

See discussions, stats, and author profiles for this publication at: <https://www.researchgate.net/publication/7052626>

Errors in clinical laboratories or errors in laboratory medicine?

Article in *Clinical Chemistry and Laboratory Medicine* · February 2006

DOI: 10.1515/CCLM.2006.123 · Source: PubMed

CITATIONS

767

READS

33,347

1 author:



Mario Plebani

University of Padua

2,123 PUBLICATIONS 67,612 CITATIONS

SEE PROFILE

Review

Errors in clinical laboratories or errors in laboratory medicine?

Mario Plebani*

Department of Laboratory Medicine, University Hospital of Padova and Center of Biomedical Research, Castelfranco Veneto, Italy

Abstract

Laboratory testing is a highly complex process and, although laboratory services are relatively safe, they are not as safe as they could or should be. Clinical laboratories have long focused their attention on quality control methods and quality assessment programs dealing with analytical aspects of testing. However, a growing body of evidence accumulated in recent decades demonstrates that quality in clinical laboratories cannot be assured by merely focusing on purely analytical aspects. The more recent surveys on errors in laboratory medicine conclude that in the delivery of laboratory testing, mistakes occur more frequently before (pre-analytical) and after (post-analytical) the test has been performed. Most errors are due to pre-analytical factors (46–68.2% of total errors), while a high error rate (18.5–47% of total errors) has also been found in the post-analytical phase. Errors due to analytical problems have been significantly reduced over time, but there is evidence that, particularly for immunoassays, interference may have a serious impact on patients. A description of the most frequent and risky pre-, intra- and post-analytical errors and advice on practical steps for measuring and reducing the risk of errors is therefore given in the present paper. Many mistakes in the Total Testing Process are called “laboratory errors”, although these may be due to poor communication, action taken by others involved in the testing process (e.g., physicians, nurses and phlebotomists), or poorly designed processes, all of which are beyond the laboratory’s control. Likewise, there is evidence that laboratory information is only partially utilized. A recent document from the International Organization for Standardization (ISO) recommends a new, broader definition of the term “laboratory error” and a classification of errors according to different criteria. In a modern approach to total quality, centered on patients’ needs and satisfaction, the risk of errors and mistakes in pre- and post-examination steps must be minimized to guarantee the total quality of laboratory services.

Keywords: errors; intra-analytical; laboratory medicine; mistakes; post-analytical procedures; pre-analytical; total testing process.

Introduction

The Institute of Medicine (IOM) report, *To Err Is Human: Building a Safer Health System* (1), galvanized a dramatically expanded level of debate and concern about patient injuries in healthcare. Patient safety, a topic that had been little understood, and even less discussed in healthcare systems, became a frequent focus for journalists, healthcare leaders, and concerned citizens (2). The IOM report has far-reaching implications for all disciplines, including pathology activities and laboratory medicine (3). Laboratory services have a great influence on clinical decision-making: 60–70% of the most important decisions on admission, discharge, and medication are based on laboratory test results (4). With this high degree of influence, the quality of laboratory testing and reporting is of utmost importance. The overwhelming dependence of clinical decision-making and patient-management processes on laboratory reporting (5) must induce laboratory medicine to set higher quality standards. Unlike many other medical processes, activities in laboratory medicine are precisely defined and are therefore more controllable than a procedure or treatment in an emergency department or other medical settings. Laboratory medicine enjoys another unique advantage in that it pioneered statistical quality control (QC) activities and it is leagues ahead of other clinical disciplines in introducing quality improvement initiatives. However, the real number of mistakes made in laboratory testing is not fully recognized, because no widespread process is in place to either determine how often mistakes occur or to systematically eliminate sources of errors. Moreover, total testing is complex, consisting of a series of inter-related processes, each involving a series of process steps, every one of which can result in an error. Laboratory activities have been traditionally classified as pre-, intra- and post-analytical. In the past, laboratory professionals focused their attention on intra-analytical errors and on mistakes resulting in adverse events, but overlooked the near misses that, apparently, cause no harm. Other well-recognized limitations of our knowledge regarding errors and mistakes in laboratory medicine are derived from the scarce scientific literature dealing with this topic, from practical difficulties in study design, as well as in meas-

*Corresponding author: Mario Plebani, Department of Laboratory Medicine, Azienda Ospedaliera-Università di Padova, Via Giustiniani 2, 35128 Padova, Italy
Phone: +39-049-8212792, Fax: +39-049-663240,
E-mail: mario.plebani@unipd.it

uring and reporting the number of errors and, above all, in defining what a laboratory error actually is.

Changing the perspective

In the past, the perspective under which most studies on errors in laboratory medicine were performed was limited to what happened inside the clinical laboratory. Thus, only analytical and some pre-analytical errors (those affecting the so-called “within laboratory pre-analytical steps”) were detected. This approach, however, is not consistent with the concept of patient-centered care, which is one of the six specific aims for improvement of the healthcare system suggested in the IOM report *Crossing the Quality Chasm* (6). The promotion of patient-centered care should be translated into the need to investigate any possible defect that occurs in the total testing process and that can eventually have a negative impact on the patient. From the patient’s viewpoint, in fact, any direct or indirect negative consequence related to a laboratory test must be considered, irrespective of whether the source lies in the pre-, intra- or post-analytical step. Moreover, from the patient’s viewpoint it is irrelevant whether any error is caused by a laboratory professional (e.g., calibration or testing error) or by a non-laboratory operator (e.g., inappropriate test request, error in patient identification, etc). Therefore, the unique framework for considering where mistakes can occur in laboratory testing services is the total testing process. A mistake can occur in each of the 11 steps in this process or in any of the places where a handoff can occur, starting from test request and ending with the physician’s reaction to laboratory information. According to this perspective, the proposed definition of laboratory error is “a defect occurring at any part of the laboratory cycle, from ordering tests to reporting results and appropriately interpreting and reacting on these” (7). Recently, this definition was accepted and incorporated into the draft of the ISO Technical Report 22367 “Medical laboratories – Reduction of error through risk management and continual improvement – Complementary elements” (8). Clinical laboratories should therefore assume responsibility for the whole cycle of the testing process, from the physician ordering a laboratory investigation to recognizing the significance of the reported result in the management of the patient. However, this responsibility requires complete control of the testing process, achieved by liaising with and involving other professionals in the quality loop.

Errors in laboratory medicine: the good, the bad and the ugly

The most relevant features of studies on laboratory errors are their scarcity and their heterogeneous nature. This means that studies performed and reported in the literature have used different data collection approaches, different time spans for data collection, and have investigated different laboratory sections or activities. Moreover, different definitions

Table 1 Frequency of errors in clinical laboratories [modified from reference (3)].

One error identified every:
a) 330–1000 events
b) 900–2074 patients
c) 214–8316 laboratory results

have been used for laboratory errors and mistakes. Consequently the frequency of errors in clinical laboratories reported in the literature varies greatly, as shown in Table 1.

Data in the literature clearly demonstrate that the collection method used has an important influence on error types and their prevalence. When data collection was based on complaints (9) or on a more fortuitous finding of blunders (10), errors were mainly attributable to misidentification, and they were few: 133 errors in 6 years or 0.05% (10). Yet a careful review of the entire process revealed a far higher number of errors (189 in 3 months, 0.47% of the test results) and misidentification errors accounted for only 2.6% of all errors (11). Despite large differences between these studies, a significant decrease in error rates has been documented over the last four decades, particularly for analytical errors. In fact, in the survey carried out by Belk and Sunderman in 1947 (12), laboratory errors (expressed in parts per million, ppm) were 162,116 (16.21%), whereas in 1996 these were 12,904 (1.29%) (13) and in 1997 only 470 (0=0.47%) (14). The good news is, therefore, that error rates in clinical laboratories have been significantly reduced over time.

The second evidence is that, despite the large differences in actual error frequencies, all recently available studies demonstrate that a large percentage of laboratory errors occur in the pre- and post-analytical phases, with fewer mistakes occurring during the analytical step (15). Figure 1 shows the current stratification of errors in laboratory medicine and their distribution within the different phases of the testing process. In the Q-Probes studies performed in the USA, the frequency of errors for pre-analytic performance measures, such as procuring specimens for digoxin measurements before serum levels of the drug are in equilibrium with the level at the active site, was 24.4% (16); ordering an improper diagnostic test accounted for 23% (17), and incorrectly identifying a hospitalized patient prior to collecting a blood specimen, 6.5% (18). Lower error rates were observed for some other pre-analytic measures, such as duplicate ordering of laboratory tests (19) and rejecting unacceptable chemistry specimens (20). Post-analytical errors included 7.1% of telephoned results incorrectly transmitted (21), no result for 1.7% of ordered tests (19), 15.1% of patients dissatisfied with their phlebotomy procedure (22), and 15% of markedly high critical values not noted in the patient’s medical record (23). Performance measures for analytical processes undertaken within the clinical laboratory had the lowest error rates, and some examples in this area were the frequency of proficiency test failures (0.19%) (13) or a quality control specimen for an analyte that was out of control (0.14%) (24), as shown in Figure 2.

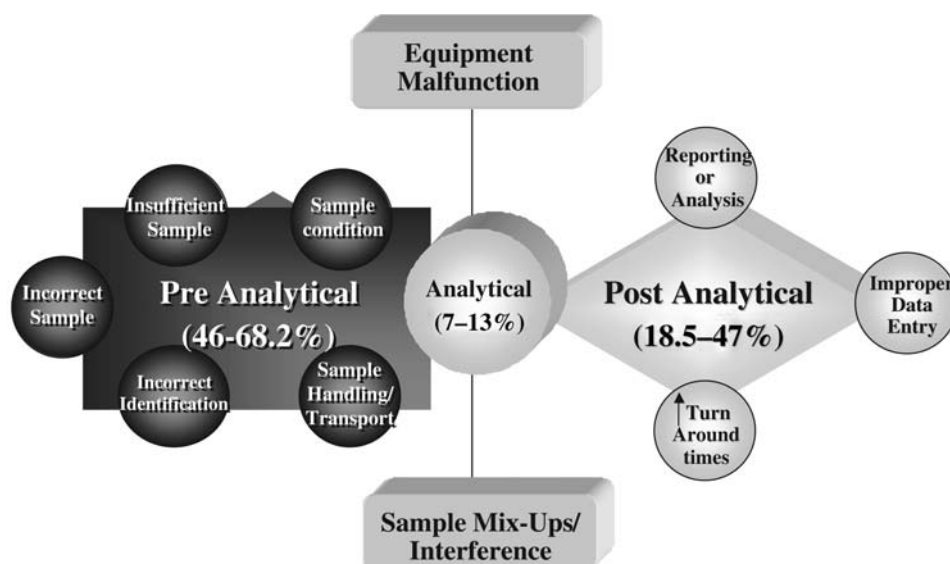


Figure 1 Types and rates of error in the three stages of the laboratory testing process (modified from reference 3).

Pre-analytical errors

Pre-analytical procedures performed outside the control of the laboratory

While the total testing process is typically divided into three main phases (pre-, intra- and post-analytical), exploration of the beginning and end of the loop reveals that currently, pre- and post-analytical steps are more error-prone than intra-analytical processes (26). In particular, in the pre-analytical phase, the existence of a pre-pre-analytical phase (i.e., procedures performed neither in the clinical laboratory nor under the direct control of laboratory personnel) must be recognized. This phase starts with test request, patient and specimen identification, blood drawing,

sample collection and handling, and ends with the transportation of specimens to the laboratory.

Findings made in several studies indicate the importance of the pre-pre-analytical phase. Misuse of laboratory services through inappropriate laboratory test requesting is under scrutiny worldwide because of its impact on total costs, and the inherent increased risk of medical errors and injury. The estimations of inappropriate laboratory tests vary widely, ranging from 11% to 70% for general biochemistry and hematology tests, 5% to 95% for urine screens and microbiology, and 17.4% to 55% for cardiac enzymes and thyroid tests (27). Numerous studies have been conducted to investigate measures to reduce the excessive and inappropriate use of laboratory tests. Combined efforts in this direction are more effective

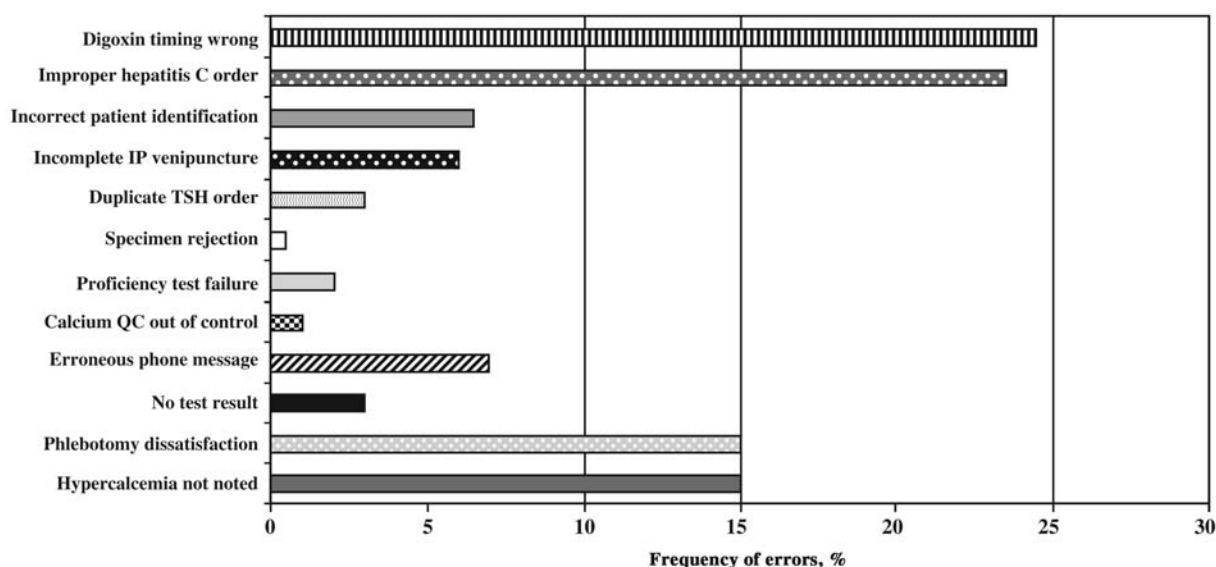


Figure 2 Error rates in the total testing process, as shown in the Q-Probes studies performed by the American College of Pathologists (25).

than single interventions. Moreover, the use and diffusion of evidence-based laboratory guidelines should be associated with continuous monitoring and clinical advice from laboratory specialists (28). It is therefore unanimously agreed that it is important to provide consultancy as part of a laboratory service in order to improve appropriateness.

Accurate patient identification is one of the first steps in ensuring correct laboratory results: misidentification of patients and specimens can have serious consequences (29). In 1995, a Q-Probes study found a mean wristband error rate of 7.4% and demonstrated that the error rate was related to hospital size, with smaller hospitals having a higher error rate (18). A subsequent Q-Tracks inter-laboratory quality improvement program, performed between 1999 and 2000, demonstrated an initial error rate of 7.4% that fell to 3.05% following continuous monitoring and educational initiatives (30). In the College of American Pathologists Q-Probe study (31) performed in 660 institutions, a total of 5514 of 114,934 outpatient requisitions (4.8%) were associated with at least one type of order entry error, including discrepancies between tests ordered and transcribed in the laboratory computer, one or more discrepancies in the identity of patients or physicians, and incorrect test priority. In an Australian survey on transcription and analytical errors, the transcription error rate was up to 39%, with the most frequent types of errors associated with misidentification of the requested tests, the requesting doctors and/or the patient (32). Further evidence has been provided by studies demonstrating the importance of the evaluation of specimen adequacy as a critical factor in test result accuracy and usefulness (20). Samples that are missing, coagulated, hemolyzed, insufficient and wrong consequent to inappropriate specimen collection and handling procedures may account for a large percentage of pre-analytical mistakes. In particular, mistakes due to the use of incorrect containers or procedures (e.g., from infusion route or with excessive aspiration force) stress the importance of inter-departmental cooperation in improving the quality of specimen collection and handling (33). In fact, some data demonstrate a significant difference regarding the frequency of these mistakes between outpatients and inpatients (7). This difference should be related, in part, to the higher complexity of examinations performed and multiple blood drawings for inpatients, but also to the more accurate control assured by laboratory personnel who perform sample drawings for outpatients. On the other hand, the blood drawing performed by ward personnel, with a higher turnover and less specific skills, may lead to an increase in the number of mistakes. Overall, inappropriate quantity and quality of specimens account for over 60% of pre-analytical errors, while additional causes, such as incorrect identification of the specimen, lack of due signature, empty tube, lack or wrong compilation of the accompanying form, sample not in ice, tube broken in the centrifuge, urine not acidified or without volume indication present, show a lower prevalence. Less identifiable pre-analytical errors

originate from variations in plasma volume and metabolites as a result of physical exercise (34–36), tourniquet placement (37) and other patient-related physical variables (diet, stress, position) (38, 39).

Pre-analytical procedures performed in the laboratory

Specimen preparation, which involves all the activities required to render a sample suitable for analysis, includes log-in, centrifugation, aliquotting, pipetting, dilution, and sorting specimens into batches for their introduction into automated analyzers. The specimen preparation step has attracted considerable academic and commercial attention in recent years because it contributes to approximately 19% of the overall cost of analyzing a single specimen and is also time-consuming (37% of time spent in producing a result). Moreover, the manual handling of samples that may be infectious constitutes a well-recognized hazard to laboratory staff (40). Indirect evidence of the risk of errors in this phase stems from some papers dealing with the effects of the introduction of automated pre-analytical robotic workstations. In particular, in a paper by Holman et al. (41), the number of sorting, routing, pour-off and labeling errors was dramatically reduced after the introduction of a pre-analytical workstation. For instance, sorting and routing errors decreased from 7950 to 477 per month, labeling errors decreased from 6668 to 33 per month, while biohazard exposure events decreased from 2658 to 6 per month.

Analytical errors

In recent decades, standardization, automation and technological advances have significantly improved the analytical reliability of laboratory results and decreased the error rates (42). One mark of the success achieved in decreasing errors in the analytical phase is the high level of accuracy that currently exists in blood product testing for infectious agents. Thanks to nucleic acid testing, the contamination rate has dropped about from 1 per 100 units to its current level of 1 infectious unit in 1,800,000 units (43). However, this is not the case in all areas of laboratory medicine: importantly “quality design in a laboratory must begin with analytical quality because it is the essential quality characteristic of any laboratory test; unless analytical quality can be achieved, none of the other characteristics matter” (44). Furthermore, some data underline the relevance of analytical errors in some areas of laboratory medicine. In particular, a body of evidence demonstrates the frequency, and the negative outcomes, of analytical interferences in immunometric assays (45, 46). Marks stressed that analytical interference can occur with most of the present immunoassays, that errors related to these interferences can be difficult to identify and that they can produce serious errors (47) and, as stated by other authors, “interference in immunoassays is insidious and could adversely affect patient care” (48). Analyt-

ical interferences may arise from unsuspected abnormal binding protein(s) in patients, such as heterophilic antibodies, anti-animal antibodies and anti-idiotypic antibodies. The exact effect of such interferences will depend on the site of their interference with the reaction, leading to falsely raised or lowered measurements (49). The magnitude of interference may vary, but in a significant percentage of cases (up to 82%) it was considered large enough to have a potentially adverse effect on cost and/or the clinical care of patients. In particular, Ismail and colleagues underlined that the most serious impact of interference on clinical decisions are immunoassays with clear "cutoff" limits, such as tumor markers and cardiac troponin (50). With the present limitations of immunoassays, therefore, the magnitude of interference, direction of bias, concentration of analyte and concentration of interferent should all be known before sound clinical decisions can be made. Further recent data underline the importance of analytical accuracy. The National Institute of Standards and Technology (NIST) report on "The impact of calibration error in medical decision making" demonstrates that calibration error, leading to analytical bias, is a key parameter affecting the number of patients passing decision thresholds in practice guidelines. Because the signs and symptoms of hypercalcemia are not specific, a hypercalcemic laboratory finding can be confirmed with follow-up procedures, such as intact parathyroid hormone measurement, chest X-rays, 24-h calcium measurement, ionized calcium measurement and thyroid imaging (51). Based on their analysis of over 89,000 patients receiving serum calcium tests at the Mayo Clinic in 1998–1999, the authors demonstrated that the cost impact of an analytical bias of 0.1 mg/dL could range from \$8 to \$31 per patient. For an analytical bias of 0.5 mg/dL, the potential healthcare cost increase ranged from \$34 to \$89 per patient. With approximately 3.55 million USA patients receiving screening serum calcium tests affected by systematic bias, the potential economic impacts range from \$60 million to \$199 million per year for analytic bias of 0.1 and 0.5 mg/dL, respectively. In addition, the psychological and emotional effects that this has on patients should be considered. The effects of analytical bias on medical and economical outcomes are widely demonstrated (52).

Post-analytical errors

Post-analytical quality, the ultimate check on the consistency of pre- and intra-analytical quality, can be considered as the overall quality (53). It ties together not only the quality of the question to be answered, the analytical quality achieved and the usefulness of the answer obtained, but also the context of the patient and the perceived abilities of the physician to interpret and utilize laboratory information. Similar to the pre-analytical step, the post-analytical phase can be subdivided into one phase performed within the laboratory and another (post-post-analytical phase) in

which the clinicians receive, interpret and react to laboratory results.

Post-analytical procedures performed within the laboratory

The post-analytical procedures performed within the laboratory include verifying laboratory results, feeding them into the laboratory information system, and communicating them to the clinicians in a number of ways (in particular, by producing a report and making any necessary oral communications regarding "alert" or panic results). In this step, the most common mistakes, accounting for 18.4–47% of total laboratory errors, are: wrong validation, results that are delayed, not reported or reported to the wrong providers, and incorrect results reported because of post-analytical data entry errors and transcription errors (11, 54). Manual test validation is a time-consuming process with large inter-individual variation; moreover, it slows down the response of the laboratory to the clinic, thus causing delay in the diagnostic and therapeutic process. This validation process can be automated; some automated validation systems with satisfactory sensitivity and specificity have been developed and introduced into clinical laboratories (55, 56). As yet, however, it has not been proven that validation systems allow clinical laboratories to reduce errors, thus improving patient safety and outcomes. This is owing to difficulties in performing longitudinal studies with a design that allows the identification of real errors and a comparison with historical error rates. However, validation systems may be considered valid "preventive action". Another well-recognized source of post-analytical problems is inter-laboratory variability and inaccuracy of reference intervals (57–60). Reference intervals for healthy subjects and diseased populations are important benchmarks for the clinical interpretation of laboratory test values. The use of different, sometimes erroneous, reference intervals may markedly affect the clinical interpretation of laboratory data, leading to errors in clinical decision-making (57). The production and release of the laboratory report is the crucial step in post-analytical procedures, as its format, content, and communication significantly affect the interpretation and utilization of laboratory data by clinicians. The importance of information technology in improving reliability and security of result reporting is widely recognized. Requirements for information technology in laboratory medicine now go well beyond the provision of purely analytical data and include fundamental aspects of data communication, namely the notification of results that fall within established critical or alert intervals (61). In particular, the possible role of interpretative comments in improving patient outcomes has generated a lot of interest. Guidelines for the provision of interpretative comments have been released (62) and schemes for assessing the quality of comments have been initiated (63). The results obtained indicate that interpretation provided by laboratory professionals with inadequate expertise can be dangerous, and highlight the need for improve-

ment in the standard of interpretation currently provided (64, 65).

Post-analytical procedures performed outside the laboratory

In the post-analytical phase performed outside laboratory control (post-post-analytical phase), the clinician receives, reads and interprets the results, and makes a decision on the basis of information from the laboratory and other sources. There is evidence that laboratory information is only partially utilized: a recent report demonstrates that 45% of the results for urgent laboratory tests requested by the Emergency Department of one hospital were never accessed, or were accessed far too late (66). In addition, numerous errors can occur at this stage, as admitted by some clinicians on completing questionnaires (26), but problems can be generated at the laboratory-clinician interface. In fact, results released by the laboratory may not contain all the information needed by the clinician; the laboratory report may even contain information that the clinician considers superfluous or irrelevant. It has also been underlined that the introduction of new and complex tests, including genetic testing, may increase the complexity of medical management, and this, in turn, may influence the interpretation and clinical applicability of new and promising laboratory tests. Laposata and coworkers have demonstrated the usefulness of a laboratory interpretive service based on a pathologist's written, evidence-based, patient-specific interpretation that automatically accompanies the results of complex laboratory testing panels in several areas of laboratory medicine (67–69). The core of this service is the substitution of individual test requests by clinicians with the clinical question, the use of reflex testing to increase appropriateness of test selection, and the provision of a patient-specific narrative interpretation of test results. The results of a survey conducted by the same group demonstrate physician satisfaction in nearly 80% of responses and a significant reduction in test-ordering errors per requisition after 2.5 years of this service (69).

Effects of laboratory errors on patient outcomes

Pre- and post-analytical errors, which are frequent, undermine the quality of laboratory testing and can have an unacceptable impact on patient care (Table 2).

The risk of inappropriate care, and therefore of adverse events, due to laboratory errors ranges from

6.4% to 12%, while in a larger percentage of cases (26–30%) a laboratory error translates into a patient care problem. In a study by Plebani and Carraro (11), 6.4% of errors translated into inappropriate transfusions, modifications in heparin infusion, infusions of electrolyte solution and modifications in digoxin therapy. The incidence of further inappropriate investigations is much higher. Approximately 30% of laboratory errors can lead to undue repetition of laboratory tests, more invasive testing (CAT scan, NMR, biopsies, etc.), and consultations that create discomfort and increased costs for patients and the healthcare system, respectively. Among errors due to analytical interference in immunoassays, 21% were potentially misleading and likely to have adverse clinical effects. Anecdotal evidence indicates that one error can translate into 15 clinical consultations with primary-care physicians and hospital specialists, 77 laboratory tests, a pituitary computed tomography scan and inappropriate treatment (49).

Classification, prevention and correction of laboratory errors

The heterogeneity of criteria used in the literature on laboratory errors has led to different classification proposals. Table 3 shows a classification proposal aimed at identifying errors both within and outside of the direct control of the laboratory (72).

According to recently proposed ISO Technical Specifications (8), laboratory errors, non-conformities and incidents can be classified as follows:

- Cycle phase of event (pre-, intra- or post-analytical);
- Recognition of where the event has been generated (internal or external to the laboratory);
- Responsibility for event (latent or active, cognitive or non-cognitive);
- Preventability (from not preventable to highly preventable);
- Impact on patient care (none or minimal to inappropriate treatment/diagnosis).

The above classification should enable medical laboratories to: a) recognize the cause of errors; b) identify high-risk processes where the potential for error could lead to a risk for patients; c) identify real incidents associated with deviations from standard requirements; d) estimate and evaluate the associated risk to patient care; e) control these risks; and f) monitor the effectiveness of the controls undertaken.

ISO Technical Specifications are useful for classifying laboratory errors and, above all, stressing the importance of identifying potential errors and non-

Table 2 Effects of laboratory errors on patient outcomes.

	Number of errors	Effect on patient care	Risk of inappropriate care
• Ross and Boone (70)	336	30	7
• Nutting et al. (71)	180	27	12
• Plebani and Carraro (11)	189	26	6.4

Table 3 Classification of errors in laboratory practice.**1. Errors exclusively within the laboratory**

- *Pre-analytical*
 - Acceptance of improper specimens
 - Mismatch during the analysis
- *Intra-analytical*
 - Failure of the diagnostic system
 - Analytical interference
 - Procedure not followed
 - Undetected failure in quality control
- *Post-analytical*
 - Erroneous validation of analytical data
 - Failure in reporting
 - Excessive TAT

2. Laboratory errors caused by organizational problems outside the laboratory

- Wrong identification of a patient at the bedside
- Sample mismatch during blood withdrawal performed by non-laboratory personnel
- Wrong procedure for specimen collection
- Errors in specimen transport to the laboratory

3. Errors at the laboratory-clinical interface

- Appropriateness of test request
- Appropriateness of test interpretation
- Appropriateness of test utilization

TAT, turnaround time.

conformities through a planned review of processes and corrective and preventive action. Moreover, the management's responsibility in implementing preventive and corrective actions is clearly stated. A review of laboratory non-conformities, errors and incidents at regular intervals, as well as of the effects of preventive and corrective actions, should allow clinical laboratories to improve the quality of laboratory services and patient safety. Moreover, the identification, implementation and monitoring of indicators that effectively evaluate the quality of pre-, intra- and post-analytical phases can drive assessment and continuous improvement programs for laboratory services (73, 74). Introduction into the laboratory arena of some methodologies that identify the most critical steps in the total testing process, such as cognitive task analysis, HAZard and Operability study and the Absolute probability Judgement (75–77), should allow us to identify the risk of errors and to at least reduce the errors that are more likely to affect patient outcomes. Another quality tool, Six Sigma, incorporating management commitment and support, a basic problem-solving methodology relying heavily on metric analysis and a management system that supports continual improvement, has been successfully introduced into some clinical laboratories (78).

Laboratory automation provides for standardized workflow and helps to eliminate many error-prone steps undertaken by humans. Automation and robotics are effective in decreasing the likelihood of laboratory errors occurring from active human factors such as stress, fatigue, and cognitive impairment. Clinical laboratories must identify areas in which human involvement can be reduced and the use of automation and robotics increased. However, effective control of the total testing process will further

reduce laboratory errors. This should be achieved through more sophisticated control of laboratory processes thanks to affective integration between automation and information management. In particular, while automation is responsible for sample assessment at the beginning of the process, optimized routing and scheduling, and accurate and reliable measurements, information management involves access processes, specimen tracking, data logging and reporting, and quality control documentation.

Conclusions

Recent years have seen a significant improvement in our perception of the importance of patient safety and the need to reduce medical errors. As they are part of the overall healthcare system, clinical laboratories are prone to medical errors. A body of evidence demonstrates that, currently, the pre- and post-analytical steps of the laboratory testing process are more error-prone than the analytical steps. However, some points deserve further consideration:

- a) Although analytical methods and systems have been significantly improved in recent decades, we should not become complacent. There is much room for improvement, particularly in areas such as immunoassays, and for more effective procedures for quality assessment and control.
- b) More effective integration between automation and information management is crucial for assuring process control that allows us to identify and improve on the critical steps in pre-, intra- and post-analytical phases.
- c) Technological solutions, such as computerized order-entry systems, bar-coding identification of

patients and related samples, and strategies for sharing information, have the potential to make laboratory services safer, but they cannot be considered a panacea.

- d) Probably the most frequent pre-analytical errors are due to inappropriate choice of laboratory tests or panel of tests, and most post-analytical errors arise from inappropriate interpretation and utilization of laboratory results. This underpins the need to improve the laboratory-clinic interface. It is now known that interpretative and narrative comments are effective, and substitution of the traditional test request with a clinical question to be answered, with the laboratory taking a proactive role through effective utilization of reflex, reflective testing and narrative interpretation, should lead to safer and less expensive diagnoses.
- e) As stated by David Blumenthal in an editorial concerning two reports on laboratory errors and mistakes, the greatest quantitative reductions in laboratory errors are likely to be achieved through interdepartmental cooperation designed to improve the quality of specimen collection and data dissemination (79).
- f) Teamwork and good communication within the laboratory and, more importantly, with clinicians and patients are crucial to improving our knowledge on laboratory errors and developing practical remedies. The cornerstone to identifying aberrant laboratory test results remains clinical context and common sense.
- g) A characteristic of safe organization is that every individual feels personally responsible for ensuring safety. In a safety-oriented laboratory, personnel have a healthy skepticism about everything they do: they are proud of their high standards, but are constantly on the look out, because they are aware that they can, and will, make mistakes from time to time (80). The concept that bad systems, not bad people, lead to the majority of errors and medical injuries and the creation of a no-blame environment is a crucial scientific foundation for improving on safety in clinical laboratories.
- h) The availability of an ISO Technical Specification document should allow us to achieve a consensus on the definition and classification of laboratory errors and on the importance of implementing and reviewing corrective and preventive measures at regular intervals.

References

1. Kohn KT, Corrigan JM, Donaldson MS. *To Err Is Human: building a safer health system*. Washington, DC: National Academy Press, 1999.
2. Leape LL, Berwick DM. Five years after *To Err Is Human*. *J Am Med Assoc* 2005;293:2384–90.
3. Kalra J. Medical errors: impact on clinical laboratories and other critical areas. *Clin Biochem* 2004;37:1052–62.
4. Forsman RW. Why is the laboratory an afterthought for managed care organizations? *Clin Chem* 1996;42:813–6.
5. Plebani M. Charting the course of medical laboratories in a changing environment. *Clin Chim Acta* 2002;319: 87–100.
6. Institute of Medicine. *Crossing the quality chasm: a new health care system for the 21st century*. Washington, DC: National Academy Press, 2001.
7. Bonini P, Plebani M, Ceriotti F, Rubboli F. Errors in laboratory medicine. *Clin Chem* 2002;48:691–8.
8. ISO/PDTS 22367 *Medical laboratories – reduction of error through risk management and continual improvement – complementary elements* [Draft, August 2005].
9. Goldschmidt HM, Lent RW. Gross errors and work flow analysis in the clinical laboratory. *Klin Biochem Metab* 1995;3:131–40.
10. Lapworth R, Teal TK. Laboratory blunders revisited. *Ann Clin Biochem* 1994;31:78–84.
11. Plebani M, Carraro P. Mistakes in a stat laboratory: types and frequency. *Clin Chem* 1997;43:1348–51.
12. Belk WP, Sunderman FW. A survey of the accuracy of chemical analyses in clinical laboratories. *Am J Clin Pathol* 1947;17:853–61.
13. Steindel SJ, Howanitz PJ, Renner SW. Reasons for proficiency testing failures in clinical chemistry and blood gas analysis. *Arch Pathol Lab Med* 1996;120:1094–101.
14. Witte DL, VanNess SA, Angstadt DS, Pennell BJ. Errors, mistakes, blunders, outliers, or unacceptable results: how many? *Clin Chem* 1997;43:1352–6.
15. Boone DJ. Is it safe to have a laboratory test? *Accred Qual Assur* 2004;10:5–9.
16. Howanitz PJ, Steindel SJ. Digoxin therapeutic drug monitoring practices: a College of American Pathologists Q-Probes study of 666 institutions and 18,679 toxic levels. *Arch Pathol Lab Med* 1993;117:573–7.
17. Schiffman RB, Meier FA. Viral hepatitis serology test utilization. Q-Probes 93-01. Northfield, IL: College of American Pathologists, 1993.
18. Renner SW, Howanitz PJ, Bachner P. Wristband identification errors reporting in 712 hospitals: a College of American Pathologists Q-Probe study of quality issues in transfusion practice. *Arch Pathol Lab Med* 1993;117: 573–7.
19. Valenstein PN, Howanitz PJ. Ordering accuracy: a College of American Pathologists Q-Probes study of 577 institutions. *Arch Pathol Lab Med* 1995;119:117–22.
20. Jones BA, Calam RR, Howanitz PJ. Chemistry specimen acceptability: a College of American Pathologists Q-Probes study of 453 laboratories. *Arch Pathol Lab Med* 1997;121:19–26.
21. Schiffman RB, Steindel SJ, Howanitz PJ. Quality of telephone support by clinical laboratories: a College of American Pathologists Q-Probes study involving 459 institutions. *Am J Clin Pathol* 1996;105:517A–518A.
22. Dale JC, Howanitz PJ. Patient satisfaction in phlebotomy: a College of American Pathologists Q-Probes study. *Lab Med* 1996;27:188–92.
23. Howanitz PJ, Cembrowski GS. Postanalytical quality improvement: a College of American Pathologists Q-Probes study of elevated calcium results in 525 institutions. *Arch Pathol Lab Med* 2000;124:504–10.
24. Steindel SJ, Tetrault G. Quality control practices for calcium, cholesterol, digoxin and haemoglobin: a College of American Pathologists Q-Probes study in 505 hospital laboratories. *Arch Pathol Lab Med* 1998;122:401–8.
25. Howanitz PJ. Errors in laboratory medicine. Practical lessons to improve patient safety. *Arch Pathol Lab Med* 2005;129:1252–61.
26. Stroobants AK, Goldschmidt HM, Plebani M. Error budget calculations in laboratory medicine: linking the concepts of biological variation and allowable medical errors. *Clin Chim Acta* 2003;333:169–76.

27. Silverstein MD. An approach to medical errors and patient safety in laboratory services. A white paper. The Quality Institute Meeting, Atlanta, April 2003.
28. Solomon DH, Hashimoto H, Daltroy L, Liang MH. Techniques to improve physicians' use of diagnostic tests: a new conceptual framework. *J Am Med Assoc* 1998; 280:2020-7.
29. Altman DE, Clancy C, Blendon RJ. Improving patient safety. Five years after the IOM report. *N Engl J Med* 2004;351:2041-2.
30. Howanitz PJ, Renner SW, Walsh MK. Continuous wristband monitoring over 2 years decreases identification errors: a College of American Pathologists Q-Tracks study. *Arch Pathol Lab Med* 2002;126:809-15.
31. Valenstein P, Meier F. Outpatient order accuracy. A College of American Pathologists Q-Probes study of requisition order entry accuracy in 660 institutions. *Arch Pathol Lab Med* 1999;123:1145-50.
32. Khoury M, Burnett L, McKay MA. Error rate in Australian chemical pathology laboratories. *Med J Aust* 1996;165: 128-30.
33. Plebani M, Bonini P. Interdepartmental cooperation may help avoid errors in medical laboratories. *Br Med J* 2002;324:423-4.
34. Lippi G, Brocco G, Franchini M, Schena F, Guidi G. Comparison of serum creatinine, uric acid, albumin and glucose in male professional endurance athletes compared with healthy controls. *Clin Chem Lab Med* 2004;42: 644-7.
35. Lippi G, Franchini M, Guidi G. Haematocrit measurement and antidoping policies. *Clin Lab Haematol* 2002;24: 65-6.
36. Lippi G, Brocco G, Salvagno GL, Montagnana M, Dima F, Guidi G. High-workload endurance training may increase the serum ischemia modified albumin concentrations. *Clin Chem Lab Med* 2005;43:741-4.
37. Lippi G, Salvagno GL, Montagnana M, Guidi GC. Influence of short-term venous stasis on clinical chemistry testing. *Clin Chem Lab Med* 2005;43:869-75.
38. Romero A, Munoz M, Ramos JR, Campos A, Ramirez G. Identification of preanalytical mistakes in the stat section of the clinical laboratory. *Clin Chem Lab Med* 2005;43: 974-5.
39. Young DS. Conveying the importance of the preanalytical phase. *Clin Chem Lab Med* 2003;41:884-7.
40. Auchinleck GF, Lines RB, Godolphin WJ. Cost-effectiveness and benefits of automation and robotics. In: Kost GJ, editor. *Clinical automation, robotics and optimization*. New York: John Wiley & Sons, 1996.
41. Holman JW, Mifflin TE, Felder RA, Demers LM. Evaluation of an automated preanalytical robotic workstation at two academic health centers. *Clin Chem* 2002;48: 540-8.
42. Stankovic AK. The laboratory is a key partner in assuring patient safety. *Clin Lab Med* 2004;24:1023-35.
43. Busch MP, Kleinman SH, Nemo GJ. Current and emerging infectious risks of blood transfusions. *J Am Med Assoc* 2003;289:959-62.
44. Westgard JO. Six Sigma quality design & control. Madison, WI: Westgard QC, Inc., 2001.
45. Kricka LJ. Interferences in immunoassays - still a threat. *Clin Chem* 2000;46:1037-8.
46. Bjerner J, Nustad K, Norum LF, Olsen KH, Bormer OP. Immunometric assay interference: incidence and prevention. *Clin Chem* 2002;48:613-21.
47. Marks V. False-positive immunoassay results: a multicenter survey of erroneous immunoassay results from assays of 74 analytes in 10 donors from 66 laboratories in seven countries. *Clin Chem* 2002;48:2008-16.
48. Ismail AA, Barth JH. Wrong biochemical results. *Br Med J* 2001;323:705-6.
49. Kazmierczak SC, Catrou PG. Analytical interference. More than just a laboratory problem. *Am J Clin Pathol* 2000;113:9-11.
50. Ismail AA, Walker PL, Barth JH, Lewandowski KC, Jones R, Burr WA. Wrong biochemistry results: two case reports and observational study in 5310 patients on potentially misleading thyroid-stimulating hormone and gonadotropin immunoassay results. *Clin Chem* 2002;48: 2023-9.
51. National Institute of Standards and Technology. Planning Report 04-1: The impact of calibration error in medical decision making. www.nist.gov/director/prog-ofc/report04.pdf (accessed 23 November 2005).
52. Klee GG, Schryver PG, Kisabeth RM. Analytical bias specifications based on the analysis of effects on performance of medical guidelines *Scand J Clin Lab Invest* 1999;59:509-12.
53. Goldschmidt HM. Postanalytical factors and their influence on analytical quality specifications. *Scand J Clin Lab Invest* 1999;59:551-4.
54. Astion ML, Shojana KG, Hamil TR, Kim S, Ng VL. Classifying laboratory incident reports to identify problems that jeopardize patient safety. *Am J Clin Pathol* 2003; 120:18-26.
55. Oosterhuis WP, Ulenkate HJ, Goldschmidt HM. Evaluation of LabRespond, a new automated validation system for clinical laboratory test results. *Clin Chem* 2000; 46:1811-7.
56. Valdigué PM, Rogari E, Philippe H. VALAB: expert system for validation of biochemical data. *Clin Chem* 1992;38:83-7.
57. Zardo L, Secchiero S, Sciacovelli L, Bonvicini P, Plebani M. Reference intervals: are interlaboratory differences appropriate? *Clin Chem Lab Med* 1999;37:1131-3.
58. Henny J, Petersen HP. Reference values: from philosophy to a tool for laboratory medicine. *Clin Chem Lab Med* 2004;42:686-91.
59. Grasbeck R. The evolution of the reference value concept. *Clin Chem Lab Med* 2004;42:692-7.
60. Klee GG. Clinical interpretation of reference intervals and reference limits. A plea for assay harmonization. *Clin Chem Lab Med* 2004;42:752-7.
61. Jones R, O'Connor J. Information management and informatics: need for a modern pathology service. *Ann Clin Biochem* 2004;41:183-91.
62. The Royal College of Pathologists. Guidelines for the provision of interpretative comments on biochemical reports. *Bull R Coll Pathol* 1998;104:25-8.
63. Vasikaran SD, Penberthy L, Gill J, Scott S, Sikeris KA. Review of a pilot quality-assessment program for interpretative comments *Ann Clin Biochem* 2002;39:250-60.
64. Laposata M. Patient-specific narrative interpretations of complex clinical laboratory evaluations: who is competent to provide them? *Clin Chem* 2004;50:471-2.
65. Kim EK, Sikaris KA, Gill J, Calleja J, Hickman PE, Beilby J, et al. Quality assessment of interpretative commenting in clinical chemistry. *Clin Chem* 2004;50:632-7.
66. Kilpatrick ES, Holding S. Use of computer terminals on wards to access emergency test results: a retrospective study. *Br Med J* 2001;322:1101-3.
67. Kratz A, Soderberg BL, Szczepiorkowski ZM, Dighe A, Versalovic J, Laposata M. The generation of narrative interpretations in laboratory medicine. *Am J Clin Pathol* 2001;116(Suppl 1):S133-40.
68. Dighe AS, Soderberg BL, Laposata M. Narrative interpretations for clinical laboratory evaluations *Am J Clin Pathol* 2001;116(Suppl 1):S123-8.
69. Laposata ME, Laposata M, Van Cott EM, Buchner DS, Kashalo MS, Dighe AS. Physician survey of a laboratory medicine interpretive service and evaluation of the influence of interpretations on laboratory test ordering. *Arch Pathol Lab Med* 2004;128:1424-7.

70. Ross JW, Boone DJ. Institute on critical issues in health laboratory practice. Wilmington, DE: DuPont Press, 1989:173pp.
71. Nutting PA, Main DS, Fisher PM, Stull TM, Pontius M, Seifert M, et al. Problems in laboratory testing in primary care. *J Am Med Assoc* 1996;275:635–9.
72. Plebani M, Bonini P. In: EUROMEDLAB, 15th IFCC-FESCC European Congress of Clinical Chemistry and Laboratory Medicine, Barcelona, 1–5 June 2003.
73. Ricos C, Garcia-Victoria M, de la Fuente B. Quality indicators and specifications for the extra-analytical phases in clinical laboratory management. *Clin Chem Lab Med* 2004;42:578–82.
74. Plebani M. Towards quality specifications in extra-analytical phases of laboratory activity. *Clin Chem Lab Med* 2004;42:576–7.
75. Draft Federal Information Processing Standards Publication 183. Integration DEFinition for function modelling (idef). www.ldef.com/Downloads/pdf/idef0.pdf, 1993.
76. Redmill F, Chudleigh M, Catmur J. System safety: HAZOP and software HAZOP. New York: John Wiley & Sons, 1999:258pp.
77. Schraagen JM, Chipman SF, Shalin VL. Cognitive task analysis. Mahwah, NJ: Lawrence Erlbaum Associates, 2000:531pp.
78. Kazmierczak SC. Laboratory quality control: using patient data to assess analytical performance. *Clin Chem Lab Med* 2003;41:617–27.
79. Blumenthal D. The errors of our ways. *Clin Chem* 1997; 43:1305.
80. Leape LL. Striving for perfection. *Clin Chem* 2002;48: 1871–2.