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The Future of Laboratory Medicine: review of Understanding the New Pressures

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Abstract: **Since the future role of Laboratory Medicine is strongly and equally challenged by economic and new technological pressures, itis essential to take a broad view of the discipline and present to the administrators and other decision-makers the full spectrum ofactivities and benefits Laboratory Medicine can provide. In particular, the importance and the true impact of Laboratory Medicinecan only be achieved by adding value to laboratory tests, represented by their effectiveness in influencing the management of patients and related clinical outcomes.**

Keywords: **Laboratory Medicine, laboratory tests, patients, clinical outcomes.**

I. INTRODUCTION

Clinical laboratories represent an area of healthcare that has always undergone major changes because of technological advances and external economic pressures.[1] In the recentpast, many new diagnostic techniques and laboratory tests have been introduced as a result of both research on the fundamental pathogenesis of diseases and the development ofnew methods in themselves.

The two Nobel prizes awarded respectively to the inventors of monoclonal antibodies (G. Koehler and C. Milstein, 1984) and the polymerase chain reaction (K.B. Mullis, 1993) are only the more visible tips of a huge iceberg of innovationin the field. Without these techniques, many immunoassays and methods of molecular genetic testing that are currently taken for granted would simply have been impossible. Onthe other hand, in recent years, significant changes havebeen made to health care systems and care policy, largely because governments have had to address extremely complexeconomic issues.[2]

Experiencing a Paradigm Shift

The response of administrators and policy makers to the shrinking of available funds has begun on multiple fronts, and the financial health of clinical laboratories worldwide is becoming increasingly critical. In fact, because of their technological characteristics, laboratories are easy targets for financial constraints and limitations.2 In addition, laboratory tests on hospitalized patients are generally reimbursed as part of a diagnosis-related group (DRG). Under this arrangement, the hospital receives a flat fee for a DRG, regardless of how many (or few) tests are actually performed. Therefore, reducing laboratory costs will improve the hospital's profit margin.3In clinical laboratories, cost savings have often been achieved by merging laboratory areas through the creation of central core laboratories. Additional economies of scale have been sought through the regionalization of laboratory services through the creation of individual laboratories for different healthcare facilities.4 In some situations, purported savings have also been achieved through the addition of automated handling of pre-analytical samples using robotic systems.5Unfortunately, this “technological” approach to lowering the cost per assay has often been used to undermine the influence of laboratory professionals and further isolate them from clinical problems.1 On the other hand, laboratory professionals are generally trained to focus on technical performance. and in achieving and maintaining the highest quality test results achieved in laboratories.The value of clinical information related

to clinical laboratory testing is often forgotten. But it is obviously not enough to report the correct results if this data is not used for patient care. From the patient's perspective, only the transformation of data into useful information matters.6 The big picture requires a common knowledge model that moves from laboratory data to information and new knowledge to facilitate medical decisions. of nurses and ultimately intervention and outcome.7 This integration and understanding is the real challenge for pathologists and laboratory scientists at a time when the number of test parameters available has increased tremendously and the available resources have decreased significantly. Therefore, the survival of laboratory medicine in such an environment ultimately depends on its ability to add value to patient care. The key to realizing the importance and true impact of diagnostic testing can only be achieved by considering cost issues in the broader general context of health economics and not in the narrower realm of pure laboratory economics, where almost by definition every test involves a cost whose value is outside laboratory practice is.8

Measuring the Outcome of Laboratory Practice

How can this reflection be applied in the medical laboratory? It is clear that the "reason for existence" of laboratories should only be evaluated in the context of the impact of their production on clinical services and other laboratory service benefits. In other words, clinical laboratories must use outcome research to compete in the new healthcare landscape characterized by financial challenges and in the use of multiple medical technologies and processes. economic. studies demonstrating the impact of laboratory tests on a patient's overall health, patient care costs, and other less tangible pragmatic measures, such as quality of life and patient satisfaction.10 Understanding relevant laboratory results allows the clinical laboratory to participate in improving facility processes, including developing practice guidelines, equipment redesign laboratory service and apply patient satisfaction measures within the organization.11 However, the assessment of clinical outcomes relative to the clinical diagnosis is difficult. laboratory medicine, such as the difference between outcome measurements and biochemical tests.1 Often, surrogate markers have a role to play in assessing the clinical impact of laboratory practice. experiment (Table 1).10 In practice, it is more useful to measure changes in resource use, such as length of hospital stay or clinic visits, than to assess the number of years of life achieved. These results may not be traditional, but they are valuable, and we should start using them. One of the best examples of surrogate outcomes is glycated hemoglobin (HbA1c), which can be used as a surrogate marker of glycemic control and to assess adherence in patients with diabetes. Three levels of laboratory-related patient test results have been identified.11 A primary test result is simply the performance of a given test result, in terms of sensitivity and specificity in practice. Therefore, each test is associated with at least four result sets; namely the consequences of true positives, true negatives, false positives and false negatives. A quadratic test result is the patient's likelihood of disease as estimated by the caregiver receiving the test result; that is, the predictive value of the test is determined by Bayes theorem. Tertiary test results are the actual likelihood of a change in a patient's health as a result of any treatment intervention being performed or discontinued based on the test.

Table 1. Types of outcome measures.

Clinical outcome	Surrogate outcome
Mortality	Length of stay
Morbidity	Number of clinic visits
Quality of life, e.g. quality-adjusted life year (QALY)	Disease markers, e.g. HbA_{1C}, LDL cholesterol
Cost of episode	Complication rate
Cost of treatment	Readmission rate

Presently, there are good examples of situations where the judicious choice and use of diagnostic testing can significantly reduce the overall costs of treating the patient, accompanied frequently by a better overall clinical outcome for the patient. One example of this is the introduction of cardiac troponin for the diagnosis and treatment of patients with diseases in the spectrum of acute coronary syndrome. 13 Cardiac troponins could be the paradigm of the new role of Laboratory Medicine in many diseases. 14 As yet, no other clinical information or any other diagnostic test can replace the information provided by the measurement of troponin. Cardiac troponins are presently regarded as the most specific and sensitive of the currently available diagnostic techniques for myocardial damage, and the redefined criteria used to classify acute coronary syndrome patients presenting with ischemic symptoms as myocardial infarction patients are heavily predicated on an increased concentration of these markers in blood. 15 Troponins also are the only markers identifying high-risk coronary patients who should be treated with anti-thrombotic agents, such as glycoprotein IIb/IIIa antagonists, and referred for invasive evaluation at the earliest convenience.16 When compared with the traditional diagnostic approach (elevated CK-MB), troponin is markedly effective in altering patient management by enabling early discharge of patients, resulting in significant cost savings and increasing bed availability. In a British study conducted over six months, the introduction of troponin led to a

saving of more than £20,000 to the hospital from fewer bed days and reduced patient episode cost. 17 In another study of more than 850 consecutive patients presenting to the emergency department with suspected myocardial infarction who were randomized to receive a standard evaluation with serial electrocardiograms and CK-MB tests (control group) with or without a serial cardiac troponin evaluation, the length of stay was significantly shorter and hospital charges were less for patients who had troponin measurements, with an impressive potential annual saving of about US$4 million. 18 Collinson et al. recently showed that 5% of all admissions in their hospital for suspected acute coronary syndrome were incorrectly classified as myocardial infarction using the traditional WHO criteria. 19 The potential annual drug cost for treatment of these patients as infarction patients was approximately £56,000, with a 10-year estimated cost close to half a million pounds in wasted resources.19 In a recently published analysis, screening of high risk individuals by BNP before echocardiogram appeared to be more cost-effective than referring all subjects for echocardiography, with a reduction in the cost of screening per detected case of left ventricular systolic dysfunction by 21%. 20 But it has recently been reported that HbA1c also predicts mortality in non-diabetic men, with an increasing risk as the concentration increases, even below the commonly used upper reference limit. 22 A last example is a recently published study, demonstrating that procalcitonin- guided treatment of lower respiratory tract infections is able to significantly reduce antibiotic use in this type of disease without any compromise in outcome. 23 Low serum procalcitonin concentrations identified patients without clinically relevant bacterial infections, in whom antimicrobial therapy can be safely withheld. Thus, in view of the current overuse of antibiotics in acute respiratory tract infections, treatment based on procalcitonin measurement may have important financial and clinical implications. In addition to lower costs, a reduction of antibiotic use also results in fewer side effects and, in the long-term, leads to diminishing drug resistance.

Changing Role for Medical Laboratory Professionals

To meet the changing testing needs, the role of the laboratory in patient management should therefore be improved by adding value to laboratory tests derived from appropriate test request and utilization. On the other hand, physicians who frequently request laboratory tests outside of their field of expertise lack the knowledge base to order the optimal sequence of tests and to correctly interpret the results. 24 Conversely, medical laboratory professionals, combining clinical knowledge with experience in the performance of laboratory assays, have the unique expertise to advise their clinical colleagues in regard to the appropriate test selection and interpretation of laboratory results. 25 Knowledge of analytical and biological variation and the influence of physiological status and co-morbidities are critical in the interpretation of laboratory results, but many clinicians are unaware of these. For example, the reliability of information derived from a laboratory test may heavily depend on the quality of the analytical performance of the assay being used for the corresponding measurement. It is well demonstrated that the use of the more sensitive cardiac troponin instead of the traditional criteria for the diagnosis of myocardial infarction leads to an average increase in the number of infarcts diagnosed, from 20 to 30%, in patients admitted with suspected acute coronary syndrome. 26 However, the percentage of patients re-categorized from angina to myocardial infarction is also critically dependent on the performance of the troponin assay used.27 Since experimental data indicates that various commercial methods have significantly different sensitivities for detection of cardiac troponin in blood samples with very low concentrations of this biomarker, the selection of the troponin assay by the clinical laboratory represents one of the major factors influencing the clinical performance of this important biomarker. 28 Biological variation is frequently the most important source of variability in laboratory measurements. Knowledge of the biological variability is critical to understanding the significance of a laboratory result (Table 2). Recent studies have provided information on the biological variation of BNP and N-terminal proBNP, showing broad fluctuations of their concentrations in the blood of healthy subjects. 30 The critical difference for these markers has been calculated as being approximately 70- 90%. A demonstration of the possible influence of the physiological situation on the clinical value of laboratory tests can be derived from the behaviors of pancreatic amylase in infants and children. Due to the slow development and maturation of some functions of the exocrine pancreas, pancreatic amylase reaches adult concentrations only after the fifth year of life.32 As a consequence, the use of this enzyme for the diagnosis of acute pancreatitis in young children should be avoided and be replaced with the measurement of pancreatic lipase. Co-morbidities are also critical in test interpretation, as in the case of the influence of a reduction in the glomerular filtration rate on blood concentrations of C-telopeptide of type I collagen (CTx), a biomarker of bone resorption. 34 Thus, in patients with impaired renal function, measurement of serum CTx needs to be interpreted with great caution. In this type of patient, other serum markers of bone resorption, such as tartrate-resistant acid phosphatase 5b isoform, which is not influenced by renal function, should be considered. 35 It is clear from my personal experience that physicians are greatly confused by the amount of information and make many errors in the selection and interpretation of laboratory tests. audit on the reasons for the request of measurement of bone turnover markers in different clinical departments done in my hospital some years ago. Other authors have shown that the involvement of laboratory professionals in test selection and interpretation can significantly decrease the likelihood of some types of medical errors.

Promoting the Laboratory-Clinic Interface

The laboratory-clinic interface is, therefore, of fundamental importance to ensure that the patient is given high quality care, because it provides the boundary for the multidisciplinary activities which result in the improvement of the appropriateness of test requests and in the exchange of information on test results.36,37 use of reflex testing and algorithms; 2. Many examples demonstrate the effectiveness of reflex testing and algorithms for shortening the time of diagnosis and rationalising the use of laboratory testing. The most common example where a cascade of tests is performed based on an abnormal (frequently chance) biochemical finding, is in the case where monoclonal gammopathy is suspected. In this case, an abnormal band found on protein electrophoresis might trigger the performance of immunofixation and monoclonal protein quantitation to confirm the presence of this abnormality. Figure 2 shows another example related to an algorithm proposed for the interpretation of hyperamylasaemia.38 This work-up begins with the measurement of amylase in serum. A high value leads to reflexive testing for pancreatic lipase, followed by serum creatinine or isoamylase assays. The algorithm is able to determine, with a high degree of confidence, if the underlying pathophysiology is due to the presence of acute pancreatitis or of other causes of hyperamylasemia, such as extra-pancreatic abdominal disorders or renal insufficiency.38

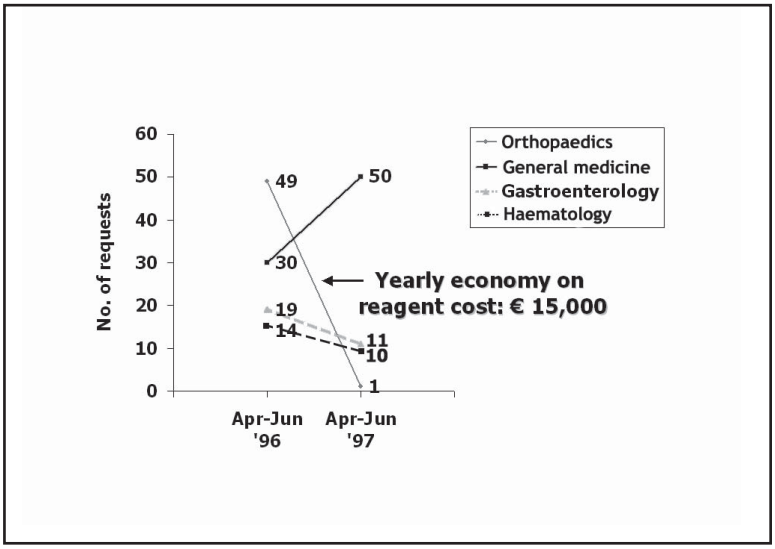

Figure 1. Results of an audit on the reasons of the request for measurement of bone turnover markers. Apr-Jun '96: numberof profiles before the introduction of the specific request; Apr-Jun '97: number of profiles after the introduction of the specific request.

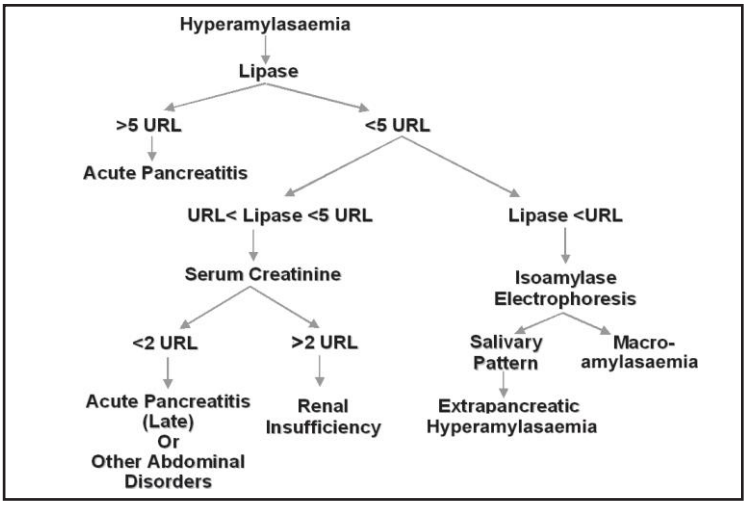

Figure 2. Proposed algorithm for the interpretation of hyperamylasemia. Adapted from ref. 38. URL, upper reference limit.

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II. CONCLUSIONS

Some years ago, presidents of European Societies of Laboratory Medicine were asked what they considered to be the most relevant issues for the future development of their profession.51 The implementation of request strategies, the diagnostic validation of tests and knowledge of test interpretation were indeed ranked as the most important issues. Today, the complexity of the health-care environment and the availability of an ever-expanding array of laboratory tests have further increased the need for more integration between clinical information and laboratory data.6 This is especially true in genetic testing, because it should be performed as an adjunct to the management of the individual and must be used in conjunction with the total information concerning the patient. The impact of the clinical laboratory on the medical environment of the future will be not only to maintain the highest quality generated data and to improve the total quality of the process of providing laboratory information, but also By integrating pathophysiologic rationale and preferences of the clinicians responsible for the care of the patient with valid and up- to-date clinical research evidence, Laboratory Medicine, supported by computerized information and expert systems, will promote the use of this new knowledge in a timely and responsible manner, contributing to the provision of better care more economically. As laboratory professionals, we will remain viable only if we build our own future and educate others about the contribution that Laboratory Medicine can and does make to health care.

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