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REVIEW

Meeting the challenges of globalisation and miniaturisation in laboratory services

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Abstract

In the recent years, two trends emerged in the clinical laboratory: the miniaturisation of equipments to provide point-of-care testing (POCT) and a concentration of laboratories through mergers and acquisitions. New technology has expanded both opportunities. POCT provides the benefit of a convenient test where it is needed, i.e. near the patient. For companies, it is easier and cheaper to develop such tests, since technical requirements are somewhat less stringent, being an interesting area for start-ups. Nanotechnology is one of the most fascinating technical advances, with some advocating a US$1 trillion market-size for it by 2015. Laboratory tests and biomaterials will probably be greatly influenced by it, with new approaches for molecular diagnosis, with tests that can target both DNA and proteins in a process that eliminates PCR and allows multiplex analysis. On the other hand, there is a strong trend towards the globalisation of clinical laboratories and that occurs in four areas: a) Consumption of health services abroad; b) Movement of Health Personnel; c) Cross-Border delivery of trade; and d) Commercial presence. Each of these areas presents new challenges and opportunities for clinical laboratories, what will certainly shape the way we work today and in the future.

Keywords: miniaturization, nanomedicine, telemedicine, health services, International cooperation

INTRODUCTION

Laboratory medicine practice evolves somewhat differently than other medical specialties, due to its greater technological dependence and its commercial nature. Among the new factors that shape our profession are globalisation of laboratory services and miniaturisation of equipment. These factors have been recently discussed as the central theme of the 24th World Congress of Pathology and Laboratory Medicine, held in Kuala Lumpur, Malaysia, in 2007. It is important to understand these forces in order to be prepared for changing environments.

MINIATURISATION

Miniaturisation is a trend that became well-known due to the advancement of *point-of-care testing* (POCT) in the last decade.[1] POCT is the fastest growing area in a US$30 billion market, the in-vitro diagnostic (IVD) industry,[2] with an annual growth rate of over 15%.[3] POCT devices are attractive to manufacturers not only due to the economic perspective but also because these devices are somewhat simpler to develop, as they provide less analytical sensitivity and the cost per test is higher as an exchange for convenience. Another important aspect is that there is less competition with large diagnostic companies, and no need to have a full line of reagents since many devices are analyte-specific (eg. Glucosimeters, A1c measurement, etc) therefore it is easier for start-ups to enter this market.

Miniaturisation of devices is being further developed as nanomedicine evolves. *Nanomedicine* uses tools sized from one to a few hundred nanometers for the diagnosis, prevention and treatment of disease and to gain increased understanding on its pathophysiology.[4] Market specialists evaluate that nanotechnology will be a US$1 trillion market by 2015, and many groups have raised the question on focusing more

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on the economic aspect of nanomedicine, with multidisciplinary approach and more patents.[5-7] Nanotechnology presents a huge opportunity for POCT devices, since it enables greater analytical sensitivity and multiplexing of proteins and nucleic acids markers evaluation in the same assay.[8,9] In the last few years, many companies targeted their POCT initiatives to multi-parameter devices,[10,11] and the perspective of multiplexed analysis can make economic sense since with a greater availability of tests in a single equipment, it would be possible to address a major concern of POCT devices that is the maintenance of multiple devices.

Biosensors are devices that combine a diagnostic sensor with a transducer that enable real-time monitoring of several parameters, such as oxygen saturation, but in the near future they will be capable of detecting even molecular targets.[12] Potentially, sensors could detect environmental hazards both in military (e.g. toxins, bacteria) and occupational settings (e.g. mercury vapours).

There are several ways nanomedicine can improve quality of laboratory medicine, such as improved detection of predisposition, better disease characterization, identification of new targets for therapy and therapy selection, monitoring disease progression and response to therapy.[13,14] It is likely that many diagnostic applications will rely on the analysis of multiple targets simultaneously and this trend already started.[15-17] Nanotechnologies and other approaches to detect gene or protein profiles are becoming available and challenging current reimbursement practices in many parts of the world, as physicians increasingly ask for these tests.[18] Clearly, these new multianalyte tests will also require greater test validation and physician education, but there is great expectation that these tests will reach the market soon.[19] Nanomedicine will likely be used also for treatment purposes, since with nanorobots it is possible to improve drug delivery,[20,21] to perform gene-based immunotherapy[22] and even tissue repair.[23]

Personal sensor technologies that enable patients to monitor a high-risk situation, such as breast or colon cancer, in their homes, are another possibility for the future. Breast cancer could be monitored using a shower with thermal scanning capabilities that allows detection of small nodules and serially evaluates the data on breast temperature and nodule size, and colon cancer could be detected by (occult) blood (or other substances) evaluation in the toilet. Prompt detection of diseases in high-risk groups, could lead to less aggressive and less expensive therapeutics. Emotional and psychological issues are to be discussed when technology proves its feasibility.

An interesting technology that is under research is the *electronic nose* (e-nose). A set of sensors made from various polymers can be trained to identify certain substances, in a variety of applications such as detection of volatile organic compounds in the air,[24] detection of tumour cells[25] and bacteria classification in ear-nose-and-throat infections.[26] E-nose reminds us that good use of technology often makes us appreciate the history of medicine even more, since early physicians both in the east and the west relied on smelling their patients' breath and secretions.

Increased availability of micro-sensors will widen the possible applications of *telemedicine*. Currently, there are commercially available devices that can measure blood pressure, glucose, INR and many more laboratory parameters integrated with question-based algorithms and even video at the patient home, delivered to a health-care provider through the internet. This is likely to evolve as technology makes them cheaper and we have independent evidence of good cost-benefit. Laboratories should identify this as a potential growth-area that could be controlled by a central laboratory, since it essentially involves QC, managing critical alerts and contacting physicians. The evolving near-patient testing industry and the potential for lowering the actual price-per-test of POCT may dominate great part of routine testing and radically transform the laboratory industry to a platform for esoteric testing and an intelligent medical data management centre.[27]

GLOBALISATION OF MEDICAL SERVICES

Laboratories are also facing challenges due to the globalisation of medical services. These include new threats that spread rapidly (e.g. SARS), changes in lifestyle and epidemiology of diseases (e.g. obesity, alcohol and tobacco consumption), microbial resistance due to difficult control of internet pharmacies and changes in global trade.[28,29] According to Dr. Chanda,[30] from the World Health Organization, there are 4 types of global trade:

Consumption of health services abroad
Consumers move to countries providing diagnosis and treatment, usually seeking specialized healthcare, lower prices and easier access to medications. This can be exemplified by the growing popularization of plastic surgery in Brazil, treatment of skin diseases in Cuba (with more than 25million US dollars annually, from foreign patients) and many treatments in India.[31] Laboratory demand usually "tag-along" with other specialties, mostly with pre-operatory and follow-up tests. This provides additional revenues for countries and acts as a buffer for professional-shortages. One risk is the creation of a two-tier system, with resource-constrained medical services for the poor and a distinct service for wealthy nationals and foreigners.

Movement of health personnel
There are both temporary and permanent flows, for training and seeking better work conditions and salaries. The major flow (56%) is from developing countries to developed ones. This is a challenging problem in certain areas, like Zimbabwe and Lithuania**,** where a great exodus of health care professionals took place.[32,33] Laboratory societies and governments should try to develop international guidelines on professional standards, immigration and licensing of professionals, as well as recommendations on working conditions for resource-poor countries, but most likely an economic aid will be necessary.[34,35]

Cross-border delivery of trade
This includes shipment of laboratory samples and telemedicine, areas well-known to many services. Performing esoteric tests is benefited for the economies of scale, and even international shipping of specimens can make sense for some tests. Second-opinions and consultations can be greatly facilitated by telemedicine technologies, what can improve the capitalization of expertise that can be seen as a source of income, diminishing medical errors and insurance costs.[36,37] This can be very difficult in some countries, however, due to poor infra-structure.[38] It is important to notice that although many African countries lack proper internet infra-structure, cell phones are advancing at greater pace in Africa than in many emergent markets. In order to enable telemedicine efforts in these countries, there is a need to understand the available infra-structure and adapt or change the telemedicine technology, but if the aim is to spread e-health initiatives beyond medical facilities, improving education and other actions will probably be necessary as well.[39,40]

Commercial presence
The establishment of laboratories in other countries has been commonplace in recent years, and even the US has been challenged by this.[41] Large test volumes are accompanied by greater economies of scale, especially in the highly automated and in the least requested tests. In Brazil, only 70 types of tests are associated with 90-95% of all laboratory volume (Rosenfeld LG, unpublished data). Larger laboratories achieve great economy when performing low-frequency tests (approximately 430 types of tests that account for an additional 4.5% of all tests). Esoteric testing (thousands of types of tests that account for only 0.5% of laboratory volume) are economically challenging, since there are huge costs involved (test development, setup, QC, etc) for a very small number of tests performed.[42,43]

Globalisation of medical services raises important concerns, for laboratories and countries alike. To date, there is no international regulation on privacy of information, for example. Patient data could be used for a myriad of purposes, from marketing to the development of ethnic-oriented gene-based therapies (or threats). Medical dependence is a critical problem in times of war. Insensitivity to local cultures and aggressive commercial behaviour in poor countries, leading to further impoverishment are other frequently raised problems.[44,45] The benefits of globalisation should be balanced with the potential perils in each country, and adequate legal measures should be taken proactively.

The changing environment for laboratories indicates that there is a trend towards greater laboratory utilization worldwide, mostly due to greater access to services, the availability of new markers and new technologies. Laboratory consolidation through mergers and acquisitions in a globalised world presents challenging perspectives in the nearer-term whereas novel nanotechnology devices may provide better cost-effectiveness in near-patient testing and a greater challenge to laboratories in the future. Successful labs will learn how to keep an eye on the market, regarding test utilization, prices and location; will learn how to best use capital for investments, transforming processes using automation and new management principles, such

as lean six-sigma, for continuous cost-reduction. Certification of quality and accreditation will continue to be seen as important factors to success. Probably a major transformation will be that laboratories will ultimately move from producing data for producing knowledge.

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