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Opinion: redefining the role of the physician in laboratory medicine in the context of emerging technologies, personalised medicine and patient autonomy ('4P medicine')

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ABSTRACT

The role of clinical pathologists or laboratory-based physicians is being challenged on several fronts—exponential advances in technology, increasing patient autonomy exercised in the right to directly request tests and the use of non-medical specialists as substitutes. In response, clinical pathologists have focused their energies on the pre-analytical and postanalytical phases of Laboratory Medicine thus emphasising their essential role in individualised medical interpretation of complex laboratory results. Across the European Union, the role of medical doctors is enshrined in the Medical Act. This paper highlights the relevance of this act to patient welfare and the need to strengthen training programmes to prevent an erosion in the quality of Laboratory Medicine provided to patients and their physicians.

INTRODUCTION

The wide-ranging responsibilities of physicians in Laboratory Medicine have been recently defined in an European position paper.¹ In these introductory paragraphs, we discuss selected examples to highlight the changing role of doctors in medical laboratories.

In the constant quest to develop new laboratory biomarkers, it is essential to provide robust evidence of how this leads to improved clinical outcomes.² The evaluation of the medical value of these biomarkers is complex and is highly dependent on the medical context.³ In many countries, such an evaluation includes the assessment of clinical outcome studies in diagnostic assessment programmes.^{4,5} However, country-specific differences exist for the utilisation of a given test, for example, in terms of indication and frequency of use. Some of these country-specific differences may depend on the expertise of those providing the Laboratory Medicine input. Absence of such expertise may lead to inappropriate recommendations as evidenced by UK guidelines recommending the use of faecal occult blood tests in symptomatic patients with suspected colonic cancer.⁶

Several processes are now well embedded in Laboratory Medicine to ensure provision of reliable and timely test results, thus enhancing quality of care and patient safety. In recent decades, the

standardisation and harmonisation of methods and reference intervals, test names and laboratory practices⁷ as well as of pre-analytical quality indicators⁸ in Laboratory Medicine have been core activities of the International Federation of Clinical Chemistry and Laboratory Medicine and the national societies for Laboratory Medicine. This is also reflected by the recent introduction of the In Vitro Diagnostic (IVD) Regulation directive from the European Union (EU) which requires rigorous external oversight of evidence, as in the USA, before the introduction of IVD tests. There is a similar view that harmonisation can also be achieved for individuals working in medical laboratories⁹ and that voluntary technical standards developed to facilitate world trade such as International Organisation for Standardisation (ISO) norms can be used for this purpose. However, ISO standards focus on processes and do not assess clinical outcomes.

The patients' well-being is the primary focus of all procedures performed in healthcare such that, by implication, healthcare is different from trade and other services. Specific ethical guidelines from the World Medical Association ('Declaration of Geneva') and the complex network of EU and national legislation regulate healthcare issues.

To safeguard patients, national, federal and regional legislation restrict the practice of medicine to (licensed) physicians. Such physicians generally must have, as a minimum, a medical degree from a medical school/university on the World Directory of Medical Schools, previously established by the WHO and now as a joint venture between the World Federation for Medical Education (which also sets standards and accredits) and the Foundation for Advancement of International Medical Education and Research. Inclusion on the directory means that each medical school will have provided medical students with the minimum required time period (5500 hours in the EU¹⁰) of theoretical and practical training in a structured, supervised, standardised programme with appropriate professional assessments to provide assurance that the doctor has acquired the required knowledge and skills. National laws may also restrict the bodies that can hold qualifying examinations, for example, in the UK.¹¹ In addition, EU law requires that each country has a minimum compulsory period of



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structured and supervised training (internship) before a basic license to practice is issued, in addition to a rigorous programme of postgraduate training before certification as a specialist.¹⁰ In most countries, the activities requiring physician competencies (as stated in the Medical Act¹²) include all aspects of the investigation, diagnosis and management of illness.¹³ As such activities are restricted to physicians, this means that they are clearly responsible for the consequences of such activities. This definition of the Medical Act is currently challenged by the move to delegate some well-defined procedures to other professions (mainly due to financial constraints or a shortage of skilled professionals).

THE RELEVANCE OF THE MEDICAL ACT TO THE DIAGNOSTIC LABORATORY AND NEW TECHNOLOGIES

In Laboratory Medicine (clinical pathology), complex processes in a medical laboratory can be dissected into many small segments starting from the request form or electronic order for obtaining the patient's sample up to the issuing of the medical report and discussion about how these results might influence patient management. It is obvious that many of these small segments can be performed by persons who are trained for individual specific tasks, irrespective of their educational background. This situation is like the division of work in an operating theatre between physicians (surgeons and anaesthetists), nursing staff, semiskilled healthcare workers and trainees, where nobody would question that the whole process of surgery requires rigorous medical training as enshrined in the Medical Act. It is indisputable that safe medical practice requires a solid grounding in the basic sciences underpinning clinical medicine coupled with knowledge and experience of disease states. All of these attributes are relevant to physicians in Laboratory Medicine in addition to active engagement in research, development and innovation.¹⁴

Ideally, the patient's well-being should be explicitly stated within this definition independent of financial resources and the availability of pathology services. However, there are differences in how healthcare has evolved between different nations, federations and regions. Harmonisation in healthcare such as the delegation of subtasks to certain professions should consider such differences in the healthcare systems between countries. Laboratory physicians work in collaboration with other personnel at the laboratory who are responsible for patient hospitality, sample collection, pre-analytical, and postanalytical and analytical phases of sample management and provide their medical expertise to the whole process. Reliable laboratory results are the result of complementary interaction between physicians and non-medical biomedical scientists/technologists in the medical laboratory. Heterogeneity and cost constraints in healthcare systems in different countries result in differences in the role of these professions.⁹ However, in many countries, it is the clinical pathologist who carries ultimate responsibility for provision of a high-quality service, with some countries legally mandating this.

In recent decades, technological advances have transformed virtually all fields of medical practice, bringing with it an important role for scientists, physician assistants and IT specialists. These developments contrast with the historic context of the Medical Act with its pre-eminent role for physicians responsible around the clock for patients with very little assistance from co-workers.¹³

These changes in the perception of medicine as a vocation to that of a commodity are also calling into question the Medical Act, notably challenging the grey zone between qualified and non-qualified practitioners from a medical perspective. Why

should the patient see a physician to get an ultrasound when they can go to a physician assistant trained specifically in sonography? Why should the patient see a radiologist to get a CT scan when a radiographer can perform and email the image files for interpretation to a call centre somewhere else in the world? Why should the patient see a cardiologist when the smart watch ('wearable') or the smart phone automatically interprets his or her ECG? It is without doubt that some simple, brief and clearly defined processes of the Medical Act such as performing routine vaccinations, administering certain drugs (eg, analgesics for headaches) or taking the blood pressure can be delegated and even substituted by non-physician professionals. The delegation of these Medical Acts poses only a very limited risk for the patient once proper processes to ensure oversight are in place; as a result, the employer's liability insurance will usually cover the risk of the non-physician healthcare professionals. Directive 2001/24/EU of the European Parliament and of the Council of 9 March 2011 on the application of patients' rights in cross-border healthcare states 'systems of professional liability insurance, or a guarantee or similar arrangement that is equivalent or essentially comparable as regards its purpose and which is appropriate to the nature and the extent of the risk, are in place for treatment provided on its territory'. As a result of this, all UK state registered professional groups must have indemnity insurance though some state registered professional groups have had difficulty in obtaining such indemnity insurance for private practice independent of physicians or hospitals with physicians.¹⁵

The relevance of the Medical Act in clinical pathology is particularly challenged by these new developments. The situation gets even more complicated since the complexity and the volume of testing differs markedly between laboratories. While the level of direct intervention by the clinical pathologists in many cases is not as prominent as in the example of surgery and the personal contact between clinical pathologist and patients in most cases is indirect and often invisible to the patient; nonetheless, laboratory physicians play an important role in improving clinical outcomes for individual patients¹⁶ (box).

Developments in IVD marketing have led to direct selling to physicians and also to consumers (direct-to-consumer testing, DTC).¹⁷ As a result, IVD diagnostics could potentially be performed by non-qualified practitioners or even by lay persons in the future if there are no regulations concerning the professional qualification of staff employed by laboratories. The patient could just submit his sample to any laboratory for testing. Consequently, in some laboratories, Laboratory Medicine would no longer be a part of healthcare as we know it. The medical aspects of oversight and interpretation would be removed and only an analytical service would remain. The most prominent example of DTC was Therasano, a company that tried to revolutionise the US market for Laboratory Medicine by testing capillary samples drawn in the neighbourhood pharmacy and transmitting the test results directly to the patient.¹⁸ It is worth noting that Therasano received sanctions from the Centers for Medicare and Medicaid Services in July 2016 including the revocation of its Clinical Laboratory Improvement Amendments certificate and prohibition of the owners and operators from owning or operating a laboratory for 2 years for multiple deficiencies, including producing inaccurate results.¹⁹ While some believe that the regulatory framework is too lax in the USA,²⁰ it is noteworthy that some countries such as the UK have no specific laws or regulations governing the ownership of a laboratory (with the exception of blood transfusion and embryology), requiring only registration with the devolved national independent regulator of health and social care services.

Box Examples of laboratory testing requiring supervision by a physician in Laboratory Medicine

International normalised ratio (INR) self-testing

INR self-testing must be under the supervision of physicians, directly or indirectly. The reason for this is that patients must have an access to a physician for medical advice for the dosing of their anticoagulants. Drug prescription and dosing adjustment is a Medical Act and requires a medical license. In many countries, the monitoring of patients on therapy with oral anticoagulants is done by clinical pathologists since it entails some knowledge of Laboratory Medicine and prescribing. However, it can be performed by general practitioners, but this is usually done with laboratory support in view of the associated difficulty of assuring the quality of the analyser.

The reporting of complex laboratory tests

Complex analyses that can have significant therapeutic consequences associated with interpretation require medical interpretation and are also examples of the Medical Act. Additional examples include reporting of monoclonal gammopathy, autoimmune profiles, therapeutic drug monitoring, toxicology analyses, dynamic stimulation and suppression testing, prenatal and newborn screening, and intraoperative testing.

Blood coagulation

Testing and test interpretation is complex and includes careful assessment of the medical history, drug treatment, pre-analytical and analytical factors, mixing studies and additional tests of biomarkers. The laboratory testing of patients with suspected coagulation disorders requires specialist expertise and should be performed in conjunction with specialists in internal medicine and haematology. The situation is similar in other areas such as medical genetics, endocrinology and specialised haematology (eg, haemoglobin variants).

Assessing medical necessity

Medical doctors have the legal obligation to offer the medical services necessary for their patients (*primum non nocere, secundum cavere, tertium sanare*) and accordingly clinical pathologists are part of the critical infrastructure of a national healthcare system. On the other hand, laboratories are contacted by in vitro diagnostic (IVD) companies who want to sell their instruments and tests. Clinical pathologists will choose tests by their clinical relevance, reliability and robustness. Cost-effectiveness is evaluated as well, but it is not a dominating factor for the decision. Clinical pathologists can assess the need for new biomarker and can prioritise the development of biomarkers in the academic and commercial setting.

When biomarker testing is moved out of healthcare and laboratory testing becomes a commodity, the rules of the marketplace will remove costly but medically important tests from the laboratories. This effect can already be seen when certain tests, such as certain coagulation tests or previously intraoperative (PTH) assays, were not or are not performed by for-profit laboratories in some countries.

Establishing clinically relevant cut-offs

With the advent of electronic patient records ('e-health'), standardisation of testing including common reference intervals is of special interest. The selection of tests and the directory of services ('Laboratory book') is a continuous task of the clinical pathologist. It contains information on each analysis including medical indications for the test, reference and/or decision intervals, a guideline how to interpret the results and clinical cut-offs. Writing and updating the Laboratory User Handbook is a Medical Act, which includes selection of the appropriate test including the removal of archaic tests from the scope of the laboratory and the introduction of newer tests, setting clinically relevant cut-offs and establishing guidelines how to interpret the laboratory results.

One might argue that these guidelines can be written by national committees. However, often methods are so different that clinical decision limits of certain tests are highly method dependent (eg, many endocrine tests are prone to cross reactivity,⁴¹ calibrators are not commutable or assays are not harmonised or standardised). Even when the test behaviour is similar in one patient group, good medical knowledge is needed when the test used in other patient groups (such as in stimulation tests or hormone replacement therapy) to provide medical decisions for a given test result.

Verification of methods: a medical evaluation

In most countries, only laboratory tests with a proven medical use should be used. Therefore, the usage of the test by the attending physician should be medically assessed by the clinical pathologist. Typical challenges include tests being used for medical applications in which the expected serum concentration is below the level of detection of the assay (such as with some methotrexate assays despite being Conformité Européenne (CE) marked for clinical use or in continuous aminoglycoside infusion for gentamicin) or when changes of the tests results cannot be detected due to low performance of the test (eg, many complement-binding assays or prostate-specific antigen (PSA)⁴²) or a long half-life of the biomarker such a procalcitonin to assess efficacy of antibiotic treatment.

Evaluation of the laboratory errors: a medical act

Internal quality controls are used as tools to monitor the bias and precision of the operational process. There is extensive knowledge about the biostatistical caveats of analysing quality control data, in regard of false-negative and false-positive results and biomedical analysts as well as other laboratory professionals are trained to analyse internal quality control data.

However, if a laboratory internal quality control error occurs, the medical consequences (clinical importance) of the error should be assessed in an appropriate time period by the clinical pathologist as part of the Medical Act. For example, if there is a bias that is medically significant, the results in question should ideally be voided and the samples reanalysed. If there is no clinical consequence of this failure ('false alarm'), there is little benefit in informing the requesting physician and/or the patient. However, in each case, an appropriately competent individual is required to take responsibility for the situation. Assessing the medical consequences is a challenge in high-volume tests in which both decreased and increased values can have medical consequences, be they for individuals or for a population, for example, thyroid-stimulating hormone (TSH), glucose, HbA1c or INR. The default situation of informing all requesters and patients because there is no individual available who is competent to make the medical decision is not appropriate as it will inappropriately add to the anxiety of many patients.

Continued

Setting up and updating rules autovalidation rules

IT-based rules are increasingly used in Laboratory Medicine to improve turnaround times (autovalidation), to detect results that have significantly changed from the previous result (delta checks) and to stop impossible results being released by the laboratory information system. Such rules require a thorough knowledge of human physiology and pathophysiology to ensure patient safety. Accordingly, only those with such knowledge can take responsibility for the setting up and improvement of such rules. It would be professional negligence if medically implausible test results were released to the medical record. Particular challenges to the use of such IT rules occur in endocrinology, for example, thyroid-related tests due to the combination and permutation of the potential tests, the variety of the clinical conditions associated with abnormalities and the variety of associated treatment, immunoassays interferences (human anti-mouse antibodies, heterophilic antibodies, rheumatoid factor and so forth) or the effect of daratumumab treatment on interpretation of blood transfusion serology.⁴³

This argument, however, focuses only on a few selected aspects of analytics and does not consider the whole complex process associated with IVDs. This whole in vitro testing process has been aptly conceptualised as the ‘brain-to-brain loop’²¹: this loop covers the entire process from obtaining the patient’s sample to selection of appropriate test(s) and through to the analytical and postanalytical processes, including interpretation, which then contributes to patient management—all key elements described in the Medical Act. In addition, there are legal issues which prohibit delegation of certain tasks in clinical pathology to non-qualified practitioners or lay persons: blood transfusion, genetic testing²² and investigation of contagious diseases in most countries are restricted to physicians only and certain diagnostic kits can only be obtained by a physician’s prescription.

The consequences highlighted here of unfettered marketing of IVD have parallels with indiscriminate testing across medicine. By their training, physicians in Laboratory Medicine are well placed to address these issues by ensuring provision of appropriate test repertoires, guiding test selection and audit, thus ensuring cost-effective use of finite resources.^{23–25}

PERSONALISED MEDICINE AND PATIENT AUTONOMY

Closely related to DTC testing are proposed initiatives from the EU legislation to empower patients by direct transmission of results. This is done in the context of P3 medicine (predictive, personalised, preventive), a concept, however, which to date has had only limited success. Extension of this view to include active participation of the patient would lead to the concept of P4 medicine (predictive, personalised, preventive, participatory), which is likely to have a greater chance of success. It also lends itself to salutogenesis, an approach focusing on factors that support human health and well-being, rather than on factors that cause disease.^{26 27} The concept of P4 medicine heavily relies on technology, big data and on social networks for commenting on the data of consumers (the word patient is avoided intentionally) by peers in the general public. An immediate challenge to conventional thinking is the difference between classical laboratory medicine which could be called decision diagnostics (figure 1) and the concept of big data which focuses heavily on statistical associations. The imminent danger of false interpretation of health data is obvious. The P4 medicine concept is based on the idea that the patient collects his data in a data cloud to be used effectively to optimise wellness and minimise disease.²⁶ The consumer/patient is not left alone, without professional help. Supporters of P4 medicine see a strong requirement for trusted interpreters of these data clouds for each patient,²⁶ in regard to laboratory testing and the correct interpretation of IVD results. This interpretation should ideally be done soon after the analytical step since the release of raw analytical data (ie, the

uninterpreted test results) may pose a risk to some patients²⁸: for a very limited number of tests such as blood glucose in diabetics with self-monitoring²⁹ or luteinising hormone-based ovulation tests—classical DTC, the interpretation of laboratory results can be done by patients themselves. However, for most tests, medical interpretation should ideally be done either by a physician such as the clinical pathologist (especially for more complex laboratory tests) or, for basic tests, by the attending physician (figure 1) rather than by individuals without appropriate training such as a ‘healthcare and wellness’ coach.^{26 28–31}

FOCUS ON MEDICAL INTERPRETATION INSTEAD OF ANALYTICAL EVALUATION

With the exception of very few tests mentioned above, it is obvious that all other tests need medical interpretation, both in patients and in consumers.²⁸ Medical interpretation goes far beyond flagging up a result outside defined reference ranges and, as a part of the Medical Act, should be done by a physician.¹ In the ideal world, this physician should know the limits of the analytical phase (ie, the testing process) and should be experienced in the consequences of a certain test result, in the context of other diseases, certain therapies and in the clinical course of the disease. It is debatable whether this task is better done by a medical laboratory specialist who subspecialises in certain areas

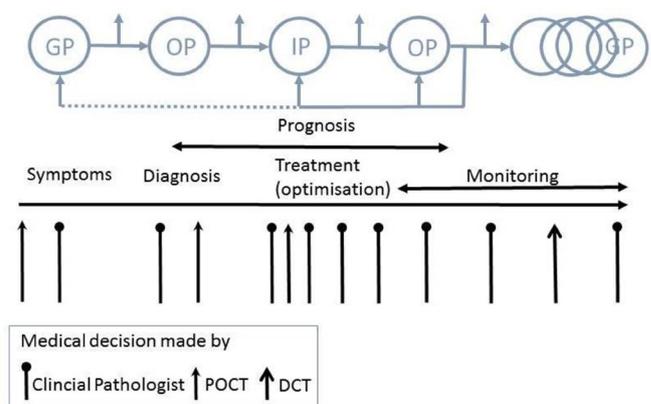


Figure 1 Laboratory testing is pivotal at numerous time points during a single patient episode. The laboratory reports of clinical pathologists of (mostly) panels of laboratory tests as well as the results of single tests in point of care testing (POCT) and direct-to-consumer testing (DTC) are used for necessary medical decisions by the general practitioner (GP) as well as from the outpatient (OP) and inpatient department (IP) of the hospital. The patient-specific selection of the best suited biomarker as well as the medical interpretation of the test results relies heavily on medical knowledge.

of clinical pathology (such as endocrinology or blood coagulation) or by a generalist covering all subjects of *in vitro* testing (ie, haematology, clinical chemistry, immunology, laboratory genetics and often microbiology).¹ In our experience, depending on the local situation both specialists and generalists can give adequate advice to requesting physicians and patients. From the patient's perspective, proliferation of subspecialties in clinical pathology could potentially be confusing in contrast to having unified advice from a generalist. In certain situations, however, in particular in very complex patients, the expertise of two or even more laboratory specialists is likely to be in the best interests of such patients. It is not unusual for specialist clinical scientists and biomedical scientists/technologists to participate in clinical rounds and share their advice, like nurse consultants or pharmacist consultants. In hospitals with clinical rounds, there is a long tradition of sharing knowledge between different professions with mutual respect. However, in these clinical rounds, the final responsibility as envisaged in the Medical Act for integrating advice given by non-medical specialists and consequent management decisions remains with the attending physician.

The biggest evolution in the laboratory over recent decades has occurred in the supply of robust tests, technologies and instruments: huge improvements in instrument design together with the successful standardisation of reagents and instruments allow IVD companies to offer nearly perfect diagnostic systems for most areas of the clinical laboratory. Because of these rigorous improvements in the analytical process, many technical chores such as the preparation of reagents or tedious adjustments of instruments regularly performed in the laboratories in the past have been transferred to the IVD companies. With the widespread use of CE-marked or equivalent reagents, problems associated with assay verification are less frequent than previously. In addition, a wide array of improvements in the pre-analytical processes (such as electronic orders, diagnostic pathways, barcode coding of primary samples, robot-assisted aliquoting, permanent temperature control of reagents and samples, automatic checks for clots, haemolysis, lipaemia and icterus),⁸ analytical processes (in particular by using highly standardised techniques with low intra-assay and inter-assay variation) and postanalytical processes (such as autovalidation and sending reports electronically directly in the health record) have occurred in the last years.³² These improvements enable clinical pathologists to spend less time with analytical processes and assign most of their time to being a partner to treating physicians (and to patients) for selecting and interpreting laboratory tests and advising on appropriate therapies. Extensive practical and theoretical medical expertise is essential for these tasks, which is reflected in recent modifications to the curricula for clinical pathology in different European countries, with a special focus on medical knowledge and practical experience, in particular in Internal Medicine and laboratory management skills rather than on analytical techniques.³³

PATIENT VERSUS CUSTOMER

Justifiable moves to empower patients have led to a change in the dynamics of the doctor–patient relationship, with the patient frequently being regarded as a consumer. This has led to the promotion of inexpensive appliances such as smart watches and fitness trackers (wearables) capable of monitoring physiological data previously only accessible by sophisticated medical equipment under medical supervision. The overall value of these wearables is currently under intense discussion. Notwithstanding possible benefits in the context of P4 medicine, self-monitoring

contains the risk of potential harm.³⁴ For example, in diabetics, intense self-monitoring has been shown to increase depressive symptoms.³⁵ In addition, sophisticated regulations safeguard the patient but not the customer. In general, the patient–physician (such as a clinical pathologist) relationship is based on trust. For example, the patient can rely on very high levels of data protection regulated by the declaration of Geneva. On the contrary, the relation between a customer and a vendor (such as the vendor of DTC tests) is markedly influenced by competition, the law of the marketplace and even the interests of others, such as buyers of consumers' health data ('big data').^{26,36} In this context, consumer rights are often used as false pretences to eliminate essential barriers currently present in healthcare. Instead, many perceived or apparent restrictions of trade may be necessary to guarantee quality and competence. For example, one important aspect of healthcare performed by clinical pathologists is the obligation to use only tests with proven medical value,^{2,37} in contrast to the many unvalidated lifestyle tests that are offered to customers (quackery) without regulatory control.

DIRECT ACCESS OF PATIENTS TO BIOANALYTICAL SPECIALISTS (NON-MEDICAL LABORATORY SPECIALISTS)

In the interests of empowerment, it has been proposed that patients should be able to obtain laboratory test results directly without the involvement of physicians, with efforts to allow non-medical laboratory specialists direct access to patients in the outpatient setting.³⁰ However, offering patients bald numerical values without appropriate individualised clinical interpretation of results is counterproductive and could be considered to be unethical.^{28,38} In this setting, the patient's safety would rely primarily on the medical knowledge and medical skills of the non-medical laboratory specialist, an obvious oxymoron. The safeguards to patients of the Medical Act are further compromised when considering the type of clinical sample for analysis. Except for saliva and urine testing, potentially risky and or invasive sampling (like phlebotomy, bone marrow aspiration or a spinal tap) precedes the testing process. For this reason, most countries stipulate that clinical samples for analysis should only be performed by a physician or under a physician's supervision.

SUBSTITUTION OF CLINICAL PATHOLOGISTS BY BIOANALYTICAL SPECIALISTS

If fundamental elements of the Medical Act in Laboratory Medicine to be carried out by non-clinical pathologists,³⁰ then a rigorous system of standardised, supervised and structured training complemented by formative and summative assessment of competencies would be required to ensure patient safety. In fact, the possibility of clinical training for non-medical laboratory specialists is under intense discussion. To overcome the current lack of necessary knowledge and skills in non-medical specialists in the pre-analytical and postanalytical phases, a separate graduate programme for Laboratory Medicine might be an option, like the brief human medicine curriculum taught in dentistry to provide assurance that the required theoretical and practical skills have been obtained. However, unlike with dentistry which has a limited interface with medicine, Laboratory Medicine is integrally involved in decision-making across Internal Medicine and related subspecialties. For a non-medical specialist to be accepted as an equal peer by other physicians, the clinical training should be at a similar level of competence as that obtained by physicians in Laboratory Medicine. The challenges of doing so should not be underestimated given the statutory length of undergraduate and postgraduate training required for

attaining competence by specialists in Laboratory Medicine in the EU.¹⁰

In a multifaceted and innovative specialty such as clinical pathology, continuing professional development (CPD) or continuing medical education (CME) is a crucial plank of patient well-being: physicians are obliged to participate successfully in life-long learning CPD-CME programmes both to ensure high standards and their fitness to practice in medicine. These unique CPD-CME programmes are well structured with standards in regard of content (both covering clinical leadership and specialty knowledge) and conflict of interest.³⁹

In some countries, participation in an appropriate and accredited scheme is a legal requirement for registered doctors,⁴⁰ including physicians in Laboratory Medicine, with statutory consequences for those who fail to comply. While this requirement for mandatory participation is not universal for non-medically trained laboratory specialists, it is clear that the trend is definitely in this direction.

Therefore, current efforts to develop curricula for non-medical laboratory specialists should take into account the wide-ranging knowledge base and interpretative skills required for these individuals to function independently as effective substitutes for physicians. Political pressures to use free movement of professionals across the EU to plug workforce shortfalls should not be used as an excuse to dilute the rigour of training.

CONCLUSIONS

While the focus of this review has been on the changing role of the laboratory-based physician, it is important to acknowledge that a physician in laboratory medicine does not practice in isolation. Instead, a high-quality laboratory medicine service is critically dependent on the complementary roles of medical doctors, scientists and related laboratory personnel.

Self-empowerment of patients, DTC testing, free movement and internet technology currently challenge the established role of the laboratory-based physician and the standards included in the Medical Act, which are meant to ensure the practice of high-quality Laboratory Medicine. In the last few decades, a high level of standardisation of the tests used in the clinical laboratory has been accomplished. Together with the improvements made by IVD vendors, the role of the physician in Laboratory Medicine has changed fundamentally to focus on the diagnosis and management of disease, interacting with both physicians and patients. There is an urgent need for training curricula in Laboratory Medicine to reflect and support these changes in practice. Any moves to broaden direct access to laboratory testing for patients need to be accompanied by appropriate safeguards including provision of appropriate advice and interpretation.

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REFERENCES

- Misbah SA, Kokkinou V, Jeffery K, et al. The role of the physician in laboratory medicine: a European perspective. *J Clin Pathol* 2013;66:432–7.
- Horvath AR, Lord SJ, StJohn A, et al. From biomarkers to medical tests: the changing landscape of test evaluation. *Clin Chim Acta* 2014;427:49–57.
- Price CP, John AS, Christenson R, et al. Leveraging the real value of laboratory medicine with the value proposition. *Clin Chim Acta* 2016;462:183–6.
- National Institute for Health and Clinical Excellence. *Diagnostic assessment programme manual*. Manchester: NHS, 2011.
- Wegscheider K, Drabik A, Bleich C, et al. Nutzenbewertung aus Sicht der Versorgungsforschung und der Epidemiologie. *Bundesgesundheitsblatt gesundheitsforschung gesundheitsschutz*, 2015;58:298–307.
- Hamilton W, Hajioff S, Graham J, et al. Suspected cancer (part 2—adults): reference tables from updated NICE guidance. *BMJ: British Medical Journal* 2015;350.
- Plebani M. Harmonization in laboratory medicine: the complete picture. *Clin Chem Lab Med* 2013;51:741–51.
- Lippi G, Banfi G, Church S, et al. Preanalytical quality improvement. In pursuit of harmony, on behalf of European Federation for clinical chemistry and laboratory medicine (EFLM) Working group for Preanalytical Phase (WG-PRE). *Clin Chem Lab Med* 2015;53:357–70.
- Oosterhuis WP, Zerah S. Laboratory medicine in the European Union. *Clin Chem Lab Med* 2015;53:5–14.
- Directive 2005/36/EC of the European Parliament and of the Council of 7 September 2005 on the recognition of professional qualifications. <http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=celex:32005L0036> (accessed 30 Sep 2017).
- Government of the United Kingdom. Medical act. 1983.
- UEMS News Brussels. European definition of the medical act. 2005.
- Beard JA. To what extent did the 1858 Medical Act bring unity to the British medical profession? *J Med Biogr* 2013;21:95–9.
- Ferraro S, Braga F, Panteghini M. Laboratory medicine in the new healthcare environment. *Clin Chem Lab Med* 2016;54:523–33.
- United Kingdom Department of Health. Independent midwives: insurance options outlined, 2017. <http://www.gov.uk/government/news/independent-midwives-insurance-options-outlined>. (accessed 30 Sep 2017).
- Aarsand AK, Sandberg S. How to achieve harmonisation of laboratory testing -The complete picture. *Clin Chim Acta* 2014;432:8–14.
- Orth M. Direct-to-consumer testing: the business with lifestyle tests. *Point of Care* 2017;16:124–7.
- Diamandis EP. Theranos phenomenon: promises and fallacies. *Clin Chem Lab Med* 2015;53:989–93.
- Carreyrou J, Siconolfi M, Weaver C. Theranos dealt sharp blow as Elizabeth Holmes is banned from operating labs. *Wall Street Journal* 2016.
- Gabler E. Hidden errors - a watchdog report - common medical tests escape scrutiny but often fall short. *Milwaukee Journal Sentinel* <http://archive.jsonline.com/watchdog/watchdogreports/common-medical-tests-escape-scrutiny-but-often-fall-short-1-b9957094521-338990781.html/> (accessed 30 Sep 2017).
- Plebani M, Lippi G. Closing the brain-to-brain loop in laboratory testing. *Clin Chem Lab Med* 2011;49:1131–3.

- 22 Orth M, Rost I, Hg F, *et al.* Practical implications of the german genetic diagnostics act (gendg) for laboratory medicine, the human genetics laboratory and for genetic counseling. *LaboratoriumsMedizin* 2011;35:243.
- 23 Hiatt HH. Protecting the medical commons: who is responsible? *N Engl J Med* 1975;293:235–41.
- 24 Kim JY, Dzik WH, Dighe AS, *et al.* Utilization management in a large urban academic medical center. *Am J Clin Pathol* 2011;135:108–18.
- 25 McGuire AL, Burke W. An unwelcome side effect of direct-to-consumer personal genome testing: raiding the medical commons. *JAMA* 2008;300:2669–71.
- 26 Hood L, Auffray C. Participatory medicine: a driving force for revolutionizing healthcare. *Genome Med* 2013;5:110.
- 27 Hood L, Flores M. A personal view on systems medicine and the emergence of proactive p4 medicine: predictive, preventive, personalized and participatory. *N Biotechnol* 2012;29:613–24.
- 28 Weinert K, Gyorda P, Rifai N, *et al.* Triangulating dynamic of clinical laboratory testing. *Clin Chem* 2015;61:1320–7.
- 29 Bresó A, Sáez C, Vicente J, *et al.* Knowledge-based personal health system to empower outpatients of diabetes mellitus by means of p4 medicine. *Methods Mol Biol* 2015;1246:237–57.
- 30 Watson ID, Siodmiak J, Oosterhuis WP, *et al.* European views on patients directly obtaining their laboratory test results. *Clin Chem Lab Med* 2015;53:1961–6.
- 31 Orth M, Luppa PB. Direct-To-Consumer-Testing: Fluch oder Segen für die Patienten? *Dtsch Arztebl International* 2015;112:174.
- 32 Armbruster DA, Overcash DR, Reyes J. Clinical chemistry laboratory automation in the 21st century - amat victoria curam (Victory loves careful preparation). *Clin Biochem Rev* 2014;35:143–53.
- 33 Badrick T, Gay S, McCaughey EJ, *et al.* External quality assessment beyond the analytical phase: an australian perspective. *Biochem Med* 2017;27:73–80.
- 34 Redman BK. Responsibility for control; ethics of patient preparation for self-management of chronic disease. *Bioethics* 2007;21:243–50.
- 35 Dennick K, Bridle C, Sturt J. Written emotional disclosure for adults with Type 2 diabetes: a primary care feasibility study. *Prim Health Care Res Dev* 2015;16:179–87.
- 36 Tolan NV, Parnas ML, Baudhuin LM, *et al.* "Big Data" in laboratory medicine. *Clin Chem* 2015;61:1433–40.
- 37 Cornel MC, van El CG, Borry P. The challenge of implementing genetic tests with clinical utility while avoiding unsound applications. *J Community Genet* 2014;5:7–12.
- 38 European Society of Human Genetics. Statement of the ESHG on direct-to-consumer genetic testing for health-related purposes. *Eur J Hum Genet* 2010;18:1271–3.
- 39 Maillat B, Maisonneuve H. Apprentissage tout au long de la vie pour les médecins spécialistes en Europe : formation médicale continue, développement professionnel continu et qualifications. *Presse Med* 2011;40:357–65.
- 40 Government of Ireland. Medical practitioners act. 2007.
- 41 Cavalier E, Delanaye P, Vranken L, *et al.* Interpretation of serum PTH concentrations with different kits in dialysis patients according to the KDIGO guidelines: importance of the reference (normal) values. *Nephrol Dial Transplant* 2012;27:1950–6.
- 42 Australian commission on safety and quality in health care. Review of serious failures in reported test results for prostatespecific antigen (PSA) testing of patients by SA pathology. Secondary Review of serious failures in reported test results for prostatespecific antigen (PSA) testing of patients by sa pathology. 2016 <https://www.hcasa.asn.au/documents/273-psa-review/file> (accessed 30 Sep 2017).
- 43 De Vooght KM, Oostendorp M, van Solinge WW. New mAb therapies in multiple myeloma: interference with blood transfusion compatibility testing. *Curr Opin Hematol* 2016;23:557–62.