

Narrative Interpretations for Clinical Laboratory Evaluations

An Overview

Anand S. Dighe, MD, PhD,^{1,2} Britt L. Soderberg,² and Michael Laposata, MD, PhD²

Key Words: Laboratory tests; Laboratory medicine; Clinical pathology; Value-added services

Abstract

As the clinical laboratory test menu has significantly expanded in volume and complexity, there is a rapidly growing need by clinicians for narrative interpretations of complex studies that resemble those provided in anatomic pathology and radiology. In this report, the impact of advice on laboratory test selection and interpretation is presented with regard to providing adequate quality of care, reducing medical error, and reducing the cost for health care. In addition, past and current attempts to address the physician's need for advice on laboratory test selection and interpretation are also described. These include curbside consultations, intelligent laboratory information systems, and medical information from the Internet. Each is presented with examples from the literature and with its advantages and disadvantages for practicing clinicians confronting large, expensive test menus and the results of esoteric assays.

During the past decade, physicians in the United States have reported an increasing need for consultative advice on the selection and interpretation of laboratory tests. As the laboratory test menu rapidly expanded through the 1990s with the discovery of the molecular basis for many disorders, and as health care dollars have become limited, it has become increasingly more difficult for primary care physicians to know the appropriate (and often expensive) laboratory tests to select to make a diagnosis in the most efficient and cost-effective manner. At most community and academic medical centers, there has been no single group of physicians who can readily provide expert consultative advice in all areas of the clinical laboratory.

With regard to the selection of laboratory tests, the use of diagnostic algorithms in laboratory test selection permits reflexive testing to indicate the appropriate next test and permit an entire evaluation to be completed within minutes to hours instead of days, using a single blood specimen. **Table 1** indicates the test options offered from our coagulation laboratory in which reflexive testing is used extensively. The goals of reflexive testing algorithms, defined and modified by experts, are shorter time to diagnosis, shorter length of stay in a hospital, and decreased laboratory test utilization. In the absence of reflexive testing, as shown in **Table 2**, the ordering physician must select the appropriate coagulation tests from an extensive list of assays. There is likely to be an excessive number of visits to the physician to minimize the number of laboratory tests or an excessive number of tests ordered to minimize the number of patient visits.

Consider a patient being evaluated before a surgical procedure who has a prolonged partial thromboplastin time (PTT) of 65 seconds, which is unexpected. **Figure 1** illustrates the evaluation of a prolonged PTT with reflexive

Table 1
Coagulation Studies Available From Massachusetts General Hospital Clinical Coagulation Laboratory With and Without Reflexive Testing

With reflexive testing
Prolonged prothrombin time evaluation
Prolonged partial thromboplastin time evaluation
Hypercoagulation studies
von Willebrand studies
Antiphospholipid antibody assessment
Without reflexive testing
Anticardiolipin antibody measurement (only)
Factor assay quantitation (list specific factors)
Platelet aggregation studies
Other specific tests in coagulation (please list)

testing. If the physician selects the correct tests without any additional tests ordered to evaluate the cause of the prolonged PTT, a second visit will be required for a PTT mixing study and interpretation of the results, and a third visit will be needed to determine the levels of factor assays or inhibition studies associated with the PTT prolongation. Thus, in this simple example, there is a minimum of 3 visits with approximately 6 laboratory tests performed. Conversely, to minimize the number of patient visits, if all of the testing was ordered that was necessary to explain a prolonged PTT in the single visit, there would be at least 9 tests performed, with assays for the PTT mixing study; levels of factors VIII, IX, XI, and XII; lupus anticoagulant screening and confirmatory assays; and potentially a Bethesda unit assay for a factor VIII inhibitor, which is extremely labor intensive and costly.

It is difficult to imagine a situation in which a biopsy specimen is obtained by a surgeon and then processed by a histology laboratory technologist and then returned to the surgeon for diagnosis, with the anatomic pathologists making themselves available for questions only if necessary. It would be similarly absurd to consider the review of a computed tomography scan involving a lung mass without the automatic review by a skilled radiologist. However, we constantly provide complex batteries of tests performed by clinical laboratory technologists and return the results to primary care physicians examining patients on the order of 1 every 15 minutes without any assistance in test interpretation, no matter how complex the evaluation.

Therefore, to address the issue of interpretation of test results, in our institution we developed daily interpretive rounds in the field of coagulation during a 2-year period (1993-1995), whereby every complex evaluation beyond those involving a simple prothrombin time (PT) or PTT would be accompanied by a narrative paragraph that describes the differential diagnosis and identifies any additional informative tests that should be considered in the evaluation of the patient. Currently in our institution, the

Table 2
Coagulation-Related Assays Available to Clinicians to Illustrate the Challenge of Test Selection Without Reflexive Testing

Activated protein C resistance
Anticardiolipin antibody
Antiphosphatidylserine antibody
Anti-plasmin assay
Antiplatelet antibody
Antithrombin plasma activity/antigen
Antithrombin serum activity
Anti-Xa danaparoid
beta-2 Glycoprotein I
beta-Thromboglobulin
C4b binding protein
Cryofibrinogen
D-dimer quantitative/semiquantitative
Dilute Russell viper venom test
Euglobulin lysis time
Factor activity (II, V, VII, VIII, IX, X, XI, XII, XIII)
Factor antigen (VII, IX, X)
Factor inhibitors (V, IX, VIII human/porcine)
Factor V Leiden mutation
Factor VIIa
Factor X chromogenic assay
Fibrin monomer
Fibrinogen activity/antigen
Fibrin(ogen) degradation products
Fibrinopeptide A
Fletcher factor (prekallikrein) screen/assay
Heparin absorption of plasma
Heparin (unfractionated, low-molecular-weight) anti-Xa activity
Heparin cofactor II
Heparin-induced antibody/antibody titer
Hexagonal phospholipid neutralization
High-molecular-weight kininogen assay
Homocysteine
Lipoprotein (a)
MTHFR (methylene tetrahydrofolate reductase)
Partial thromboplastin time (PTT)
PTT mixing study
Plasminogen activator inhibitor-1
Plasminogen activator inhibitor-2
Plasminogen activity and antigen
Platelet aggregation with agonists: adenosine diphosphate, arachidonic acid, collagen, epinephrine, spontaneous, or ristocetin
Platelet factor 4
Platelet neutralization procedure
Proconvertin prothrombin assay
Protein C activity (chromogenic/clot based)/antigen
Protein S activity/free and total antigen
Prothrombin G20210A
Prothrombin fragment 1+2
Prothrombin time
Prothrombin time mixing study
Reptilase time
Stypven time
Thrombin time
Thrombin time mixing study
Thrombin-antithrombin complex
11-dehydrothromboxane B ₂ /creatinine ratio
Tissue factor pathway inhibitor antigen
Tissue plasminogen activator activity/antigen
Tissue thromboplastin inhibition test
von Willebrand factor activity/antigen/multimers

interpretive rounds in various stages of development involve coagulation, toxicology, hemoglobin/anemia, blood transfusion, protein electrophoresis, molecular diagnosis in infectious disease, and autoimmune disorders.

There have been many limitations that have prevented an interpretive service for clinical laboratory test results from reaching the same level of success as in anatomic pathology and radiology. An interpretive service that is not available at all times for clinical laboratory tests has minimal clinical usefulness. An interpreter who does not have expert knowledge cannot consistently provide the necessary information. Handwritten comments, which often are illegible, on the bottom of a laboratory report are not acceptable. Interpretations that do not consider important clinical information (when it exists and influences the evaluation) also are not useful. Interpretations that are too short or too general, such as “canned” comments that are not patient specific, have minimal value. We have avoided all of these limitations in our current service.

The Need for Advice on Laboratory Test Selection and Interpretation

To Provide Adequate Quality of Care

A report in the *New England Journal of Medicine* in 1999 by St Peter et al¹ based on the responses of 7,015 primary care physicians and 5,092 specialists indicated that nearly 1 in 4 primary care physicians believes that the scope of the care they are expected to provide is greater than it should be. The specialists whose referrals were received by the primary care physicians indicated by even a greater percentage (38% of those surveyed) that the physicians in primary care are being deluged with issues beyond those they can diagnose and treat with confidence. This admission on the part of physicians has been demonstrated in a number of publications. In a 1997 report, physicians identified patient-specific interpretive comments as a valuable addition to the test results, as opposed to standard comments from a package insert. These included an explanation of antinuclear antibody patterns, cardiac enzyme indices, and results for uncommonly ordered tests such as osteocalcin. Some physicians asked for a narrative explanation for every laboratory evaluation that contained an abnormal test result.² Another study demonstrated that even when physicians do not have adequate knowledge to make a diagnostic or management decision, in situations where a mistake may result in decreased quality of care or a case of medical malpractice, they obtain the definitive answers to address their uncertainties only 30% to 50% of the time.³ This is not significantly different from a report in 1985 in the *Annals of Internal Medicine*, in which only 30% (14/47) of physicians during a half day of typical office practice reported that their informational needs per patient visit were met.⁴ Thus, in the majority of cases, now and in years past, there is still guesswork

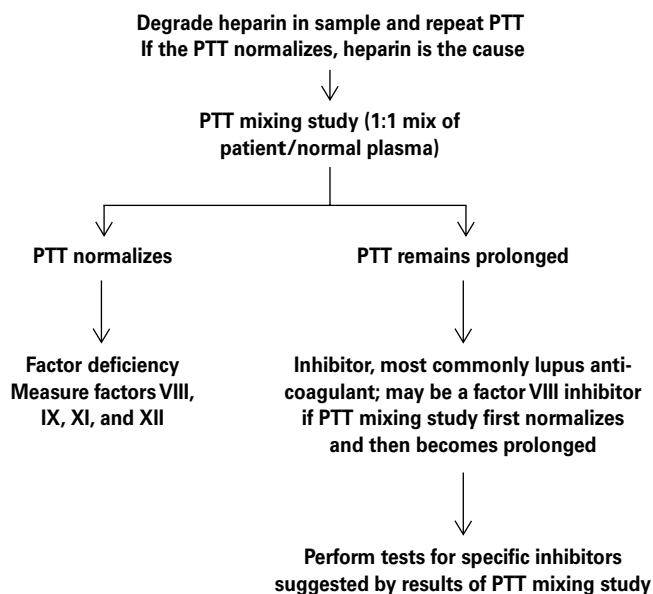


Figure 1 Laboratory evaluation of a prolonged partial thromboplastin time (PTT).

involved in diagnostic and treatment issues. The results of a survey of practicing clinicians published in 1998 revealed that the greatest value that can be provided by a clinical laboratory director is to serve as a consultant on the selection and interpretation of laboratory tests.⁵

A survey in our institution was performed in which coagulation interpretations that were more than a simple sentence or two in length were returned to physicians, and the physicians were asked several questions about the value of the interpretation. In this study, in which 46 of 90 surveys were returned, 98% (45/46) of the physicians indicated that they found the interpretations useful or informative; 59% (27/46) indicated that the interpretation shortened the time to diagnosis; 72% (33/46) indicated that the interpretation probably reduced the number of laboratory tests required to make a diagnosis; and, notably, 72% (33/46) indicated that the interpretation helped avoid a misdiagnosis (unpublished data, 1998). Thus, there is a clear need articulated by clinicians for a simple, automatically provided, and inexpensive mechanism to obtain information on the appropriate laboratory tests to select in a given clinical situation and the clinical meaning of the test results.

To Reduce Medical Error

The Institute of Medicine (IOM) report on medical error⁶ has brought to light the dramatic observation that the number of Americans who die each year as a result of hospital medical errors is, at a minimum, 44,000 to 98,000. There has been much exchange of correspondence in the *New England Journal of Medicine* regarding this report,

Table 3
Medical Errors by Type

May be directly decreased by reflexive testing and systematically provided clinical laboratory narrative interpretations by experts

Incorrect diagnosis is made
 Time to diagnosis is unnecessarily prolonged
 Appropriate diagnostic test is not ordered
 Outdated tests or therapies are used
 Slow or incorrect response to the results of tests or monitoring occurs

Most likely would not be affected by reflexive testing or narrative interpretations

Operational mistake is made during a procedure
 Treatment is incorrectly used or distributed
 Medication dosing error occurs
 Communication between the staff and patient is insufficient
 Equipment malfunctions
 Prophylactic therapy is not supplied
 Case is managed inappropriately

much of which suggests that this is a substantial underestimate. One letter notes that the data pertain only to hospitalized patients, and, therefore, errors with outpatients are not included.⁷ Another letter points out that the IOM report focused only on medical errors that are relatively easy to document.⁸

Errors associated with a failure to select a necessary laboratory test to provide an accurate diagnosis in a timely fashion or an error from the misinterpretation of a laboratory test result were not included in the tally in the IOM report. **Table 3** lists the types of medical errors that can occur.⁹ The likelihood for recognition of a medical error is high with the incorrect administration of a drug or with technical errors in surgical procedures. It is clear from our personal experience of more than 5 years of daily interpretive rounds in coagulation that physicians are greatly confused by the amount of information and make many errors in the selection and interpretation of laboratory tests. Among dozens of commonly encountered examples, it is quite common to have a physician order a factor V test when seeking the result of a screening test for the factor V Leiden mutation, and it is equally common for a physician to order a particular coagulation factor assay measurement that is not relevant to the evaluation of a prolonged PT or PTT.

We performed an informal survey of physicians to determine whether they knew which tests should be performed to evaluate a genetic predisposition to thrombosis in a 28-year-old man who developed a deep vein thrombosis and subsequently a near-lethal pulmonary embolism. Most of the physicians did not know of the existence of a high-incidence mutation known as the prothrombin G20210A mutation, and many physicians were still unaware that the factor V Leiden mutation was assessed by an inexpensive screening test known as the activated protein C resistance test. The patient

in this case had the prothrombin mutation, which was missed because the physician did not test the patient for it. This omission led to an inappropriate discontinuation of anticoagulant therapy 6 months after the deep vein thrombosis, thereby permitting a near-lethal pulmonary embolism to occur 2 months later.

A sounding board editorial in the *New England Journal of Medicine*, which summarizes the IOM report, notes that there is a need to use systematic approaches to prevent mistakes.¹⁰

To Reduce the Cost of Health Care

A third major driver for a systematic consultative program in laboratory medicine is the continuous need for reduction in the cost of care. It has been reported that laboratory services make up 3% to 5% of a hospital's budget but leverage 60% to 70% of all critical decision making such as admissions, discharges, and medications.¹¹ Therefore, the development of a program for expert-based diagnostic test selection and interpretation is likely to lead to reductions in time to diagnosis and length of stay, which contribute far more to reducing costs than a limited reduction in the number of laboratory tests. As noted earlier, in our institution the provision of a narrative paragraph for complex evaluations in coagulation was found in a survey of our own physicians to have been useful in preventing a misdiagnosis in 71% of the cases for which it was provided. A cost analysis, with certain reasonable assumptions, indicates that the coagulation interpretation service accounts for a cost avoidance in our institution in excess of \$1 million annually (unpublished data, 1998).

Thus, the desire of physicians to provide a high quality of care to patients, the need to reduce medical error, and the need to minimize the cost to obtain a diagnosis are the 3 main drivers to develop a better system nationwide for selection and interpretation of laboratory tests.

Attempts to Address Physicians' Need for Advice on Laboratory Test Selection and Interpretation

The Curbside Consultation

There have been a number of possible solutions tested over the years to address the need of clinicians for information on the selection and interpretation of laboratory tests. One of these is the "curbside consultation," a process in which a physician seeks information or advice about patient care from another physician who has a particular expertise without obtaining a formal consultation at that time.¹² Two studies appeared in the *Journal of the American Medical Association* in 1998 surveying physicians about curbside consultations, with one study surveying Massachusetts

physicians¹³ and another surveying Rhode Island physicians.¹¹ Both of these studies showed a growing use of curbside consultation by primary care practitioners and a reluctance to provide them by specialist physicians. From these and other related studies,¹⁴⁻¹⁷ there are some general conclusions. One is that most of the requests for curbside consultations are from general internists and primary care practitioners. A second was a concern by specialist physicians who do not have an abundance of revenue-generating procedures about the potential loss of revenue from fewer formal (and paid) consultations. Third, there is concern among specialists that their verbal curbside comments may be misinterpreted or taken out of context when the primary care physician diagnoses or treats the patient. One major disadvantage of the curbside consultation is that the expert usually is not given the opportunity to review any additional patient data, while there is still some potential for legal responsibility if a note is made in the patient's chart commenting on the expert's input. Fourth, there is an association between the increase in capitated payment systems and the increase in the curbside consultations. A final comment was that curbside consultations varied substantially in quality, depending on the expertise of the physician who was consulted.

The Intelligent Laboratory Information System

A second possible solution that has been offered to assist physicians requesting advice on the selection and interpretation of laboratory tests is an "intelligent" laboratory information system that guides the ordering physician. It has been demonstrated with pharmaceuticals¹⁸ that providing computerized advice to physicians ordering medications can lead to appropriate changes in the selection of medications, resulting in the use of more effective and less expensive drugs. It was thought that the same might be true for laboratory test selection, such that when a physician orders a particular laboratory test, an intelligent system provides advice on test selection. However, this is extremely difficult because of the different clinical situations in which a particular test might be requested. For example, a factor V Leiden assay might be requested for a patient who has a family member who suffered a thrombosis, for a woman taking oral contraceptives, for a person with recurrent thrombosis, for a person with calf pain and unilateral leg swelling, or for an asymptomatic person with a negative personal and family history of thrombosis. The advice on the appropriateness of that test varies tremendously in these different clinical situations.

In one institution a "laboratory advisory system" was used to interact with clinicians to assist them in the laboratory investigation of a patient's condition.¹⁹ This study showed that physicians who ordered tests through the laboratory advisory system ordered fewer laboratory tests during a diagnostic evaluation, with fewer blood samples obtained from the

patient and a lower cost associated with laboratory tests. Importantly, there also was a shortened time to diagnosis. The disadvantage of the system was that there was no expert physician input on each case and, therefore, no data on whether the information generated by the computer system was correct. Fixed algorithms for diagnosis or treatment probably are effective in no more than approximately 70% of cases. For the patient who seeks care because of chest pain, for example, the recommended treatment steps in a clinical pathway to obtain an electrocardiographic tracing, perform appropriate laboratory tests, and provide treatments will not be correct in all cases. To prevent this extremely high error rate in clinical pathway management, just as in the case of laboratory test selection and result interpretation, there has to be an expert physician involved in each clinical case.

Medical Information From the Internet

A third possible solution that has been offered to address the growing need for information on test selection and interpretation is to help physicians obtain medical information from the Internet. One review²⁰ cited 5 top physician Web portals, providing information on MD consult, Medscape, WebMD, Doctors Guide, and Physicians on Line. Each of these provides a clinical library, continuing medical education opportunities, drug information, health news, MEDLINE access, patient education, and a search engine. However, they are not associated with a panel of experts who can provide advice in a timely manner for clinical cases, but instead represent the equivalent of a current and electronically searchable medical library.

In a study published in 1995,²¹ a group of physicians in a large practice had the benefit of dedicated individuals to perform searches to obtain medical information for their cases, and much of the information requested was related to appropriate laboratory test selection. The searches were provided in a relatively short time (an average of 43 minutes) at a total (modest) cost of \$27.37 per case. However, the information was contained in an average of 19.6 pages from the medical literature for the physicians to read. The physicians reported that they found it more useful to discuss their questions directly with expert physician colleagues rather than read 19.6 pages per case to obtain an answer.²¹

Conclusion

The use of curbside consultations, intelligent computer systems that attempt to identify appropriate laboratory tests without physician intervention, and Web-based clinical information fall short of what is needed to provide consultative advice to clinicians on the selection and interpretation of laboratory tests.

Given the limitations of the curbside consultation, the intelligent laboratory information system, and obtaining medical information from the Internet, our system of daily interpretive rounds, which provides advice in the selection and interpretation of laboratory tests in the field of coagulation, has worked exceedingly well at our institution. It has offered our clinicians informative and valuable interpretations to enhance their ability to provide timely, accurate, and effective care.

From ¹American Medical Diagnostics, Vienna, VA; and the ²Division of Laboratory Medicine, Department of Pathology, Massachusetts General Hospital and Harvard Medical School, Boston, MA.

Address reprint requests to Dr Laposata: Director of Clinical Laboratories, Room 235 Gray Bldg, 55 Fruit St, Massachusetts General Hospital, Boston, MA 02114.

References

1. St Peter FR, Reed MC, Kemper P, et al. Changes in the scope of care provided by primary care physicians. *N Engl J Med.* 1999;341:1980-1985.
2. Jahn M. Doctors speak their minds on lab profiles and problems. National Survey of Physicians. *MLO Med Lab Obs.* June 1997:32-38.
3. Green ML, Ciampi MA, Ellis PJ. Residents' medical information needs in clinic: are they being met? *Am J Med.* 2000;109:218-223.
4. Covell DG, Uman GC, Manning PR. Information needs in office practice: are they being met? *Ann Intern Med.* 1985;103:596-599.
5. Horowitz RE. The successful community hospital pathologist: what it takes. *Hum Pathol.* 1998;29:211-214.
6. Kohn LT, Corrigan JM, Donaldson MS, eds. *To Err Is Human: Building a Safer Health System.* Washington, DC: National Academy Press; 2000.
7. Richardson WC, Berwick DM, Bisgard JC. The Institute of Medicine report on medical errors [letter]. *N Engl J Med.* 2000;343:663-664.
8. Melker RJ. The Institute of Medicine report on medical errors [letter]. *N Engl J Med.* 2000;343:664-665.
9. Leape LL, Lawthers AG, Brennan TA, et al. Preventing medical injury. *QRB Qual Rev Bull.* 1993;19:144-149.
10. Brennan TA. The Institute of Medicine report on medical errors: could it do harm? *N Engl J Med.* 2000;342:1123-1125.
11. Forsman RW. Why is the laboratory an afterthought for managed care organizations? *Clin Chem.* 1996;42:813-816.
12. Keating NL, Zaslavsky AM, Ayanian JZ. Physicians' experiences and beliefs regarding informal consultation. *JAMA.* 1998;280:900-904.
13. Kuo D, Gifford DR, Stein MD. Curbside consultation practices and attitudes among primary care physicians and medical subspecialists. *JAMA.* 1998;280:905-909.
14. Manian FA, McKinsey DS. A prospective study of 2,092 "curbside" questions asked of two infectious disease consultants in private practice in the Midwest. *Clin Infect Dis.* 1996;22:303-307.
15. Bergus GR, Sinift SD, Randall CS, et al. Use of an e-mail curbside consultation service by family physicians. *J Fam Pract.* 1998;47:357-360.
16. Myers JP. Curbside consultation in infectious diseases: a prospective study. *J Infect Dis.* 1984;150:797-802.
17. Manion FA, Janssen DA. Curbside consultations: a closer look at a common practice. *JAMA.* 1996;275:145-147.
18. Teich JM, Merchia PR, Schmitz JL, et al. Effects of computerized physician order entry on prescribing practices. *Arch Intern Med.* 2000;160:2741-2747.
19. Smith BJ, McNeely MDD. The influence of an expert system for test ordering and interpretation on laboratory investigations. *Clin Chem.* 1999;45(8 pt 1):1168-1175.
20. Berkowitz LL. Portals that shine. *e.MD.* Fall 2000:13-23.
21. Gorman PN, Ash J, Wykoff L. Can primary care physicians' questions be answered using the medical journal literature? *Yearbook of Medical Informatics.* 1995:175-179.