an additional order for

Table 5. Assays Used to Monitor Low-Molecular-Weight Heparin (LMWH) Therapy				
Assay Used to Monitor LMWH Therapy*	Large Hospitals, % (No.)	Small Hospitals, % (No.)	Estimated Proportion of Hospitals, %†	*P*
aPTT	58 (23)	96 (24)	79	.001
Antifactor Xa	65 (32)	18 (3)	38	.001
Factor Xa (inhibitor assay)	8 (3)	6 (1)	7	.79
Thrombin inhibitor assay (HEP test)	0	0	0	. . .

* aPPT indicates activated partial thromboplastin time; HEP, heparin.

† Estimated by weighing reported responses using relative proportions of large and small hospitals in the sampling frame, the proportions that reported performing coagulation testing, and the proportions of the latter that reported monitoring LMWH therapy.

the mixing study (46.7%; 77.7% of large vs 34.4% of small hospitals).

- They always did so when PT was prolonged (2.2%; 3.4% of large vs 1.8% of small hospitals).
- They did so only if PT was ordered as part of the lupus anticoagulant profile (1.0%; 3.4% of large vs no small hospitals).
- They did so under other unspecified circumstances (2.6%; 3.1% of large vs 2.5% of small hospitals).

The responses from large and small hospitals were significantly different ($P < .001$).

Respondents chose from among the following possible responses for what they would do if an aPTT result was prolonged, in reference to when respondents performed a mixing study:

- Their laboratory did not offer mixing studies for aPTT (44.4%; 10.3% of large vs 58.0% of small hospitals).
- They did so only if there was an additional order for the mixing study (48.8%; 78.4% of large vs 37.1% of small hospitals).
- They always did so when aPTT was prolonged (2.5%; 4.1% of large vs 1.9% of small hospitals).
- They did so only if aPTT was ordered as part of the lupus anticoagulant profile (1.3%; 4.5% of large vs no small hospitals).
- They did so under other unspecified circumstances (3.0%; 2.7% of large vs 3.0% of small hospitals).

Again, the responses from large and small hospitals were significantly different ($P < .001$).

Of hospitals offering mixing studies for aPTT, if the results did not correct to normal, an estimated 11.7% of the respondents (20.5% of large vs 8.2% of small hospitals, $P = .004$) reported routinely initiating a workup to diagnose a lupus anticoagulant.

Practices Relating to Monitoring of LMWH Therapy

Monitoring LMWH Therapy.—Only an estimated 12.1% reported monitoring LMWH therapy (18.6% of large vs 9.5% of small hospitals, $P = .002$). In our survey, however, we did not ask participants if they actually used LMWH therapy; rather, we asked only if they monitored it. Therefore, we could not determine what proportion of those using LMWH monitored it. Because LMWH has greater bioavailability than heparin and a more predictable anticoagulant response, anticoagulation can be achieved effectively by calculating dosages based on patients' weight without the need for laboratory monitoring.[39]

Assays Used to Monitor LMWH Therapy.—We asked participants if they used the following tests to monitor LMWH therapy: aPTT assay, antifactor Xa assay, factor Xa assay (inhibitor assay), and thrombin inhibitor assay (heparin test) (Table 5). When monitoring LMWH therapy, 58% of large hospitals reported using aPTT assay, compared with 96% of small hospitals ($P = .001$). However, 65% of large hospitals reported using antifactor Xa assay, compared with 18% of small hospitals ($P = .001$). Small hospitals mostly used aPTT assay in lieu of anti-Xa assay to monitor LMWH therapy, probably because few of them reported performing an in-house anti-Xa assay (Table 1). In the 1998–1999 Canadian survey, 71% of those monitoring LMWH did so by a chromogenic anti-Xa assay, and the remaining 29% used an anti-Xa clotting assay. Our results were in agreement with this Canadian survey, which noted that no respondents reported using thrombin inhibitor assay (heparin test) to monitor LMWH therapy (Table 5). The chromogenic antifactor Xa assay is recommended for monitoring LMWH, but the aPTT assay is not[22] because of the lack of impact of LMWH on aPTT. This is because LMWH achieves most of its anticoagulant effect by inhibiting factor Xa, rather than thrombin or factor IXa. Use of an inappropriate aPTT assay, instead of an antifactor Xa assay, may trigger modification of patient anticoagulation therapy, leading to adverse clinical outcomes.

Use of Calibration Curves.—The CAP has recommended that laboratories use different calibrations for LMWH and unfractionated heparin[22] and that laboratories establish calibration curves for each lot and type of LMWH.[25] An estimated 70% of the respondents (76% of large vs 50% of small hospitals, $P = .26$) used different calibration curves for LMWH and unfractionated heparin, and 43% (41% of large vs 50% of small hospitals, $P = .74$) used different calibration curves for each type of LMWH.

Timing of Specimen Collection for Antifactor Xa Assay.—We asked participants if they recommended an optimal time after subcutaneous administration of LMWH to collect specimens for antifactor Xa testing (Table 6). More than half (51%) did not recommend a time for testing, whereas almost a third (31%) recommended testing 4 hours after injection. According to the CAP recommendation, to monitor LMWH therapy, the sample should be obtained 4 hours after subcutaneous injection of LMWH.[22]

Information Requested and Noted on Requisition Forms

An estimated 60.8% of respondents (45.9% of large vs 66.7% of small hospitals, $P < .001$) stated that they used test requisition forms. Some hospitals may have given negative responses to this question because they order coagulation tests electronically, without using a paper-based requisition form. There was a wide variation in the proportion of respondents requesting and noting specific information items on test requisition forms (Table 7). Al-

Table 6. Timing of Specimen Collection for Antifactor Xa Assay

Time of Specimen Collection After Subcutaneous Administration of LMWH*	Large Hospitals, % (No.)	Small Hospitals, % (No.)	Estimated Proportion of Hospitals,%†	*P*
Our coagulation laboratory does not recommend a time for testing	42 (14)	75 (3)	51	.22
4 Hours after injection	33 (11)	25 (1)	31	.74
Between 2 and 4 hours after injection	15 (5)	0 (0)	11	.40
Do not know	6 (2)	0	4	.61
5 Hours or more after injection	3 (1)	0	2	.72
Other	0	0	0	. . .

* LMWH indicates low-molecular-weight heparin.

† Estimated by weighing reported responses using relative proportions of large and small hospitals in the sampling frame, the proportions that reported performing coagulation testing, the proportions of the latter that reported monitoring LMWH therapy, and the proportions using an anti-Xa assay to monitor LMWH.

Table 7. Information Requested and Noted on Requisition Forms

Information Item Requested or Noted*	Large Hospitals, % (No.)	Small Hospitals, % (No.)	Estimated Proportion of Hospitals,%†	*P*
Diagnosis	78.4 (105)	82.1 (156)	81.0	.40
ICD-9 code	71.5 (88)	54.0 (88)	59.0	.003
Warfarin use	56.9 (74)	50.6 (86)	52.4	.28
Unfractionated heparin use	48.8 (59)	31.0 (49)	36.0	.003
Heparinoid use	39.5 (47)	27.9 (43)	31.2	.04
CPT code	26.2 (28)	27.5 (42)	27.1	.82
Low-molecular-weight heparin use	28.6 (32)	18.2 (28)	21.1	.045
Salicylate use	16.8 (18)	16.1 (25)	16.3	.88
Oral contraceptive use	9.3 (10)	4.0 (6)	5.5	.09

* *ICD-9* indicates *International Classification of Diseases, Ninth Revision*; *CPT, Current Procedural Terminology.*

† Estimated by weighing reported responses using relative proportions of large and small hospitals in the sampling frame, the proportions that reported performing coagulation testing, and the proportions of the latter that reported using coagulation test requisition forms.

Table 8. Reasons for Rejection of Coagulation Specimens

Rejection Criterion	Large Hospitals, % (No.)	Small Hospitals, % (No.)	Estimated Proportion of Hospitals,%*	*P*
Clotted specimen	100 (312)	100 (300)	100	>.99
Improperly anticoagulated specimen	99.0 (308)	99.0 (296)	99.0	.96
Insufficiently labeled specimen containers	99.0 (306)	98.7 (297)	98.8	.68
Conflicting patient information	91.0 (273)	92.9 (274)	92.3	.40
Excessive specimen transport time	92.4 (279)	92.2 (270)	92.2	.91
Specimen stored at inappropriate temperature	83.4 (251)	86.6 (251)	85.7	.28
Hemolyzed specimen	86.1 (266)	85.1 (252)	85.4	.74
Lack of hospital medical record number	58.9 (175)	31.2 (88)	39.1	<.001
Specimen collected via indwelling catheter	32.7 (96)	32.1 (90)	32.3	.90

* Estimated by weighing reported responses using relative proportions of large and small hospitals in the sampling frame, the proportions that reported performing coagulation testing, and the proportions of the latter that reported using coagulation test requisition forms.

though most requisition forms provided information on diagnosis (81.0%), *International Classification of Diseases, Ninth Revision* code (59.0%), and warfarin use (52.4%), a minority provided information pertaining to patient medication, such as use of heparinoid, unfractionated and low-molecular-weight heparin, salicylate, and oral contraceptives.

Rejection of Coagulation Specimens

Although most (more than 85%) respondents rejected coagulation specimens for various appropriate reasons (Table 8), a minority reported rejecting specimens collected via indwelling catheter (32.3%) or when medical record numbers were missing from specimen labels (39.1%; 58.9% of large vs 31.2% of small hospitals, $P < .001$). Because of the presence of anticoagulants in indwelling catheters, it has been recommended that specimens used for monitoring heparin therapy be collected from a different site than the site used for heparin infusion.[25]

Test Report Content

The information items most frequently provided on laboratory reports for 4 coagulation tests were measurement units, reference intervals, and specimen comments (Table 9). Items least often provided by the respondents on coagulation reports for PT, aPTT, vWF antigen, and protein C were possible drug interactions; suggested diagnosis; testing methodology and reagents; therapeutic ranges for protein C and vWF antigen; written interpretation; and recommendations for further testing, treatment, and test-

Table 9. Test Report Content*

Item Reported	PT, % (No.)	aPTT, % (No.)	vWF Antigen, % (No.)	Protein C, % (No.)
Measurement units	96.8 (592)	97.7 (589)	62 (38)	74 (58)
Reference (normal) interval	95.9 (591)	96.6 (585)	63 (39)	75 (60)
Specimen comments (if needed)	87.8 (535)	88.0 (528)	23 (33)	46 (48)
Therapeutic ranges	52.5 (331)	35.7 (229)	1 (2)	1 (3)
Written interpretation	5.7 (38)	3.7 (24)	6 (9)	7 (14)
Testing methodology or reagent	4.1 (26)	3.9 (23)	37 (2)	25 (4)
Suggested diagnosis	2.1 (13)	1.4 (10)	39 (5)	26 (6)
Possible drug interactions	0.8 (5)	0.8 (7)	37 (3)	30 (13)
No test result interpretation	28.4 (179)	29.7 (182)	10 (14)	9 (19)
Recommendations for further testing	1.9 (11)	2.3 (14)	4 (5)	4 (9)
Recommendations for treatment	0.8 (5)	0.7 (4)	1 (2)	1 (2)
Recommendations to test family members	0.1 (1)	0.1 (1)	3 (4)	2 (5)
No recommendations	50.9 (312)	49.8 (302)	49 (20)	37 (29)

* Percentages were estimated by weighing reported responses using relative proportions of large and small hospitals in the sampling frame and the proportions that reported performing coagulation testing. In parentheses are the actual numbers that gave a particular response. PT indicates prothrombin time; aPTT, activated partial thromboplastin time; and vWF, von Willebrand factor.

Table 10. Repeating a Coagulation Test

Circumstance to Repeat a Coagulation Test	Large Hospitals, % (No.)	Small Hospitals, % (No.)	Estimated Proportion of Hospitals,%*	*P*
Control(s) was (were) out of range	97.7 (296)	99.0 (288)	98.6	.23
Results were outside instrument technical ranges	97.1 (297)	98.6 (285)	98.2	.19
Results were critical (panic) values	90.9 (280)	99.0 (291)	96.7	<.001
Results did not agree with previous results	75.3 (226)	71.0 (198)	72.2	.24
Results were outside of reference (normal) range	12.5 (35)	20.1 (52)	17.9	.02

* Estimated by weighing reported responses using relative proportions of large and small hospitals in the sampling frame and the proportions that reported performing coagulation testing.

ing of family members. These results suggest a need for further research to determine how coagulation laboratories are providing relevant information, interpretations, and recommendations to those involved in patient care.

Process of Reporting Laboratory Results

Reporting of Critical Values.—An estimated 99.2% of hospitals (99.0% of large vs 99.3% of small hospitals) noted that they reported critical values for coagulation tests ($P = .69$). Hospitals that affirmed that they did responded to questions about the following practices in reporting critical values:

- Critical values telephoned to clinician and call documented (99.1%; 99.3% of large vs 99.0% of small hospitals, $P = .61$)
- Critical values repeated and documented as confirmed (92.2%; 88.2% of large vs 93.8% of small hospitals, $P = .02$)
- Critical values telephoned to clinician and call not always documented (8.1%; 3.0% of large vs 10.1% of small hospitals, $P = .002$)
- Critical values indicated on report and no further action taken (5.4%; 5.1% of large vs 5.5% of small hospitals, $P = .84$)

In a 1996 survey of Canadian medical laboratories, 75% of laboratories reported critical results by telephone.[3] The CAP requires laboratories to notify medical staff immediately when a critical value is obtained so that appropriate action can be taken.[3] According to the CLIA regulations, the laboratory must immediately alert the individual or entity that requested the test and, if applicable, the individual responsible for using the test results whenever any test result indicates an imminent life-threatening condition or panic or alert values.[17] As these data show, an estimated 0.8% of hospitals did not report critical values for coagulation laboratory tests ($P = .03$), and 0.9% did not bring critical values to the immediate attention of the clinician ($P = .01$).

Repeating a Coagulation Test.—We asked respondents if they repeated coagulation tests when (1) controls were out of range, (2) results were outside instrument technical ranges, (3) results were outside of the reference (''normal'') range, (4) results were critical values (panic values), and (5) results did not agree with previous results (Table 10). Except for repeating tests when results were outside of the reference interval, most hospitals (more than 70%) repeated coagulation tests in these circumstances. Compared with the large hospitals, the small hospitals more often reported repeating tests when results were critical values ($P < .001$) and when test results were outside of the reference interval ($P = .02$).

QA Practices

Adherence to established QA practices is an important failsafe mechanism that is needed to prevent laboratory errors, thus maintaining patient safety and improving health outcomes. In this survey, we tried to establish the level of compliance with a selected subset of QA practices. To do so, we asked participants a series of questions on QA practices (Table 11) relating to matching of patient information, checking and reviewing laboratory results, validating test systems, and checking plasma for platelet count after centrifugation to achieve platelet-poor plasma

Table 11. Quality Assurance Procedures

Quality Assurance Procedure Used	Large Hospitals, % (No.)	Small Hospitals, % (No.)	Estimated Proportion of Hospitals,%*	*P*
Review critical (panic) values†	97.4 (300)	99.7 (296)	99.0	.02
Bring critical values to immediate attention of the clinician†	98.1 (302)	99.3 (296)	99.0	.17
Periodically verify calibration of all instruments‡	99.4 (307)	97.6 (290)	98.1	.08
Validate new analytic methods‡	99.0 (304)	96.6 (283)	97.3	.04
Match patient information and laboratory-generated labels	96.7 (297)	89.1 (261)	91.3	<.001
Match specimen label and requisition form	88.3 (265)	90.8 (267)	90.1	.32
Compare instrument printout to reported value	81.9 (249)	82.6 (238)	82.4	.82
Check patient's previous results (Delta check)	85.9 (263)	66.3 (193)	71.9	<.001
Run specimens in duplicate§	32.6 (99)	46.3 (136)	42.4	.001
Run controls in duplicate§	31.9 (97)	44.9 (132)	41.2	.001
Check plasma for platelet count after centrifugation	34.4 (105)	11.3 (32)	17.9	<.001

* Estimated by weighing reported responses using relative proportions of large and small hospitals in the sampling frame and the proportions that reported performing coagulation testing.

† An estimated 0.8% of hospitals noted that they did not report critical values for coagulation tests ($P = .03$).

‡ An estimated 1.9% of hospitals noted that they did not periodically verify calibration of all instruments ($P = .003$), and an estimated 2.7% of hospitals stated that they did not validate new analytic methods ($P < .001$).

§ Not a universally accepted quality assurance procedure (see "Results and Comment").

(platelet count of $<10\,000/\mu L$), a recommended procedure for tests in which phospholipids influence test results, such as the test for lupus anticoagulant.[27] Although duplicate testing of controls and samples for commonly used automated tests is not recommended as a QA practice, we also asked if respondents analyzed controls and samples in duplicate.

Most (71.9%–99.0%) responded affirmatively to all but 3 questions. The 3 practices that were followed by a minority of participants were specimens being tested in duplicate (42.4%), controls being tested in duplicate (41.2%), and plasma being checked for platelet count after centrifugation (17.9%). There are conflicting reports relating to the need to perform replicate analyses in hospital coagulation laboratories. Replicate analyses have been reported to enhance neither precision nor accuracy of coagulation studies.[53] Another study, however, indicated that the frequency of errors produced by single estimations was too high for satisfactory clinical practice.[54] The CLIA regulations require that patient and control specimens be tested in duplicate only for manual coagulation tests but not for automated tests, which are done almost universally in US hospitals.[16] In a 1996 survey of licensed Canadian medical laboratories, 62% of laboratories ran specimens in duplicate.[3] In the follow-up 1998–1999 survey of Canadian medical laboratories, 71% ran specimens in duplicate.[4] These findings may be compared with the 42% of hospitals reporting in the current survey that they ran specimens in duplicate.

An estimated 1.9% of hospitals did not periodically verify calibration of all instruments ($P = .003$), and 2.7% of hospitals did not validate new analytic methods ($P < .001$). According to CLIA regulations, calibration and calibration verification procedures are required to substantiate the continued accuracy of the test system throughout the laboratory's reportable range of test results.[15] In a 1998–1999 survey of Canadian medical laboratories, 59% of the respondents performed testing to verify the platelet-poor status of plasma used for aPTT testing.[4] In this survey, an estimated 18% of hospitals checked plasma for a platelet count after centrifugation.

Personnel Issues, Clinical Service, and Laboratory Capacities

To our knowledge, this is the only survey of laboratory practices that has covered coagulation laboratory personnel and resources at a national level in the United States or elsewhere.

Location of Coagulation Testing.—Respondents noted the following locations for coagulation testing:

- Core laboratory (61.6%; 40.2% of large vs 70.1% of small hospitals)
- Hematology laboratory (30.6%; 53.7% of large vs 21.5% of small hospitals)
- Coagulation laboratory (12.5%; 22.2% of large vs 8.7% of small hospitals)
- Point of care (7.0%; 18.0% of large vs 2.7% of small hospitals)
- Stat laboratory (3.3%; 9.0% of large vs 1.0% of small hospitals)
- None of the above (2.1%; 0.6% of large vs 2.7% of small hospitals)

The responses from large and small hospitals were significantly different ($P < .001$).

Number of Full-Time Equivalents.—An estimated 71.3% of the hospitals had less than 4 full-time equivalents (FTEs) performing coagulation laboratory testing (69.8% of large vs 71.9% of small hospitals), 17.9% had 4 to 9 FTEs (14.3% of large vs 19.3% of small hospitals), and 10.8% had more than 10 FTEs (15.9% of large vs 8.8% of small hospitals). The responses from large and small hospitals were significantly different ($P < .001$). The number of FTEs may relate to those working on coagulation testing only part of the time while working full-time in the laboratory, because the question was not framed to inquire about the number of FTEs devoted solely to coagulation testing.

Components of Competency Assessment Program.—Except for periodic written examination (an estimated 26.6% of hospitals), most had the following components for personnel competency assessment: successful performance of quality control (QC) with documentation of remedial actions, review of procedure manuals, analysis of

Table 12. Competency Assessment Programs*

Component of Competency Assessment Program	Large Hospitals, % (No.)	Small Hospitals, % (No.)	Estimated Proportion of Hospitals,%†
Successful performance of quality control with documentation of remedial actions	92.3 (287)	91.3 (274)	91.6
Review of procedure manuals	89.7 (279)	82.0 (246)	84.2
Analysis of unknown samples	77.2 (240)	83.7 (251)	81.8
Direct observation of a task	76.5 (238)	72.3 (217)	73.5
Participation in continuing education	67.2 (209)	53.7 (161)	57.5
Periodic written examination	38.3 (119)	22.0 (66)	26.6
None of the above	0.3 (1)	0	0.1

* The responses from large and small hospitals were significantly different ($P < .001$).

† Estimated by weighing reported responses using relative proportions of large and small hospitals in the sampling frame and the proportions that reported performing coagulation testing.

Table 13. Educational Degree and Certification of the Coagulation Laboratory Director*

Educational Degree/Certification	Large Hospitals, % (No.)	Small Hospitals, % (No.)	Estimated Proportion of Hospitals,%†
MD	94.9 (298)	87.6 (261)	89.7
PhD	7.6 (24)	6.4 (19)	6.7
Other degree‡	4.5 (14)	12.1 (36)	9.9
Board certified in clinical pathology	81.4 (250)	70.5 (206)	73.6
Board certified in anatomic pathology	72.6 (223)	53.1 (155)	58.6
Certified by the ASCP	21.2 (65)	29.5 (86)	27.1
Board certified in medicine	16.0 (49)	20.5 (60)	19.2
Board certified in hematopathology	14.3 (44)	1.4 (4)	5.0
Board certified in hematology	9.4 (29)	1.0 (3)	3.4
Certified by the NCA	1.0 (3)	1.4 (4)	1.3
Certified by the AAB	0.3 (1)	1.0 (3)	0.8
Certified by the ABCC	1.0 (3)	0.3 (1)	0.5
Certified by the NRCC	0.3 (1)	0	0.1
None of the above	1.3 (4)	0.7 (2)	0.9

* The responses from large and small hospitals were significantly different ($P = .002$ for educational degrees and $P < .001$ for professional certifications). ASCP indicates American Society for Clinical Pathology; NCA, National Certifying Agency (for Clinical Laboratory Sciences); AAB, American Association of Bioanalysts; ABCC, American Board of Clinical Chemistry; and NRCC, National Registry of Clinical Chemistry.

† Estimated by weighing reported responses using relative proportions of large and small hospitals in the sampling frame and the proportions that reported performing coagulation testing.

‡ Of the 50 respondents noting degrees other than an MD or a PhD for the laboratory director, 26% also had an MD degree. The following degrees and certifications were noted in this group: MT(ASCP), 38%; DO, 16%; BS, 12%; MBA, 10%; MLT, 6%; MS, 6%; associate degree, 2%; and unspecified, 8%.

unknown samples, direct observation of a task, and participation in continuing education (Table 12).

Educational Degrees and Professional Certifications of the Coagulation Laboratory Director.—An estimated 89.7% of the hospitals' laboratory directors had an MD degree, 6.7% had a PhD, and 9.9% had other degrees (Table 13). The responses from large and small hospitals were significantly different ($P = .002$). Of the 50 respondents noting degrees other than an MD or a PhD for the laboratory director, 13 (26%) had an MD degree in addition to the other degree. We also asked whether the coagulation laboratory director was board certified in clinical pathology, anatomic pathology, medicine, hematopathology, or hematology and whether he or she was certified by specific certifying organizations (Table 13). The responses from the large and small hospitals were significantly different ($P < .001$). Most were board certified in clinical pathology (73.6%) and anatomic pathology (58.6%).

Coagulation Service Capacity.—An estimated 48.2% of hospitals reported having a clinician for consultation with expertise in coagulation disorders, 16.4% reported having an anticoagulation outpatient clinic specializing in adjusting oral anticoagulants, and 6.1% reported having an outpatient clinic specializing in diagnosis and treatment of coagulation disorders. In all cases, a significantly ($P < .001$) greater proportion of the large hospitals reported having these capabilities compared with the small hospitals (Table 14). Outpatient anticoagulation clinic services are systems of care designed to coordinate and optimize delivery of anticoagulation therapy.[13] According to a report, patients treated at an anticoagulation clinic who received lower-range anticoagulation had fewer INRs higher than 5.0, spent more time in range, and spent less time at an INR higher than 5.0.[55] Also, patients treated at an anticoagulation clinic who received higher-range anticoagulation had more INRs within range, had fewer INRs lower than 2.0, and spent more time within range. Facilities with anticoagulation clinics also demonstrated a trend toward a lower mortality rate.[55]

Point-of-Care Testing for PT Assay

Test Availability and Laboratory Oversight.—An estimated 6.4% of hospitals (15.0% of large vs 3.0% of small hospitals, $P < .001$) reported having point-of-care testing for PT, and 87% of hospitals with point-of-care testing for PT (98% of large vs 67% of small hospitals, $P = .001$)

Table 14. Coagulation Service Capacity

Coagulation Service Capacity	Large Hospitals, % (No.)	Small Hospitals, % (No.)	Estimated Proportion of Hospitals,%*	*P*
Clinician with expertise in coagulation disorders available for consultation	74.4 (233)	37.8 (113)	48.2	<.001
Anticoagulation outpatient clinic specializing in adjustment of oral anticoagulants	26.8 (84)	12.3 (37)	16.4	<.001
Outpatient clinic specializing in diagnosis and treatment of coagulation disorders	16.6 (52)	2.0 (6)	6.1	<.001

* Estimated by weighing reported responses using relative proportions of large and small hospitals in the sampling frame and the proportions that reported performing coagulation testing.

reported that the laboratory had oversight of coagulation point-of-care testing, including certification and regulatory compliance.

Location of Point-of-Care Testing.—Respondents noted the following locations for coagulation point-of-care testing:

- Coagulation clinic (60%; 68% of large vs 44% of small hospitals)
- Cardiac catheterization laboratory (21%; 32% of large vs no small hospitals)
- Satellite laboratory (21%; 26% of large vs 11% of small hospitals)
- Operating room (17%; 26% of large vs no small hospitals)
- At the bedside (16%; 19% of large vs 11% of small hospitals)
- Dialysis clinic (15%; 11% of large vs 22% of small hospitals)
- None of the above (4%; no large hospital vs 11% of small hospitals)

The responses from the large and small hospitals were significantly different ($P = .02$).

Integration of Point-of-Care Testing Results.—An estimated 34% of hospitals with point-of-care testing for PT (43% of large vs 18% of small hospitals, $P = .23$) reported that coagulation point-of-care testing results were integrated into the laboratory's reporting system. Of those noting integration of point-of-care testing results into the laboratory's reporting system, 96% (95% of large vs 100% of small hospitals, $P = .75$) reported that point-of-care testing results were integrated in the laboratory's reporting system in the order of collection times.

Reference Interval for Point-of-Care Testing of PT.—An estimated 44% of hospitals with point-of-care testing for PT (45% of large vs 43% of small hospitals, $P = .91$) reported that the reference interval for point-of-care testing of PT was the same as the PT assay reference interval used by their coagulation laboratory. Of these, 25% (38% of large vs no small hospitals, $P = .44$) reported that the point-of-care testing reference interval was established by the same method used to establish the PT reference interval for the laboratory; the following methods were used to establish the point-of-care testing reference interval in laboratories that did not use the same method to establish the PT reference range for the coagulation laboratory testing and point-of-care testing:

- In-house testing (63%; 60% of large vs 67% of small hospitals)
- Manufacturer's insert (26%; 20% of large vs 33% of small hospitals)

Table 15. Type of Quality Control (QC) Materials and Methods Used for Point-of-Care Coagulation Instruments

QC Material or Method	Respondents, % (No.)
Electronic QC method and liquid QC material	33 (18)
Electronic QC method and lyophilized QC material	30 (16)
Lyophilized QC material only	19 (10)
Electronic QC method only	7 (4)
Liquid QC material only	7 (4)
Electronic QC method, liquid QC material, and lyophilized QC material	4 (2)

- Published values (26%; 20% of large vs 33% of small hospitals)
- Other (4%; 7% of large vs no small hospitals)

Type of QC Materials and Method Used.—The following types of QC materials and method were used: electronic (71%; 76% of large vs 63% of small hospitals), lyophilized (49%; 54% of large vs 38% of small hospitals), and liquid (46%; 43% of large vs 50% of small hospitals). The responses from large and small hospitals were not significantly different ($P = .52$). Seventy-four percent reported using electronic QC along with liquid QC materials (33%), with lyophilized QC materials (30%), with both (4%), or alone (7%) (see Table 15).

Frequency of QC Runs.—The respondents noted the following frequencies for their QC runs: once per day (53%; 54% of large vs 50% of small hospitals), once per shift (41%; 37% of large vs 50% of small hospitals), and other frequencies (20%; 24% of large vs 13% of small hospitals). The responses from large and small hospitals were not significantly different ($P = .69$).

Concluding Remarks

An inherent limitation of this and other surveys is that responses may not consistently reflect actual practices. Aside from this limitation, our findings here should accurately reflect the state of coagulation laboratory practices reported by US hospitals in 2001 because of the high response (79.0%) and hospital sampling (13.5%) rates. We did not capture data on the actual individual(s) responding at each hospital, nor did we, for practical reasons, devise any mechanisms to assess intra- and interrespondent reliabilities within the same hospital. Like any other survey, this one is subject to framing bias. It is well known that the way a question is posed (or ''framed'') may have a dramatic impact on the response.[56,57] We did attempt to reduce framing bias by having the questionnaire evaluated

by survey methodologists and coagulation laboratory experts and by pilot-testing different versions of the survey at hospital coagulation laboratories that did not participate in the final survey.

Our results showed substantial variabilities in some coagulation laboratory practices. Although in most cases, response patterns from large and small hospitals were not significantly different, several questions elicited significantly different responses. When we found significant differences, usually a greater proportion of large hospitals adhered to accepted laboratory practice recommendations and guidelines that could directly affect patient care. We do not know to what extent this differential failure to follow practice recommendations and guidelines is due to knowledge, resources, infrastructure, quality systems, cost, and reimbursement issues. These findings, however, suggest a need for timely interventions targeted for improving certain coagulation laboratory practices. In our view, and based on the results of this and other surveys, health system researchers should do the following:

- Conduct studies to understand why certain accepted coagulation laboratory practices are not consistently followed.
- Work with clinical and laboratory groups to develop quality measures and monitoring systems for ongoing quality improvement efforts in coagulation laboratory testing.
- Document the relationship between substandard testing practices and unfavorable clinical outcomes.
- Work with clinicians to incorporate recommended coagulation laboratory testing practices in medical training curricula.
- Target the most consequential and deficient areas for future intervention. These efforts should include dissemination of guidelines and administration of periodic surveys not only to assess change but also to drive improvement in laboratory practice.

Publication and dissemination of practice guidelines alone may be insufficient for quality improvement in medical and laboratory practice. Evidence-based and accepted standards of practice should be written for use by medical and health practitioners in the field; compliance with good clinical and laboratory practices should be periodically monitored; and reasons for not following accepted standards of practice should be explored to determine the root causes of noncompliance or to consider if changes in practice standards are warranted.

This report is a descriptive characterization of coagulation laboratory testing practices and makes no attempt to relate specific coagulation laboratory practices to other laboratory- and hospital-specific variables or to health outcomes. Explorations of such interrelationships using these survey results and those to be collected in specific outcome studies may be avenues for further investigation.

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