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Review article
Pregledni članak

CHALLENGES OF LABORATORY MEDICINE: EUROPEAN ANSWERS

IZAZOVI LABORATORIJSKE MEDICINE: EVROPSKI ODGOVORI

Irena Korita[1], Victor Blaton[2]

[1]Laboratory Department, Faculty of Medicine, University Hospital Centre »Mother Teresa«, Tirana, Albania
[2]KU-Leuven and Department of Clinical Chemistry, Brugge, Belgium

Summary: Medical laboratories play a vital role in modern healthcare, and qualified specialists in Clinical Chemistry and Laboratory Medicine are essential for the provision of high-quality preanalytical, analytical and consultative services. Laboratory medicine has undergone major transformations during the last decade. Ongoing technological developments have considerably improved the productivity of clinical laboratories. Information on laboratory services is globally available, and clinical laboratories worldwide face international competition and there is a huge pressure to reduce costs. To be prepared for the future, clinical laboratories should enhance efficiency and reduce the cost increases by forming alliances and networks, consolidating, integrating or outsourcing, and more importantly create additional value by providing knowledge services related to *in vitro* diagnostics. Therefore, business models that increase efficiency such as horizontal and vertical integration are proposed, based on collaborative networks for the delivery of clinical laboratory services. Laboratories should cooperate, consolidate and form strategic alliances to enhance efficiency and reduce costs. There is a growing conflict between the science and the art of clinical practice and on the role of the biomedical sciences in medical practice. We have a dehumanizing effect on medical care. Disease is defined at the level of sick molecules and cells and curative medicine is being replaced by the preventive care of the disease. Undoubtedly all those questions will raise considerable problems and challenges for the medical educators.

Keywords: laboratory medicine, education and postgraduate training, core-curriculum, network, medical cost, patient care, health care

Kratak sadržaj: Medicinske laboratorije imaju veoma važnu ulogu u modernom zdravstvu, a pružanje visokokvalitetnih preanalitičkih, analitičkih i konsultantskih usluga zahteva kvalifikovane specijaliste kliničke hemije i laboratorijske medicine. Tokom poslednje decenije laboratorijska medicina pretrpela je važne transformacije. Produktivnost kliničkih laboratorija značajno je povećana zahvaljujući tekućem tehnološkom razvoju. Informacije o laboratorijskim uslugama su globalno dostupne i kliničke laboratorije se svuda suočavaju sa međunarodnom konkurencijom, pri čemu postoji ogroman pritisak da se snize troškovi. Kako bi spremno dočekale budućnost, kliničke laboratorije bi trebalo da poboljšaju efikasnost i snize rast troškova putem stvaranja saveza i mreža, konsolidacije, integracije ili angažovanja spoljnih saradnika i, što je još važnije, obezbede dodatne prihode pružanjem stručnih usluga vezanih za *in vitro* dijagnostiku. Otud se predlažu poslovni modeli koji poboljšavaju efikasnost, kao što je horizontalna i vertikalna integracija, zasnovani na kolaborativnim mrežama za pružanje usluga kliničkih laboratorija. Laboratorije treba da sarađuju, da se udružuju i formiraju strateške saveze kako bi popravile efikasnost i snizile troškove. Sve je veći konflikt između nauke i veštine kliničke prakse i kad je u pitanju uloga biomedicinskih nauka u medicinskoj praksi. Mi imamo dehumanizirajući uticaj na medicinsku negu. Bolest se danas definiše na nivou bolesnih molekula i ćelija. Kurativnu medicinu postepeno zamenjuje preventivna nega bolesti. Sva ta pitanja nesumnjivo doneti brojne probleme i izazove za edukatore u medicini.

Ključne reči: laboratorijska medicina, obrazovanje i postdiplomska obuka, kurikulum, mreža, medicinski troškovi, nega pacijenata, zdravstvo

Address for correspondence:

Prof Victor Blaton
Department of Clinical Chemistry
Az St Jan Av Ruddershove 10, 8000 Brugge (Be)
e-mail: victor.blaton@skynet.be

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Introduction

The mission of the Federation of European Societies of Clinical Chemistry and Laboratory Medicine (EFCC) is to support and promote clinical chemistry and laboratory medicine in Europe, to aid communication between the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) and National Scientific Societies, to develop education and quality in the discipline, and to encourage young scientists to take an active role in these activities (1).

Since the Tirana Balkan Meeting in 2005 there were several visits and many exchanges between the university of KU-Leuven, the Lab in Brugge, and the laboratory staff of ASoLaM (Albanian Society of Clinical Chemistry and Laboratory Medicine). After long discussions on so many points in Tirana – education and post-graduate training on external and internal quality control, evaluation of cardiovascular biomarkers, lipid and lipoprotein structure and metabolism, accreditations and total quality management, there was a need for further considerations and discussions on the future of the profession of laboratory medicine. There were so many presentations over the last 5 years that exchanges started on the »Challenges for Laboratory Medicine: answers from Europe« (2–5).

The main ongoing issues of laboratory medicine were discussed at the Department of Laboratory Medicine of the Center University Hospital of Tirana »Mother Teresa«. The capital Tirana (Albania) is a famous place with its old mosque and the Palace of Culture. A Belgian artist and project leader has been selected and accepted in a competition for the restoration and reorganisation of the centre of Tirana. Tirana, know in the world for the use of different colours in the restoration of houses and buildings, is also famous for its greenery, long warm seasons and nice surroundings – the Adriatic sea, the mountains and the lakes. The admiration for Albania grew fast and owing to so many visits inside the country, a strong link as to a second homeland was created. Extraordinary places in the country are well reknowned: the famous Berat, »the city of the thousand windows« declared a museum city, with the famous castle and the surrounding mountains creating peace and silence, keeps a lot of history. Besides Durres, Korca and many other places, the panoramic view of Shkodra in the north, a completely different part of Albania, is breathtaking. It is an ancient city, rich in cultural heritage, a place where you can meet poets, writers, men of science and other prominent Albanians. At the coast in Shkodra nature is preserved in complete originality.

Reflect the History

The opportunity to present this lecture on invitation by the President of the Scientific Committee of the 18th Meeting of the Balkan Clinical Laboratory Federation (BCLF) caused us to reflect back on our own career in Medical Biochemistry and medicine. We are impressed and astonished by one dominant and recurring theme – how a few good ideas and the power of science can radically transform the way we live. We have to reflect first on the history and the great issues for medicine realized in the 20th century before looking to the future. From the end of the sixties the exceptional progress in the last quarter of the 20th century started with four Nobel prizes awarded respectively for the genetic code (J. Watson and Fr. Crick, 1966), the LDL cell receptors (J. Goldstein and M. Brown, 1985), to the inventors of monoclonal antibodies (G. Koehler and C. Milstein, 1984) and for the polymerase chain reaction (K. Mullis, 1993), which is only the visible tip of a huge iceberg of innovation in the field. Without these techniques, immunoassays and methods of molecular genetic testing would simply have been impossible.

To predict the future, we have to remind ourselves of and learn from history. Before 1970 medicine was very primitive by today's standards (6). There were no calcium blockers or ACE inhibitors, no statines for cholesterol, no Prozac for depression and no vaccines against hepatitis and influenza. There were no bone marrow transplantations, no liver or heart transplants. Coronary bypass operations did not exist. There were no CAT scans or MRIs. Alzheimer was a very rare disorder. AIDS was unknown. The world in general and the world of medicine have been radically changed by the turns of events in the last quarter of the 20th century. Burgers, chips and genes and space technology are the exceptional ones.

The genius of the founder of the Big Mac was in addressing the need of the people who wanted to be served in 60 seconds by creating fast food restaurants and thus completely changing the way we live and introducing the metabolic syndrome worldwide, which is our first challenge for the 21th century in preventive medicine. Without microchips there were no car phones, no cash cards and no personal computers. The year 1966 was a turning point in the history of genes, when the genetic code was completely deciphered. In 1972 the recombinant technique was discovered. Our new power to manipulate genes had led to the knowledge of the complete DNA sequence of the human genome (2003). This is our second challenge, as genomic and proteomic testing are related to the prevention of the disease. Since the Moon landing »space research« has become a new department at the Faculty of Medicine, and several new aspects should be implemented in the coming years. Great scientific discoveries always lead to applications that benefit the society. But first of all, let us now focus on our specific profession, the laboratory medicine.

Laboratory Medicine: History and Roots

Only in the late 19th century they start practicing laboratory medicine, in Brugge, at St John Hospital, founded in the 9th century. In 1905 due to the appearance of Pest the Laboratory of Bacteriology was organized and an MD was nominated as chief of the Laboratory of Medicine. Our profession is a very young discipline in the diagnostic and therapeutic world of medicine. We also need to reflect on the historical roots of Laboratory Medicine to better understand our ongoing problems and to give a correct answer about the needs for the future.

During the first half of the 19th century attempts were made in various medical disciplines to answer medical questions using chemical methods. The basic idea was to describe a disease and its development objectively by chemical and physical examinations. Chemical symptoms were employed for the first time in describing diseases. Coagulation of urine proteins in kidney diseases was well used and is a good example.

The development of biochemistry as a new discipline was of great importance for clinical chemistry. In Germany the name »physiological chemistry« was used until after the Second World War. In Austria and Switzerland one said »medical chemistry«. In the USA one spoke at first of »biological chemistry«. Finally the name »biochemistry« was adopted everywhere (7). Great development in the second part of the 19th century was registered by the foundation of the »Zeitschrift für physiologische Chemie« in 1877. Germany was the leading expert in Europe and the world and the ongoing opinion was that German medical and surgical clinics were potentially institutes for experimental pathology where also intensive clinical chemistry research was carried out. Physicians remained very interested in research until the end of the 19th century. Folin's (1867–1934) work provided the basis of the modern approach to the quantitative analysis of blood and urine (8). He introduced colorimetry, turbidimetry and the use of color filters into quantitative clinical biochemistry. Folin pioneered the use of clinical chemistry in hospitals, clinics and life insurance laboratories. He brought clinical chemists into the Hospitals of USA. The spectrum of analytical methods available in clinical chemistry was greatly extended by the contribution of natural sciences, particularly from physics and physical chemistry. Prof Otto Folin created a centre at the Medical School of Harvard University for the graduate training of clinically oriented biochemists.

It was the USA, however, which provided the decisive breakthrough leading to the establishment of the modern discipline of clinical chemistry. The medical school reform, with the backwardness of American medical colleges in biomedical sciences, made possible the sudden success of biological chemistry in the 20th century. What is very important, the goal of the reform was to adapt medical school teaching to the concept of »scientific medicine«, creating »medical chemistry« (7, 9).

A unique situation in the development of modern clinical chemistry resulted from the work of Van Slyke at Rockefeller Institute New York in the capacity to develop ingenious methods and to apply them successfully to complicated medical problems (10). He was able to conduct the problem of diabetic acidosis by the use of chemical methods and he replaced the volumetric apparatus with manometric instruments, increasing the precision. This was the start and the foundation of modern clinical chemistry and its increasing specialization.

From the 1930s on and certainly later, after World War Two, there came a gradual replacement of the chemical analysis by physical and physicochemical measurement methods. There are various reasons for the increased use of instrumental analysis:

1. Physical and physicochemical methods are often more sensitive than methods for chemical analysis.

2. They are also simpler and quicker than chemical processes.

3. The industrialization of the methods and instruments took away the construction of the methods by the user and took over the manufacture and development of these instruments. Skeggs success in mechanizing analyses (Technicon Instruments) changed the way clinical chemistry laboratories work and determined in the last decade of the 20th century the progress and the growth of laboratory work (11).

Lessons from History

What we learned from history:

1. Creation of laboratory medicine was the answer to a fundamental need for medicine in that period to understand and to diagnose the human disease.

2. Great respect for the basic sciences, physics and chemistry and later biochemistry were the leading goals.

3. There was a deep interest in science in medicine, hospitals became the centres of knowledge building, medics were science oriented.

4. The reform of medical school teaching into »science oriented« education took place.

5. The mechanization of clinical chemistry laboratories work led to the growth and the enormous progress of clinical chemistry during the sixties and seventies.

Laboratory medicine has undergone major transformations during the last decade. Ongoing technological developments have considerably improved the productivity of clinical laboratories. Information on laboratory services is globally available, and clinical laboratories worldwide face international competition and there is a huge pressure to reduce costs in the prevention of the disease. As an example, the number of recognized laboratories over the last thirty years in Belgium decreased from 2200 in 1979 to 161 in 2008 and at the same time the budget increased by 100% over the last 10 years. There is an urgent need to control the budget on the medical programs and there is a gap between the technical possibilities and available financial resources.

Challenges for the Future

Medical laboratories play a vital role in modern healthcare, and qualified specialists in Clinical Chemistry and Laboratory Medicine are essential for the provision of high-quality preanalytical, analytical and consultative services. Ongoing technological developments have considerably improved the productivity of clinical laboratories.

To be prepared for the future, clinical laboratories should enhance efficiency and reduce the cost increases by forming alliances and networks, consolidating, integrating or outsourcing and, more importantly, create additional value by providing knowledge services related to *in vitro* diagnostics. Therefore business models that increase efficiency, such as horizontal and vertical integration, are proposed, based on collaborative networks for the delivery of clinical laboratory services. The advances in information technology and internet applications allow for efficient communication between collaborating laboratories. Unfortunately, several technological approaches to lowering the cost per assay have often been used to undermine the influence of laboratory professionals and to further isolate them from the clinical problems. However, the mostly economically-driven initiatives have the potential to distance laboratories from their clinical users and from their real roles of providing knowledge and consultative services related to the use of *in vitro* diagnostics (12).

Measuring the clinical and economic impact of laboratory practice and understanding testing-related outcomes are also key focus areas especially for governments and healthcare funding agencies. However, assessing clinical outcomes and value in relation to laboratory diagnostics is very difficult. In addition to solving diagnostic problems, clinical laboratories are more and more involved in assisting medical decision-making on the appropriate use of therapeutic interventions. Key objective for the future therefore remains to demonstrate the importance of Laboratory Medicine in the provision of effective healthcare. Every test has at least four sets of outcomes associated with it:

1. The consequences of the result, positive or negative or false,

2. The probability of the disease in the patient,

3. The changes in the patient health caused by the therapeutic steps on the basis of the test data,

4. In addition to diagnostic problems, clinical laboratories are increasingly involved in assisting therapeutic decisions.

To that end the profession needs to provide an interface between clinical and laboratory medicine and should be actively engaged in the development and dissemination of the results of high quality translational research and evidence-based medicine. Clinical audits and active discussion between clinical and laboratory medicine will contribute to the rational utilization of diagnostic services and will improve the quality, effectiveness and cost-effectiveness of healthcare (13).

Challenges for the Laboratory Professionals

If laboratory professionals merely focus on the analytical aspects, then their professional status will become marginalized when tests are largely outsourced. Currently, clinical pathologists focus mainly on the analytical, technical, organizational and managerial aspects and to a lesser extent on the clinical aspects. Test selection and interpretation of results remain very much the domain of the clinician (14). To be prepared for the future, clinical pathologists should redirect their thinking and engage in clinical value innovation and in translational research and develop tools that enable measuring and monitoring of the clinical value and impact of their services. Perhaps a new core competency of a clinical pathologist should be to improve patient care by providing complementary knowledge services related to diagnostic testing.

Laboratory professionals can differentiate themselves not only by their technical skills but also by being involved in the creation, distribution, and application of knowledge related to the laboratory aspects of patient care. Such extra service should be recognized and implemented in the business strategy (15).

The laboratory test menu has expanded rapidly, thus the complexity of the laboratory investigations has increased and clinicians will need more assistance in the use of new laboratory technology, as for genomic and proteomic testing. Lab professionals should optimize their professional relationship with the clinicians serving as clinicians consultants for test ordering and interpretation. The Academy recognizes medical consultancy as a key competency of the clinical pathologist. Still, care is advised so as not to overload clinicians with data.

Therefore the laboratory–clinic interface is of the utmost importance in ensuring that the patient receives high quality care. Three strategies have been recommended for supporting and disseminating clinical consultancy in laboratory medicine:

a) use of reflex testing

b) providing interpretative comments

c) organizing clinical audits.

Laboratory specialists must educate physicians to accept laboratory results as information describing a pathophysiological process, not a morphological diagnosis, while naturally sharing responsibility for ensuring that clinical information is reliable.

Appropriate use of cost-effective laboratory tests will become increasingly important. Intelligent decision support systems should assist clinicians in ordering and using laboratory tests appropriately and more efficiently. Introduction of an electronic decision support system for ordering laboratory tests in primary care resulted in cost savings.

Sackett defines evidence-based medicine as the »conscientious, explicit and judicious use of current best evidence in making decisions about the care of individual patients«. Laboratory professionals should play a major role in promoting the evidence-based approach to laboratory medicine (16).

Laboratory information system databases are powerful resources that can be exploited for clinical research particularly. Different IT systems within the hospital should be linked and shared databases installed. The link between the pharmacy and the lab system is a real positive outcome for the patient regarding the prescription of antibiotics.

Test development is very important and the staff members should participate in the development and field evaluations of new analytical devices of the tests. A network of collaborating clinicians should support such evaluations.

Table I Major recommended answers.

Focusing on new core competencies of the Clinical Pathologist.
Comprehensive consultative support to Clinicians.
Promoting the laboratory-clinic interface.
Use of reflex testing and providing interpretative comments, organizing clinical audits.
Research and innovation.

Research and education

In the second half of the 20th century, as clinical practice has become more and more reliant on the fruits of basic science and technology, the demarcation between the producers and dispensers has become less obvious. And with the rediscovered EBM, first popularized by the Paris school in the 18th century (1780), many practitioners have relied less on dogmas.

Over the last 20 years there has been a change in the emphasis of medical research. Rather than concentrating their efforts on patients or diseased organs, scientists are now focusing their attention on pathology at the level of cells and molecules. In the 21st century the diagnosis of disease predisposing genes will alter the basic practice of medicine. Perhaps in twenty years it will be possible to take DNA from newborns and analyse 50 or more genes for the allelic forms that can predispose the infant to many common diseases, cardiovascular, cancer, autoimmune or metabolic. For its defective gene there will be therapeutic regimes that will circumvent the limitation of the defective gene. Medicine will move from a reactive mode (cure patients already sick) to a preventative mode (keeping people well). Clinical Biologist needs to take part in the ongoing research in laboratory medicine and we need much more interest in clinical research (17–19).

There is growing conflict between the science and the art of clinical practice. We have to determine the role of the biomedical sciences in medical practice. The conflicting situation of the scientific basis of medicine and its day-to-day practice has to be solved and the dehumanizing effect on medical care demands our attention. The disease is now determined at the level of sick molecules and cells. Curative medicine is now replaced by the preventive care of the disease. Pressures of the marketplace economy increase every day. Undoubtedly all those questions will raise considerable problems and challenges for the medical educators of the future (20, 21).

One of the main problems and a great challenge for the future is education, the institution of intelligence centres, creation of IT centres (Intelligence Technologies), new ways of communication and education. Another message from the DNA era, and one that also has to be emphasized in medical education, is that the study of the human genes tells us that every body is unique and brings us to personalized medicine.

The problem is that we are not producing enough physician-scientists to take advantage of the enormous technological breakthroughs that the basic scientist is giving us. We need more individuals who conduct patient-oriented research; disease-oriented research is now flourishing as never before. We need in the future a new kind of education where individuals are trained in medicine as well as in science and bring the same creativity to the bedside that the basic scientist brings to the laboratory. In our profession there is an extreme need to study both medicine and science.

In conclusion I would like to refer to *Table I* were we summarized the major recommended answers to the discussed challenges for the future of the profession of Laboratory Medicine.

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Conflict of interest statement

The authors stated that there are no conflicts of interest regarding the publication of this article.

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