Assuring the Quality of Clinical Microbiology Test Results

Michael L. Wilson
Department of Pathology and Laboratory Services, Denver Health, Denver, and Department of Pathology, University of Colorado School of Medicine, Aurora, Colorado

The role of microbiology laboratories in the care of patients with suspected or known infections has been described in previous articles in this series of medical microbiology updates. This review addresses the broader role of clinical microbiology laboratories in the quality of care and patient safety. The importance of microbiology laboratories in the care of patients with infectious diseases is obvious, but microbiology laboratories also play an indirect role in patient care that, from a broader perspective, is equally important.

Previous updates in this series presented information on the use of clinical microbiology tests and the role of the clinical microbiology laboratory for the diagnosis of infectious disease [1–27]. The purpose of this update is to provide an overview of how clinical microbiology laboratories assure that the results of these tests are accurate, precise, and reproducible. This update will include the following select issues that directly impact the quality of test results generated by clinical microbiology laboratories: laboratory accreditation, implementing new laboratory tests, quality control (QC), test ordering and result reporting, quality audits, and longitudinal collection of microbiological data.

LABORATORY ACCREDITATION

Under the Clinical Laboratory Improvement Act of 1988, clinical laboratories in the United States must be accredited to perform tests on patient specimens and to report the results of those tests to health care providers. To maintain accreditation, clinical microbiology laboratories must meet the general accreditation and regulatory requirements applicable to all clinical laboratories (table 1), as well as regulatory requirements specific to clinical microbiology laboratories. The number of accreditation and regulatory requirements runs into the hundreds and changes frequently, often annually.

Despite their large number and frequent updates, accreditation and regulatory requirements are only minimal standards; mere accreditation does not guarantee high-quality testing. There are a number of reasons for this. (1) Different accrediting organizations use similar but not identical requirements. (2) Important quality issues—particularly those related to clinical interpretation and relevance of laboratory tests—may not be addressed by accreditation requirements. (3) Some requirements are only indirectly related to test quality or patient care, because they involve broader issues, such as laboratory safety or management. (4) Some requirements can be interpreted in >1 way, limiting their use for improving quality in a standard manner. (5) Some requirements are outdated, reflecting the needs of older laboratory methods or processes. (6) Finally, because of the time needed to write and implement new requirements, the requirements may lag behind the introduction of new diagnostic methods.

In addition to accrediting requirements, a number of non-regulatory guidelines and standards have been developed. Of these, the most widely used in the United States are those of the Clinical Laboratory Standards Institute (CLSI; formerly NCCLS). Other international guidelines and standards have been developed for clinical laboratories, including those of the International Organization for Standardization (ISO), the European Committee for Antimicrobial Susceptibility Testing (which is part of the European Society for Clinical Microbiology and Infectious Diseases), and the World Health Organization (WHO). Use of these guidelines and standards is, for the most part, voluntary, although some of the guidelines have been adopted by accrediting organizations as part of their accreditation requirements.
Introduction of new tests or devices in clinical laboratories requires a robust process to determine that the tests or devices exhibit the same performance characteristics established by manufacturers as part of obtaining clearance or approval from the US Food and Drug Administration to market them in the United States. Not surprisingly, this process—termed “validation” or “verification” by different organizations—may appear to be redundant with what has already been done by manufacturers. What is often unrecognized, however, is that commercial tests and devices exhibit substantial variation in performance characteristics in different settings. There are a number of reasons for this: differences in patient populations, variations in water and electrical supplies, differences in individual practices between laboratories, and changes or deterioration in instrument components over time. All of these factors affect how laboratory tests perform; thus, tests and devices must be evaluated before they are used in clinical settings [28].

The terminology used to describe the process of introducing new tests remains somewhat inconsistent, with only subtle differences between some of the definitions. For example, the terms “validation” and “verification” are defined as follows: the ISO defines validation as “confirmation, through the provision of objective evidence, that requirements for a specific intended use or application have been fulfilled” (ISO 9000); and the WHO defines validation as “the action (or process) of proving that a procedure, process, system, equipment, or method used works as expected and achieves the intended result” (WHO-BS/95.193). The ISO defines verification as “confirmation, through the provision of objective evidence that specific requirements have been fulfilled” (ISO 9000) and performance verification as “a one-time process completed to determine or confirm instrument performance characteristics before the instrument is used for patient testing.”

Some of the steps for implementation and validation of new tests are shown in Table 2. The time required to implement and validate a new laboratory test is substantial: 3–6 months is typically required before new, commercially available tests can be used for routine patient care.

Additional steps are needed to validate antimicrobial susceptibility testing before it can be used to monitor drug resistance routinely [29]. The introduction of new antimicrobial agents into clinical practice eventually necessitates antimicrobial susceptibility testing to monitor the development of resistance to those agents. The need for antimicrobial susceptibility testing varies: for some agents, resistance is reported soon after the drug is marketed, whereas for other agents, it may take years before resistance is detected in clinical isolates. There is little need for most laboratories to test isolates for resistance to new antimicrobial agents until resistance has been reported in the literature. Although it might be argued that resistance will go undetected unless antimicrobial susceptibility test results are obtained frequently and widely, not every laboratory needs to do this: there is sufficient data collection at academic medical centers and through longitudinal studies for new types of resistance to be detected.

**QC IN CLINICAL MICROBIOLOGY**

In clinical microbiology laboratories, a large number of media and procedures may be used to generate just a single test result. For example, a routine wound culture includes a direct smear and a Gram stain, use of different aerobic and anaerobic media, possible use of fungal or mycobacterial media, Gram stains of bacterial isolates recovered in culture to guide identification of pathogens. The terminology used to describe the process of introducing new tests remains somewhat inconsistent, with only subtle differences between some of the definitions. For example, the terms “validation” and “verification” are defined as follows: the ISO defines validation as “confirmation, through the provision of objective evidence, that requirements for a specific intended use or application have been fulfilled” (ISO 9000); and the WHO defines validation as “the action (or process) of proving that a procedure, process, system, equipment, or method used works as expected and achieves the intended result” (WHO-BS/95.193). The ISO defines verification as “confirmation, through the provision of objective evidence that specific requirements have been fulfilled” (ISO 9000) and performance verification as “a one-time process completed to determine or confirm instrument performance characteristics before the instrument is used for patient testing.”

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procedures, necessary tests used for rapid or preliminary identification, tests used for confirmatory identification, antimicrobial susceptibility tests, and storage of isolates. Each type of medium used, each individual test and procedure, and even the reporting of results must undergo QC on a regular basis.

The frequency and type of QC varies by the type of test, medium, or reagent. For some tests, QC must be performed along with every test. For other tests, QC must be performed only when a new lot number is to be used. For automated assays, QC is often performed daily but is typically much more extensive than that used with manual tests. Some instruments require multiple QC tests, calibration of the instrument, and establishment that the linearity of the instrument remains stable from day to day.

Although QC results are not displayed along with test results—and, therefore, are not apparent to health care providers who order cultures or review results—infectious diseases specialists should be aware of the extent and complexity of QC used in microbiology laboratories. Such awareness aids the understanding of the time required to report test results, explains delays in reporting results (i.e., QC failure for a test), provides awareness regarding the actual costs of tests, and explains, in part, why microbiologists are unwilling to deviate from standard procedures.

**TEST ORDERING AND RESULT REPORTING**

The potential benefits of computerized provider order entry (CPOE) systems are obvious; however, <5% of American hospitals have successfully implemented such a system [30]. Even basic systems that only have the capability for computer-based order entry can improve patient care by providing standardized order sets, minimizing errors related to handwriting, eliminating use of ambiguous abbreviations, facilitating resolution of discrepant or redundant orders, and improving the ability of laboratories to report critical values. Use of a CPOE system also substantially improves the timeliness and quality of audits.

The greatest improvement in quality of care and patient safety should occur with CPOE systems that are fully integrated with other information systems, in which the available information is processed by an intelligent software system. For example, an order for an antimicrobial agent would be screened by the software for results of microbiologic cultures, antimicrobial susceptibility testing, drug levels, physiologic parameters (e.g., liver or kidney function test data), drug-drug or drug-food interactions, and other information that might affect drug selection, dosage, or route of administration. Components of such systems exist in many hospitals, but overall integration remains uncommon.

The potential benefit of such systems obviously requires accurate and up-to-date information. For microbiology laboratories, this will be a challenge, because of the time required to isolate and identify pathogenic microorganisms, themultiplicity of methods used for these procedures, and the complex nature of result reporting (i.e., the extensive use of free text to report test results, as opposed to the use of coded test results). Indeed, much of the information developed as part of diagnostic microbiology is not amenable to such a system—for example, information from cultures that are in progress, efforts to isolate pathogenic microorganisms from other contaminating flora, slow growth of some microorganisms, equivocal microbial identification results, and the need for temporary descriptions of many microorganisms (e.g., gram-negative bacilli and non–glucose fermenting organisms). It is apparent that a number of issues need to be addressed for CPOE systems to make full use of information from clinical microbiology laboratories.

**ANTIMICROBIAL SUSCEPTIBILITY TESTING**

The role of antimicrobial susceptibility tests to guide empirical therapy, to refine therapy once pathogens have been isolated and identified, and to detect new types of antimicrobial resistance is well established. Other roles of antimicrobial susceptibility testing for patient care, such as development of cumulative antibiograms, creation of antimicrobial formularies, and detection of new antimicrobial resistance strains or trends, are also well established. What may not be apparent to most providers is that generating accurate and reproducible antimicrobial susceptibility test data requires perhaps the most extensive QC program used in clinical laboratories today.

The CLSI publishes guidelines for the QC of antimicrobial susceptibility tests [29]. These guidelines are extensive and require rigorous adherence to each step of testing for results to be accurate and reproducible. Specific guidelines have been developed not only for different categories of bacteria and fungi (e.g., members of the Enterobacteriaceae family) but also for individual species. Perhaps the most important guidelines published by CLSI are that antimicrobial agents should be tested against different microbial pathogens. The information used to develop these guidelines is based on clinical, pharmacologic, and microbiologic data. It is strongly recommended that clinical microbiology laboratories and providers both adhere to these guidelines; testing antimicrobial agent–pathogen combinations that are not recommended may generate antimicrobial susceptibility test results that either are misleading or cannot be interpreted. In general, it is also strongly recommended that new antimicrobial agents should not be tested in clinical laboratories until there are sufficient data for CLSI guidelines to be developed and published.

The CLSI also publishes guidelines for the development of cumulative antibiograms [31]. When developed and interpreted correctly, these documents provide the data needed to guide empirical antimicrobial therapy as well as provide a basis for
QUALITY AUDITS

Audits in health care are widely used in other countries and are an established method for assessing and improving quality [32]. Many American health care organizations also use audits, although typically these are not called audits in America. As the term implies, an audit is an assessment of a given parameter over a limited time frame (i.e., a snapshot). Audits can be broad in scope or as specific as the data will permit. For example, an audit of prophylactic use of antimicrobial agents before surgery could include all providers and broad categories of surgical procedures, or it could be limited to specific surgical procedures or providers. Once developed, audits can be repeated to track trends, to assess the effectiveness of changes, or to assess the performance of new providers or procedures. Health care organizations with good clinical data repositories or data warehouses should be able to perform a clinical audit quickly and at low cost.

Perhaps the most important decision is to determine which audits to perform. Audits should be of high quality and provide data that can be used to improve the quality of care; audits should not be performed as an end unto themselves. Only a limited number of audits should be performed at any time, because the amount of information created by many simultaneous audits can quickly become overwhelming and render the data irrelevant. In selecting which audits to perform, one should remember that many health care organizations already track data regarding the Joint Commission’s annual National Patient Safety Goals, as well as additional information needed by other regulatory agencies, third-party payers, or government. Some of this information can be used as part of an audit, but other hospital- or clinic-specific audits also should be performed. Table 3 lists examples of audits that might be useful for infectious diseases practitioners and clinical microbiologists.

Table 3. Suggested audits for infectious diseases and clinical microbiology.

| Correlation of empirical therapy with culture results |
| Tracking the appropriateness and timeliness of changes in antimicrobial therapy after culture results become available |
| Determining the proportion of patients receiving appropriate surgical prophylaxis |
| Measuring the efficacy of infection control measures |
| Tracking the blood culture contamination rate |
| Correlation of microbiologic culture results with needed surgical procedures, line replacement or removal, and other diagnostic and therapeutic procedures |
| Tracking the compliance of providers with formulary recommendations or restrictions |
| Measuring the efficacy of changes made in response to the results of previous audits |
bacteremia [33–39]. More recent data, however, suggest that anaerobic bacteremia is once again becoming more common and that anaerobic blood culture bottles should be used routinely [40, 41]. Another example is the recognition of cases of necrotizing fasciitis caused by methicillin-resistant Staphylococcus aureus [42]. Although most cases of necrotizing fasciitis continue to be caused by Streptococcus pyogenes, cases due to methicillin-resistant S. aureus have obvious implications for patient care and infection control. Collection of data through time helps define the relative proportion of cases of infection caused by different pathogens.

Because most infections are not reportable diseases, neither clinical information nor results of microbiologic cultures are maintained in public databases. Therefore, it can be argued that individual laboratories (or hospitals) should maintain this information in permanent form. This is most easily accomplished by retaining clinical and microbiologic information in either laboratory information systems or clinical data repositories. Older laboratory information systems may not have this capability because of a lack of storage capacity or other limitations, and converting data from older laboratory information systems to newer systems—if this is even possible—can be difficult and expensive. Clinical data repositories or data warehouses can also be used, but most health care systems do not transfer all microbiology data to these systems, limiting the transfer of data to final test results. Data from these systems can be used for a number of quality assurance purposes.

DATA COLLECTION FOR PUBLIC HEALTH SURVEILLANCE

Clinical microbiology laboratories are required to collect and report data as part of active surveillance by public health departments for reportable diseases. This requires laboratories to collect data on a large number of pathogens as well as for certain patterns of antimicrobial resistance. Such requirements have grown substantially over the past few years. It is important to remember that surveillance definitions do not always match clinical or microbiologic definitions, and as a result, laboratories are required to track 2 different data sets (clinical and epidemiologic). The public health benefits of tracking reportable diseases are obvious, but both laboratory staff members and providers need to be aware of the differences between the 2 types of data.

ROLE OF THE INFECTIOUS DISEASES PROVIDER

Infectious disease providers can and should play an important role in assuring the quality of results that are generated by clinical microbiology laboratories. Their most important role is to help correlate clinical, laboratory, and radiographic data, to determine the clinical relevance, if any, of microbiology test results. In addition, they can follow best practices in infectious disease diagnosis and treatment, particularly when acting as a consultant. This complements their role as liaisons for clinical microbiology laboratories—a role of particular importance in community hospitals and other nonteaching settings. Finally, they can serve on organizational pharmacy and therapeutics (and other) committees, thereby improving the integration of laboratory, clinical, and pharmacologic data in decisions about empirical therapy, formularies, and other issues related to infectious diseases practice.

SUMMARY

Clinical microbiology laboratories play an important role in the process of ensuring quality of care and patient safety. Much of this role relates to the timely reporting of accurate test results, which depends on the practice of rigorous QC. There is no compelling reason to deviate from this practice, particularly because any test results that would be generated are likely to be clinically irrelevant, misleading, or even dangerous to patients.

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References