

Coagulation Laboratory Testing Practices in a 2001 Survey of U.S. Hospitals

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**Division of Laboratory Systems
Public Health Practice Program Office**



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During the next 30 minutes or so, I'd like to present and discuss with you some of the findings from a CDC survey that we conducted in 2001 to assess coagulation laboratory practices in US hospitals.

You can also download the full text of the report in either PDF or HTML format at this URL.

Rationale for Doing the Study

- **Public health implications of coagulopathy and bleeding disorders**
- **Impact of variability in certain coagulation testing practices on patient outcome**
- **Documented variability of specific coagulation laboratory practices implied by results of past surveys**
- **Hospital setting used because of greater spectrum of coagulation laboratory practices**



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We set out to carry out this study because

- coagulation and bleeding problems have great societal burden of suffering due to their substantial, associated morbidity and mortality;
- variation in testing practices may impact result accuracy and interpretation, and clinical outcome such as bleeding or thrombosis; and
- previous studies have demonstrated great variabilities in certain consequential practices.

We used hospitals as the testing environment to address a broader spectrum of practices that are not amenable to observation in usual office laboratories.

Purpose

Assess

- **availability of specific tests for diagnosing and treating hypercoagulability or thrombophilia, von Willebrand disease, and heparin induced thrombocytopenia and thrombotic syndrome,**
- **pre-analytical issues (e.g., collection methods, information provided with specimens and processing of specimens),**
- **analytical issues (e.g., instrumentation, QC and qualifications of testing personnel),**



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The purpose of this study was to

- evaluate availability of tests for workup of hypercoagulability, von Willebrand disease and heparin induced thrombocytopenia/thrombotic syndrome;
- assess various pre-analytical and analytical stages of the testing process; ...

Purpose (Continued)

Assess

- **post-analytical issues (e.g., result reporting, interpretations and recommendations), and**
- **use of selected laboratory practices specific to each test that are subject to variation and critical to diagnostic or therapeutic use of the test.**



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- ... evaluate various post-test issues; and
- assess some testing practices critical to patients' management.

Study Sample

- **Sampling frame: hospitals listed in 1999 directory of American Hospital Association**
- **Stratification by number of beds:**
 - <200 beds (small hospitals)
 - ≥200 beds (large hospitals)
- **Sampling method: random within each stratum**
- **Sampling rate:**
 - 9% of small hospitals
 - 26% of large hospitals



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We used hospitals listed in the 1999 directory of the American Hospital Association as the sampling frame...

... and stratified them into 2; those with less than 200 beds, labeled as “small” hospitals and those with equal to or more than 200 beds, labeled as “large” hospitals.

We randomly selected hospitals from these 2 strata—sampling 9% of the small and 26% of the large hospitals.

Response Rate

- **800 hospital laboratories contacted.**
- **632 (79%) responded in all.**
- **20 (3%) responded via the Internet.**



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We contacted the 800 hospitals in the sample by mail followed by a reminder postcard 2 weeks later. To solicit response, we subsequently called all but 7 of the institutions not responding.

79% responded. Of those responding, 3% did so via the Internet and the rest mailed the completed paper questionnaire.

Survey Content

Coagulation-Specific Laboratory Practices

- **Performance of coagulation testing**
- Coagulation test requisition
- **Practices relating to prothrombin time (PT) assay**
- **Practices relating to activated partial thromboplastin time (aPTT) assay**
- Practices relating to assays for von Willebrand disease
- Practices relating to thrombosis/hypercoagulability workup



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This slide shows some of the coagulation-specific laboratory issues this survey covered from the common PT and aPTT tests to less common testing practices to assess bleeding or thrombotic risk.

Highlighted in gold are the areas which I will partially present during this talk.

Survey Content (Continued)

Coagulation-Specific Laboratory Practices

- Algorithms for diagnosing a lupus anticoagulant (LA)
- **Practices relating to monitoring of low molecular weight heparin (LMWH) therapy**
- Availability of specific coagulation tests
- Specific test result information, interpretations and recommendations
- Point-of-care testing for PT assay



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This slide shows other coagulation-specific laboratory issues the survey addressed, ranging from practices to diagnose a lupus anticoagulant and to monitor low molecular heparin therapy to point-of-care testing for PT assay.

Again, highlighted in gold is the area I will partially cover during this presentation.

Survey Content (Continued)

General Laboratory Practices

- Specimen rejection
- Process of reporting results
- QA procedures
- Coagulation laboratory personnel and resources



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We also captured data on certain general laboratory practices, relating to specimen management, reporting of results, quality assurance, and human and facility resources which I will not present.

Performance of Coagulation Testing

- 98% of large hospitals
- 97% of small hospitals



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97% of the respondents reported performing coagulation testing. All subsequently analyzed data I will present relate to these respondents.

Practices Relating to PT Assay



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Performance of PT Assay

605 (100%) reported performing PT assay.



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All reported performing PT assay.

Recommendation for Anticoagulant Concentration

- Under-filling of specimen tubes containing 3.8% sodium citrate prolongs PT and aPTT results compared to 3.2% sodium citrate.

Am J Clin Pathol. 1998;109:754-757

- Based on *WHO* recommendations and *NCCLS* guidelines, 3.2% citrate is the anticoagulant of choice for coagulation testing.

Arch Pathol Lab Med. 1998;122:768-781



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Under-filling of 3.8% citrated tubes has been reported to prolong PT and especially aPTT results.

Both NCCLS and the World Health Organization recommend using 3.2% citrate as the anticoagulant of choice.

Anticoagulant Concentration Used

<u>Concentration</u>	<u>No. (%*) of large hospitals</u>	<u>No. (%*) of small hospitals</u>
3.2% (109 mmol/L)	244 (81%)	193 (68%)
3.8% (129 mmol/L)	60 (20%)	96 (34%)

*Percentages total >100% due to 8 respondents (4 large and 4 small hospitals) noting that they used both concentrations of sodium citrate.



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Although most respondents to this survey reported using 3.2% citrate, 20% of large hospitals and 34% of small hospitals reported using 3.8% citrate as the anticoagulant.

Exclusive Use of 3.2% Sodium Citrate

<u>No. (%) of large hospitals</u>	<u>No. (%) of small hospitals</u>	<u>P</u>
240 (80%)	189 (66%)	< 0.001



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In agreement with NCCLS and WHO recommendations, a significantly greater proportion of large hospitals exclusively used 3.2% citrate compared to small hospitals.

Recommendation for Reporting of PT Results

- Reporting PT results in seconds only may lead clinicians to inappropriately compare results between institutions.
- Reliance on therapeutic PT ratio documented to cause errors in anticoagulant therapy.
- **Reporting of PT results in INR is preferred.**

Am J Clin Pathol. 1998;109:589-594

Arch Intern Med. 1992;152:278-282



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Reporting PT results in seconds only or as therapeutic ratio is not recommended.

Current recommendation calls for PT results to be reported in international normalized ratio or INR.

Reporting of PT Results

<u>Results reported in</u>	<u>No. (Proportion)</u>
International normalized ratio (INR)	601 (100%)
Seconds	577 (97%)
Therapeutic PT ratio	77 (16%)



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In agreement with the accepted practice, all respondents noted that they reported PT results in INR; 97% also reported PT results in seconds and 16% reported results as therapeutic PT ratio.

Reporting of PT Results (Continued)

Format Used to Report PT Result by U.S. Hospitals and Canadian Medical Laboratories*			
<u>Reporting format</u>	<u>U.S., 2001</u> <u>(n = 626)</u>	<u>Canada, 1996</u> <u>(n = 649)</u>	<u>Canada, 1992</u> <u>(n = 857)</u>
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%

*Am J Clin Pathol. 1998;109:589-594

*Am J Hematol. 1995;48:237-239



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This slide shows how respondents stated reporting PT results in this survey in comparison with 2 surveys of Canadian medical laboratories in 1992 and 1996.

We can see a temporal increase in reporting PT results as INR and seconds. A larger proportion of Canadian laboratories report PT as INR only.

Recommendation for Sensitivity of PT Assay to Heparin (CAP)

- **Determine sensitivity of PT assay to heparin.**
- **Where possible, select a thromboplastin that is insensitive to heparin in the therapeutic range.**

Arch Pathol Lab Med. 1998;122:768-781



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College of American Pathologists recommends that laboratories determine sensitivity of their PT assay to heparin, and where possible, select a thromboplastin that is insensitive to heparin in the therapeutic range. In agreement with the 1st recommendation, ...

Determining Sensitivity of PT Assay to Heparin

**100 (17%) reported determining sensitivity of
their PT assay to heparin.**



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... 17% of the respondents reported determining sensitivity of their PT assay to heparin. Consistent with the 2nd recommendation, ...

Selecting Thromboplastin Insensitive to Heparin in Therapeutic Range

<u>No. (%) of large hospitals</u>	<u>No. (%) of small hospitals</u>	<u>P</u>
170 (59%)	101 (40%)	< 0.001



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... ~50% of all respondents selected thromboplastins that were insensitive to heparin in the therapeutic range.

Responses from large and small hospitals were significantly different. While ~60% of large hospitals reported selecting insensitive thromboplastins, 40% of small hospitals reported doing so.

Recommendations for International Sensitivity Index (ISI) of Thromboplastin

- **CAP recommends thromboplastins with manual ISI of 0.90 - 1.70 and toward lower end of this range.**

Arch Pathol Lab Med. 1998;122:768-781

- **American College of Chest Physicians recommends thromboplastins with ISI of ≤ 1.20 .**

Chest. 1995;108(4 Suppl):231S-246S



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Due to the increased variability in INR resulting from ISI values deviating significantly from unity, various groups have recommended using thromboplastins with ISIs closer to 1.

CAP recommends thromboplastins with ISIs not exceeding 1.70, while American College of Chest Physicians recommends ISIs not in excess of 1.20. Consistent with CAP recommendation, ...

ISI of ≤ 1.70

247 (44%) reported ISI of ≤ 1.70 .

<u>No. (%) of large hospitals</u>	<u>No. (%) of small hospitals</u>	<u>P</u>
151 (50%)	96 (36%)	0.001



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... 44% reported ISIs of less than 1.71 for their current thromboplastin lots. A significantly greater proportion of large hospitals reported ISIs of less than 1.71 compared to small hospitals. In agreement with recommendation of the American College of Chest Physicians, ...

ISI of ≤ 1.20

190 (34%) reported ISI of ≤ 1.20 .

<u>No. (%) of large hospitals</u>	<u>No. (%) of small hospitals</u>	<u>P</u>
125 (42%)	65 (24%)	0.001



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... 34% reported ISIs of less than 1.21 for their current thromboplastin lots. Again, a significantly greater proportion of large hospitals reported ISIs of less than 1.21 compared to small hospitals.

Practices Relating to aPTT Assay



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Performance of aPTT Assay

601 (99%) reported performing aPTT assay.



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99% reported performing aPTT assay.

Recommendation for Establishing Therapeutic Range for Heparin

**Each laboratory should establish an individual
therapeutic range for heparin specific to its own
reagent and instrument system.**

Am J Clin Pathol. 1988;89:19-23

J Clin Pathol. 1996;49:10-14



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Based on current recommendations, each laboratory should establish an individual therapeutic range for heparin specific to its own reagent and instrument system. In agreement with these recommendations, ...

Therapeutic Range for Heparin

355 (64%) reported having an aPTT therapeutic range for heparin when monitoring therapy.

<u>No. (%) of large hospitals</u>	<u>No. (%) of small hospitals</u>	<u>P</u>
213 (73%)	142 (53%)	<0.001



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... 64% reported having an aPTT therapeutic range for heparin when monitoring heparin therapy. A significantly greater proportion of the large hospitals reported doing so compared to the small hospitals. Half of the small hospital respondents reported not having an aPTT therapeutic range for heparin.

NCCLS Recommendation for Specimen Management in aPTT Assay

Samples should be assayed within 4 h after phlebotomy if centrifuged within 1 h of collection.

NCCLS. Document H21-A3; 1998



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NCCLS recommends assaying samples for aPTT within 4 hours after phlebotomy if specimens are centrifuged within 1 hour of collection. In agreement with this recommendation ...

Specimen Management for aPTT Assay

<u>Practices used for aPTT assay specimen management</u>	<u>Large hospitals</u>	<u>Small hospitals</u>	<u>P</u>
Specimens assayed within 4 h after phlebotomy	276 (96%)	259 (97%)	0.490
Specimens centrifuged within 1 h of collection	229 (84%)	238 (92%)	0.007
Specimens kept at room temperature prior to testing	223 (84%)	196 (80%)	0.188
Specimens kept at 4 °C prior to testing	47 (20%)	54 (24%)	0.335



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... more than 95% reported assaying samples for aPTT within 4 hours after phlebotomy, and ~90% reported centrifuging specimens within 1 hour of collection. A significantly greater proportion of small hospitals reported centrifuging specimens within 1 hour of collection compared to large hospitals.

~80% reported keeping specimens at room temperature before aPTT assay while ~20% reported keeping specimens at 4 °C.

Practices Relating to Monitoring of Low Molecular Weight Heparin (LMWH) Therapy



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Monitoring of LMWH Therapy

82 (14%) reported monitoring LMWH therapy:

<u>No. (%) of large hospitals</u>	<u>No. (%) of small hospitals</u>	<u>P</u>
55 (19%)	27 (10%)	0.002



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14% reported monitoring low molecular weight heparin therapy. A significantly greater proportion of large hospitals did so compared with small hospitals. However, we don't have denominator data in that we didn't ask respondents if they actually used low molecular weight heparin therapy before asking them if they monitored for it.

CAP Recommendation for Assay to Monitor LMWH Therapy

To monitor LMWH,

- Use a chromogenic anti-factor Xa assay;
- Do not use an aPTT assay.

Arch Pathol Lab Med. 1998;122:799-807



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To monitor low molecular weight heparin, CAP recommends using a chromogenic anti-factor Xa assay and against using an aPTT assay.

Assays Used to Monitor LMWH Therapy

Assay to monitor <u>LMWH therapy</u>	No. (%) of <u>large hospitals</u>	No. (%) of <u>small hospitals</u>	<u>P</u>
aPTT	23 (58%)	24 (96%)	0.001
Anti-Xa	32 (65%)	3 (18%)	0.001
Factor Xa (inhibitor assay)	3 (8%)	1 (6%)	0.795
Thrombin inhibitor assay (HEP test)	0	0	–



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A significantly greater proportion of large hospitals performed *anti-Xa assay*, in agreement with CAP recommendation, to monitor low molecular weight heparin compared with small hospitals.

A significantly greater proportion of small hospitals performed *aPTT assay*, in disagreement with CAP recommendation, to monitor low molecular weight heparin compared with large hospitals.

The apparent reason small hospitals mostly used aPTT assay in lieu of anti-Xa assay to monitor low molecular weight heparin therapy may be that few of them even perform an in-house anti-Xa assay as we have documented in this survey.

Comments



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Survey Validity

- **Actual practice-** Responses may not consistently reflect actual practices.
- **Representativeness-** Results expected to reflect well the state of reported coagulation laboratory practices in U.S. hospitals.



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An inherent limitation of this and any other survey is that responses may not consistently reflect actual practices.

Because of the high response and sampling rates, the findings of this survey are expected to reflect well the state of reported coagulation laboratory practices in US hospitals in 2001.

Survey Validity (Continued)

Respondents

- **Response variation depending on the person completing the survey**
- **Multiple persons completing an individual survey**



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We didn't capture data on the actual individual or individuals responding at each hospital, and we also did not devise any mechanisms—for practical reasons—to assess intra- and inter-respondent reliabilities within the same institution.

Survey Validity (Continued)

Framing Bias

Addressed by having questionnaire

- Evaluated by coagulation and survey experts and
- Pilot tested



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Like any other survey, this instrument 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. We did attempt to reduce framing bias by having the questionnaire evaluated by survey methodologists and coagulation experts as well as by testing versions of the survey by 9 hospital coagulation laboratories.

We excluded from the sampling frame hospitals participating in pilot testing and also hospitals of the coagulation experts serving as consultants in development of the questionnaire.

Conclusion

- **Variability-** Substantial variability in some coagulation laboratory practices.
- **Large versus small hospitals-** For several questions, responses from large and small hospitals were significantly different .

When significantly different, responses usually implied greater proportion of large hospitals adhering to accepted laboratory practices.



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In conclusion ...

This survey showed that there were substantial variabilities in some coagulation laboratory practices.

Although in most cases, response patterns from large and small hospitals were not significantly different, several questions solicited significantly different responses from these 2 groups.

When there were significant differences, usually a greater proportion of large hospitals adhered to published laboratory practice recommendations and guidelines.

Concluding Remarks

- **Adherence to practice guidelines-** Not known to what extent lack of adherence to practice guidelines are due to knowledge, resources, infrastructure, quality systems, or cost and reimbursement issues.
- **Laboratory improvement-** Timely interventions targeted to certain coagulation laboratory practices are needed.



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We don't know to what extent not following practice recommendations and guidelines are due to knowledge, resources, infrastructure, quality systems, cost and reimbursement issues.

These data suggest a need for timely interventions targeted for improvement of certain coagulation laboratory practices.

Next Steps

- **Conduct studies to determine why certain accepted coagulation laboratory practices are not consistently followed.**
- **Work with clinical and laboratory groups to develop quality indicators and monitoring systems for ongoing QI efforts in coagulation testing.**
- **Incorporate recommended laboratory practices in medical training curricula.**
- **Target the most consequential and deficient practice areas for future intervention.**



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Where should laboratorians go from here?

As a vital component of the health care delivery system, we should conduct studies to understand why certain accepted coagulation laboratory practices are not consistently followed;

We should work with clinical and laboratory groups to develop quality indicators and monitoring systems for ongoing quality improvement efforts in coagulation testing;

We should work with our clinical colleagues to incorporate recommended laboratory practices in medical training curricula;

We should target the most consequential and deficient practice areas for future intervention. These efforts should include dissemination of practice guidelines and administration of periodic surveys to not only assess but also lead change in improved practice patterns over time.

Next Steps (Continued)

- **Write evidence-based and accepted standards of practice for use by medical and health practitioners in the field.**
- **Monitor periodically adherence to good clinical and laboratory practice.**
- **Explore periodically underlying reasons for not following accepted standards of practice to assess root causes for not doing so.**



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Publication and dissemination of practice guidelines may be necessary but not sufficient 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;
- Adherence to good clinical and laboratory practice should be periodically monitored; and
- Underlying reasons for not following accepted standards of practice should be periodically explored to determine the root causes such as lack of knowledge, resources, infrastructure, quality systems, cost and reimbursement issues.

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This study would not have been possible had it not been for the contributions of numerous colleagues, many of whom are not listed in this limited space; and I like to take this opportunity to thank them.

Finally, I want to thank you for your attention and for your interest.

Copies of Report and Slides

- **Hard copy of report and hard/electronic copy of slides:**
SShahangian@cdc.gov
- **Electronic copy of report (HTML or PDF):**
<http://www.phppo.cdc.gov/mlp/coag2001.asp>
<http://www.cdc.gov> (June 9 - 30, 2003)



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You can download the full report of this survey at this URL. This site went live in February, and was also noted as a spotlight on CDC's home page last week. This site will again go on CDC's home page during the last 3 weeks of this month beginning on June 9.

Now, I am pleased to take the 1st question or comment.