Sources of Error in Laboratory Medicine

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Systems to prevent errors have long been in place in the practice of laboratory medicine. Statistical principles first described to monitor the quality of industrial products were extrapolated to the clinical chemistry laboratory more than half a century ago, and indeed quality control in the clinical laboratory may be the first formally introduced form of quality management in health care. Quality control, the process of ongoing performance checks of laboratory tests, allows detection and correction of major problems or errors within the test system or its performance. In addition, laboratory computer information system software often includes the “delta check” feature to warn laboratory professionals of subsequent patient values that are significantly different from previously reported values. However, control of laboratory testing alone cannot prevent all laboratory-associated errors. A patient specimen follows a journey from the bedside to the laboratory for processing and results are then issued back to the bedside. What is sometimes considered a laboratory error can and often does result from processes that occur either before the specimen arrives or after the result leaves the laboratory. This continuum, or path of workflow, has been divided into 3 phases: preanalytical, analytical, and postanalytical phases. These phases form a framework for considering strategies to prevent error and improve quality in the clinical laboratory.

Materials and Methods

To review the sources of error in laboratory medicine, several searches through MEDLINE were performed covering the period 1995 through 2002 using the key words “laboratory error” and “patient safety” combined with “laboratory.” References from articles identified through MEDLINE were also reviewed. Articles chosen had a representative example at every stage of the laboratory’s path of workflow.

Results

Sources of Preanalytical Error

Preanalytical error can occur at the time of patient assessment, test order entry, request completion, communication to the laboratory, specimen collection, specimen transport, or specimen receipt in the laboratory. In a study examining factors in the delay and treatment of breast cancer, misdiagnosis was the most frequent cause of provider delay in the diagnostic stage of the disease. This included ignoring symptoms, treating with antibiotics, and neglecting to do a biopsy.

Specimen requests must include patient identifiers and demographic data, as well as tests requested and clinical diagnosis if appropriate. If there is a mismatch between the patient and the patient information entered into the computer or written onto a paper request, test results can be issued on the wrong patient. In a recent survey of test ordering accuracy, 2.9% of test orders, representing 6,538 tests from 577 institutions were not completed. Of those not processed by the laboratory, 42% were incorrectly entered into the computer and 13% of the requisitions were improperly completed. When paper requisitions are filled out illegibly, it may result in the wrong tests being performed. Barcode labeling of patient specimens is used in many centers to reduce the numerous opportunities for transcription errors at specimen reception: barcode labels generated at the bedside offer an additional safeguard against mislabeling of the patient specimen.
Specimen collection is a multifaceted process and involves collecting the right specimen from the right patient at the right time. Blood cultures taken without adequate skin disinfection prior to culture may give false-positive results. The patient identification wristband—a vital patient identification tool—is not without error; in a nationwide survey, 2.2% of wristbands were missing or contained errors. Other common sources of preanalytical error related to specimen collection include drawing blood from an indwelling line and common sources of preanalytical error related to specimen collection include drawing blood from an indwelling line and hemolysis of the sample due to an improper draw. The recent cost-cutting trend of decentralizing blood specimen collection from laboratory phlebotomists to various personnel at the nursing stations can greatly influence the quality of specimens received in the laboratory, particularly when time and funding for training have also been reduced.

Specimen volume is critical for many tests and is dictated either by performance characteristics of the analyzer or assay, or sensitivity of the test. Washington and colleagues have shown the microbial yield in blood cultures is directly proportional to the amount of blood cultured. Failure to culture a sufficient volume may result in false-negative blood cultures, and antibiotic management may be adversely impacted.

Sampling time is important for a number of laboratory tests including monitoring of blood glucose, therapeutic drugs, and cardiac isoenzymes. Metabolic screening of infants, which should be done 24 hours after birth, may be missed in patients discharged from hospital before that time.

Specimen transport is a continuation of specimen collection. Improper post-collection handling, storage, and transport prior to testing can also affect the quality of the specimen and test results. Aspirated material for anaerobic culture should be transported to the laboratory in an anaerobic transport device within 3 hours of collection for optimum yield. Tissue or biopsy material should be transported in a sterile container, reach the laboratory within 30 minutes, and be held at room temperature until processing.

Sources of Analytical Error

The analytic phase begins when the specimen is prepared for testing and ends when the test result is interpreted in the laboratory and verified as ready to report. In the chemistry laboratory, preparation in which disposable pipettes, tubing, or vessels containing sequential specimens are used can lead to “carryover” or “sample interaction” and resultant errors. Amplification techniques such as polymerase chain reaction (PCR) are particularly prone to contamination in this way and can result in false-positive test results. Not processing a specimen properly prior to analysis can similarly lead to incorrect results. Improper preparation of a specimen for corticosteroid assay, failure to perform extraction and chromatography prior to performing the compound-S radioimmunoassay, led to near-fatal misdiagnosis of congenital adrenal hyperplasia in an infant with ambiguous genitalia. A series of errors in both the preanalytical and analytical phases of susceptibility testing of Mycobacterium tuberculosis resulted in 9 patients misdiagnosed with multidrug-resistant tuberculosis. Substances that interfere with assay performance can affect test results, (eg, rheumatoid factor in a patient’s sample is reported to lead to overestimation of von Willebrand factor in a latex immunoassay and a falsely positive cryptococcal latex agglutination.) Heterophile antibodies and fibrin clots can also interfere with assay performance. In a Virginia university, an outbreak of calicivirus infection was mistakenly attributed to Shiga-toxin producing Escherichia coli 0157:H7 on the basis of a false-positive enzyme immunoassay (EIA). False-negative PCR assays for microbes can be the result of inhibitors in the clinical specimen.

Sources of Error in Test Methods

The introduction of diagnostic tests in the clinical laboratory first requires establishment and verification of method performance specifications. For a commercial test, the 1-time verification process involves evaluating the manufacturer’s claims as they relate to the following: test accuracy (measuring what it is supposed to measure), precision (reproducibility), sensitivity (ability to measure small amounts), specificity (ability to detect only the analyte of interest and not be affected by interfering substances), and linearity (the range of clinical values supported by the methodology). A recent study examining the extent of comparability among allergen-specific IgE results from different commercial laboratories found discrepancies in precision and accuracy, which raised concerns about misclassification of patient allergy status and the potential for serious consequences. In a similar type of study, Finck and colleagues studied the variations in measurement of international normalized ratio (INR) among laboratories and point-of-care (POC) devices. Results from 1 laboratory and 1 POC device were significantly different from the other 3 devices tested, and these differences may have resulted in an erroneously founded change in treatment approximately 20% of the time.

Cytopathology is one of the major areas within the laboratory predisposed to interpretative errors because of the inherent subjectivity of the pathologist. Both exfoliative respiratory cytology and fine-needle aspiration biopsy are used to make a diagnosis of lung cancer: benign and reactive conditions with cellular changes that mimic malignancy are numerous and have recently been comprehensively reviewed. According to CLIA ‘88, an amended report is to be issued when there is a significant discrepancy between cytology and histology results that would affect patient care. In a 1995 survey on issues pertaining to quality assurance and quality control, of the 51 respondents (13.5% of total), 2 noted that no correlation between cervicovaginal cytology and pathology was done. The average total number of discrepancies was 13 per month, with 2 classified as affecting patient care. Failure to look for discrepancies denies an opportunity to uncover significant error. Although 39 of 51 respondents contacted the clinicians via telephone and written report, some used only written reports, which could have been lost or overlooked. The wide range in
false-negative rates between institutions raises the issue regarding the lack of standardized definitions.

Despite caution and caveats, and increasing number of malpractice claims are being filed against pathologists, particularly with respect to misinterpretation of cervical (Pap) smears and fine needle biopsies (BFNA) of breast masses. It is interesting to note that in an interinstitutional comparison of BFNA in which a false-negative rate of 8% was described, 7% of the error was attributed to sampling error and only 1% to professional interpretation.24

Sources of Postanalytical Error

In the postanalytical phase of laboratory testing, the test results are released to the clinician, and s/he interprets them and makes diagnostic and therapeutic decisions accordingly. The inappropriate use of a laboratory test result can have devastating consequences. Three patients were misdiagnosed with HIV when HIV-1 plasma viral load tests (which were developed for following patients already diagnosed with HIV) were used as a diagnostic test and yielded false positive results.26 This example reinforces the need to follow standard diagnostic protocols in making a diagnosis of HIV infection.

Test results reported without reference ranges and comment that advises further diagnostic tests or therapeutic options may lead to erroneous conclusions or inappropriate follow-up. Manual reporting systems are subject to transcription errors at the laboratory end. Telephoned results are subject to errors at the receiver end. Paper results may get lost. Significant results can be overlooked. Treatment delays can occur even when critical laboratory results are phoned to the caregiver.27

Discussion

Errors attributed to laboratory testing can occur anywhere across the entire path of laboratory workflow: preanalytical, analytical, and/or postanalytical activities. A recent report reviewing the literature on laboratory-associated errors found that preanalytical errors predominated, ranging from 31.6% to 75%, analytical errors from 13.3% to 31.6%, and postanalytical errors from 9 to 30.8%. Preanalytical errors are most often out of the laboratory's direct control since they occur at inpatient hospital locations and physicians' offices. This report also summarizes the results of 8 reviews of blood transfusion error showing that the majority of blood transfusion errors were due to misidentification of the patient at the time of specimen collection or blood administration; both of which are also out of the laboratory personnel's direct control.

If there is to be any significant reduction in errors in the laboratory’s path of workflow, it will come only from interdependent cooperation in designing the processes and procedures for patient identification, specimen collection, specimen labeling, and specimen transport to the laboratory. In addition, there must be adequate and effective training of personnel throughout the hospital to be competent in following those processes and procedures. Data collection needs to include not only events in which patient identification errors occur, but also monitoring of specimen acceptability at the time of receipt in the laboratory and tracing unsuitable specimens to their source location.

The significant reduction across time of analytic errors within the laboratory can be attributed to several factors such as 1) training and qualification of laboratory testing personnel; 2) rules for defining allowable error in internal test method quality control practices; 3) interlaboratory test result comparisons (proficiency testing); and 4) external quality assessments (ie, laboratory inspections).

Similar to preanalytical error, the reduction of postanalytical error will be dependent on the design and development of those processes and procedures that will ensure timely notification of critical results, transmission of the correct result for the patient, routing of test results to the correct patient record, and the appropriate use of the test result by the clinician in making a diagnosis or ordering treatment for the patient.

Summary

It is incumbent upon health professionals both inside and outside the laboratory department to collaborate in designing and developing preanalytic and postanalytic processes and procedures in order to decrease error across the total laboratory testing process. This is best accomplished by involving stakeholders at the various patient care areas (eg, emergency department, surgery). Through collaboration, improvements in patient identification, ordering practices, administration practices, and reporting practices will also reduce errors in the pathways of workflow of other clinical services such as respiratory care, diagnostic imaging, and medication use, and thereby improve the quality of patient care.