Pathology and laboratory medicine in low-income and middle-income countries 1

Access to pathology and laboratory medicine services: a crucial gap

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As global efforts accelerate to implement the Sustainable Development Goals and, in particular, universal health coverage, access to high-quality and timely pathology and laboratory medicine (PALM) services will be needed to support health-care systems that are tasked with achieving these goals. This access will be most challenging to achieve in low-income and middle-income countries (LMICs), which have a disproportionately large share of the global burden of disease but a disproportionately low share of global health-care resources, particularly PALM services. In this first in a Series of three papers on PALM in LMICs, we describe the crucial and central roles of PALM services in the accurate diagnosis and detection of disease, informing prognosis and guiding treatment, contributing to disease screening, public health surveillance and disease registries, and supporting medical-legal systems. We also describe how, even though data are sparse, these services are of both insufficient scope and inadequate quality to play their key role in health-care systems in LMICs. Lastly, we identify four key barriers to the provision of optimal PALM services in resource-limited settings: insufficient human resources or workforce capacity, inadequate education and training, inadequate infrastructure, and insufficient quality, standards, and accreditation.

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This is the first in a Series of three papers about pathology and laboratory medicine in low-income and middle-income countries

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Introduction

> "As is your Pathology, so is your Practice"
>
> *William Osler*

In a clinical vignette (panel 1), we describe two patients with similar conditions but living in different countries. The first child lives in a setting that is typical in low-income and middle-income countries (LMICs), where much of the population have little or no access to health care, particularly to pathology and laboratory medicine (PALM) services. As we have learned from global efforts to control communicable diseases such as HIV, tuberculosis, and malaria, any attempts to reduce disease burden and decrease premature mortality rates will not succeed unless clinicians have access to the high-quality PALM services necessary for diagnosis, prognosis, and guidance of therapy.[1,2] The latest convergence of the international development agenda, as expressed in the Sustainable Development Goals (SDGs), continues the health agenda of the Millennium Development Goals but expands the focus to include non-communicable diseases (NCDs), particularly cardiovascular disease, cancer, and diabetes, which are among the leading causes of global disease burden and mortality.[3,4,5] Access to PALM services is as crucial for NCDs as it is for communicable diseases, because certain NCDs cannot be detected or diagnosed on the basis of clinical history or physical examination alone (eg, diabetes or hyperlipaemia) and rely entirely on access to PALM services for effective diagnosis and subsequent care. Other diseases, such as cancer, require PALM services not only for detection and diagnosis, but also for the specific classification and staging that is needed to guide treatment and help determine prognosis. Individual diagnosis and disease detection, prognosis and treatment planning, population cancer surveillance, and global health security are not possible without access to PALM expertise and infrastructure.[1,2] As a result, without access to quality PALM services at all levels of care, achieving the SDGs, including universal health coverage, simply will not be achieved by the target year of 2030.

The scale and scope of this challenge is daunting. Of 189 World Bank member countries, 138 are defined as low-income and middle-income, with 87% of the world's population living in these countries.[6] Additionally, disease burden is higher in LMICs than in high-income countries. Communicable diseases account for 21% of deaths in LMICs, compared with 2% of deaths in high-income countries, and of the 36 million global deaths caused by NCDs in 2008, almost 80% occurred in

Key messages

- Pathology and laboratory medicine (PALM) services are cross-cutting, intersectoral, and provide the foundation for safe, effective, and equitable health-care delivery, population health, and global health security
- Access to PALM services in low-income and middle-income countries is severely inadequate and inequitable
- The Sustainable Development Goals and universal health coverage cannot be achieved without PALM services
- Four key barriers to expanding access to PALM services have been identified: insufficient human resources and workforce capacity, inadequate education and training, inadequate infrastructure, and insufficient quality, standards, and accreditation

***Panel 1*: A clinical vignette**

A mother living in rural Uganda brings her 9-year-old daughter to a rural health clinic after her daughter tells her that she has seen blood in her urine. The girl has lost weight and, some months before, had a skin condition that was treated locally by a visiting nurse. There are no written medical records for her mother to bring to the clinic, which is 1 h away by bus. At the clinic, the patient is seen by a volunteer physician who documents hypertension. The only available laboratory tests are a spun haematocrit, which reveals mild anaemia, and a urine dipstick test that reveals high concentrations of protein and blood in the urine. The physician refers the patient to a district hospital in a nearby city, where the diagnoses of anaemia and severe proteinuria are confirmed, but the hospital cannot provide a kidney biopsy. The patient is referred to a teaching hospital, where these services are available, but the mother can afford neither the cost of travel to that hospital nor the medical care provided there. The patient is subsequently lost to follow-up, without having a diagnosis made or treatment given. Her prognosis is poor and she almost certainly dies within months to a few years later.

A similar patient living in Argentina is seen in her local primary care clinic. When seen by the physician, a complete blood count is obtained, along with tests for kidney function and a complete urine analysis. The patient is shown to have acute nephritis (inflammation of the kidney) and is referred to a nearby hospital, where test results available on the same day show probable autoimmune nephritis, with systemic lupus erythematosus being the most likely cause. She undergoes a kidney biopsy the day after and the biopsy specimen is sent to a university medical centre a few miles away, where the crucial diagnostic tools of light microscopy, immunofluorescence microscopy, and transmission electron microscopy are available, as are experts in kidney pathology. In this case, a correct diagnosis of lupus nephritis is made and immunosuppressive therapy is commenced. The patient's clinical signs and symptoms eventually resolve and she continues follow-up at her local clinic, including testing for her response to therapy and to monitor the effects of her ongoing immune suppression.

LMICs.[7,8] Moreover, although these countries have a disproportionately high share of the global disease burden, they also have a disproportionately low share of the world's health-care resources,[9] particularly for PALM. Although accurate data about PALM capacity and workforce are scarce for many regions of the world (as discussed later in this Series paper), where data are available, the findings are sobering. These issues are particularly pertinent as economic growth leads to an expansion of demand for health-care services. Urbanisation and population growth increase the global disease burden, and emerging infections drive the need for access to timely and accurate diagnosis.

As global efforts to improve the health of populations are expanding to include both communicable diseases and NCDs, our knowledge of the global disease burden has increased,[9,10] and our understanding of the consequences of insufficient access to PALM services has grown. It has become apparent that there is an urgent need for nations to recognise that this is a crucial gap in the health-care systems of LMICs. A scarcity of appropriate health technologies, particularly in-vitro diagnostics and PALM services, was partly responsible for the slow progress towards achieving the Millennium Development Goals, which aimed to reduce morbidity and mortality related to HIV, AIDS, and malaria.[11] Moreover, without immediate and sustained intervention, this gap in resources will only worsen, jeopardising the ability of LMICs to meet the SDGs and, in particular, the goal of universal health coverage. This Series of three papers aims to raise awareness of this gap. This first paper examines the essential and growing role of PALM services in contemporary health care and describes four key barriers that are preventing the sustainable implementation of these services in LMICs. The second paper[12] describes potential solutions to the four barriers and proposes a package of PALM services for LMICs. The third paper[13] of the Series describes how advocacy, health-care planning, and adequate financing are needed to mobilise the necessary support to address the inadequacy of PALM services in these countries. The Series finishes with eight key recommendations to address the barriers identified and issues a call to action for all stakeholders to come together in a global alliance to ensure the effective provision of PALM services in resource-limited settings.

PALM in contemporary health care

In this section, we describe the crucial importance of PALM to high-quality, contemporary health care by examining the different roles that it plays in a health-care system (figure 1). PALM is much more than the common perception of autopsies and forensic pathology: it is a highly complex set of medical subdisciplines that span the breadth of diagnostic testing that is needed to support all health care. Human resources needed for PALM include both medically trained personnel (pathologists) and non-medically trained doctoral scientists who typically direct clinical laboratories. Most clinical laboratory testing is done by medical technologists (with bachelor degree training), medical technicians (with associate degree training), or both, who usually have specialised training in PALM sub-disciplines. Histotechnologists and cytotechnologists support anatomical pathology by providing the technical expertise needed to process tissue and fluid specimens for examination by pathologists. Depending on the size and complexity of PALM services in a given location, all personnel can be supported by information technology specialists, technicians with expertise in forensic pathology, clerical and administrative support experts, billing and coding experts, and others (figure 2). All these professionals work together in teams to provide the PALM services described in the following sections.

Individual diagnosis and disease detection

Accurate and timely diagnosis is central to health-care provision. For many diseases and medical conditions, PALM testing is the only available method for making or confirming a patient's diagnosis.[10] For example, most cancer diagnoses require anatomical pathology services for interpretation of biopsy specimens, while for most infectious diseases (including HIV, tuberculosis, and malaria), the diagnosis of the causative agents and

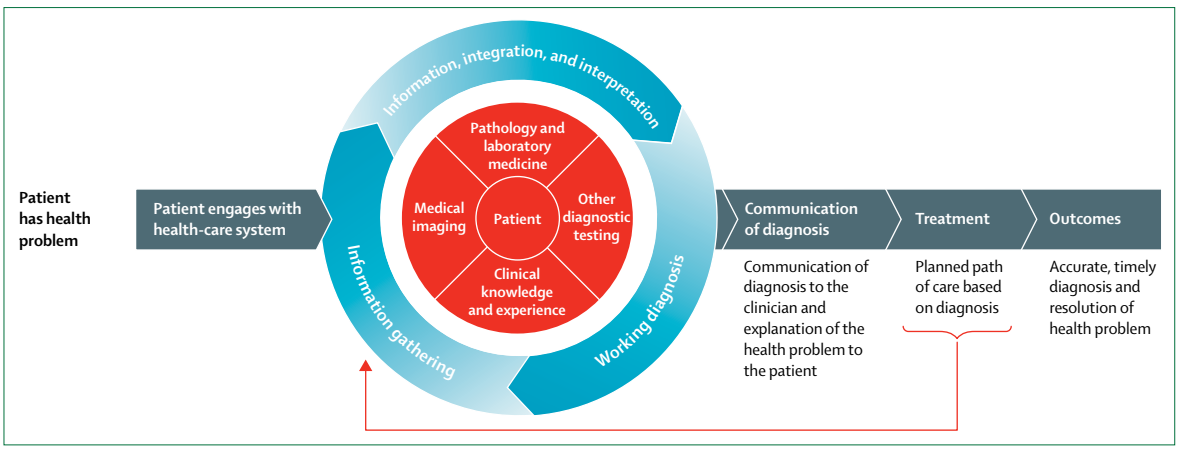

Figure 1: **The role of pathology and laboratory medicine (PALM) in patient-centred health care**
This figure shows the centrality of accurate and timely diagnosis in health care. Diagnostic information provided by PALM services is a crucial component of this process, and inadequate PALM services can preclude delivery of effective health care for patients. Adapted from Improving diagnosis in health care: quality chasm series,[14] by permission of the National Academies Press.

detection of antimicrobial resistance require access to microbiology or virology laboratory services. Similarly, many liver diseases, kidney diseases, and thyroid conditions can only be detected through testing provided by PALM services; many of these diseases and conditions are asymptomatic during early stages and, therefore, are unlikely to be detected clinically. Moreover, early detection of asymptomatic disease should result in better disease management and less consumption of the scarce resources available in LMICs. Many febrile illnesses, which are common in these countries, cannot be distinguished reliably solely on the basis of clinical signs and symptoms and require access to PALM services for correct diagnosis and treatment.[15,16]

The volume of PALM tests that are done in high-income countries reflects the importance of access to these services to deliver an accurate and timely diagnosis. In high-income countries, individual hospital laboratories do millions of tests annually, while reference laboratories do tens of millions of tests each year. This volume of testing is driven by clinical demand, with a 2016 interview-based study[17] of internal medicine specialists (cardiologists and oncologists) in the USA and Germany showing that 66% of clinical decisions are based on results generated by PALM.

Prognosis and treatment planning

Many PALM tests provide diagnostic information, but a subset of these also provides information concerning prognosis, treatment selection, response to treatment, and follow-up. Analysis of liver function by simple blood tests not only guides diagnosis of liver disease, but also allows the concentrations of specific analytes in blood to be tracked over time to establish clinical improvement or deterioration (such as monitoring serial bilirubin concentrations of a newborn baby with haemolytic disease), assess response to treatment, and establish a prognosis. Some microbiology tests, such as blood cultures, provide both diagnostic and prognostic information.[18] Simple blood tests are available to monitor response to treatment as well as recurrence of specific cancers, such as carcinoembryonic antigen in colorectal cancer. In addition to use of blood tests for monitoring biomarkers, access to accurate and timely surgical (histopathology) reports, especially in structured reporting formats, is a cornerstone of cancer care, guiding clinical oncology practice throughout the continuum of care (panel 2).[23]

However, merely providing access to results from PALM testing is insufficient to improve care because clinicians need to administer therapy on the basis of those test results.[24,25] For care providers in LMICs who have not previously had access to contemporary diagnostic testing, the introduction of new tests (as occurred with introduction of malaria rapid diagnostic tests) might not have the immediate effect on patient care and outcomes that was hoped for.[25] Replacing older tests with new ones, introducing new types of diagnostic technology that were previously not available, integrating new tests and services into health-care systems, and educating providers about test interpretation are key, if under-recognised, roles of PALM services in patient care. One successful example of these roles in a low-income or middle-income country has been the development of a national blood supply system in Ethiopia (panel 3). In this case, a need was recognised, a strategy was developed, resources were allocated, and implementation was successful, with ongoing quality audits and monitoring of effectiveness to achieve milestones and guide the future expansion of the system to meet the growing needs of the population.

Population cancer surveillance

For cancer screening, PALM also plays a crucial role. For example, many LMICs have high prevalences of cervical

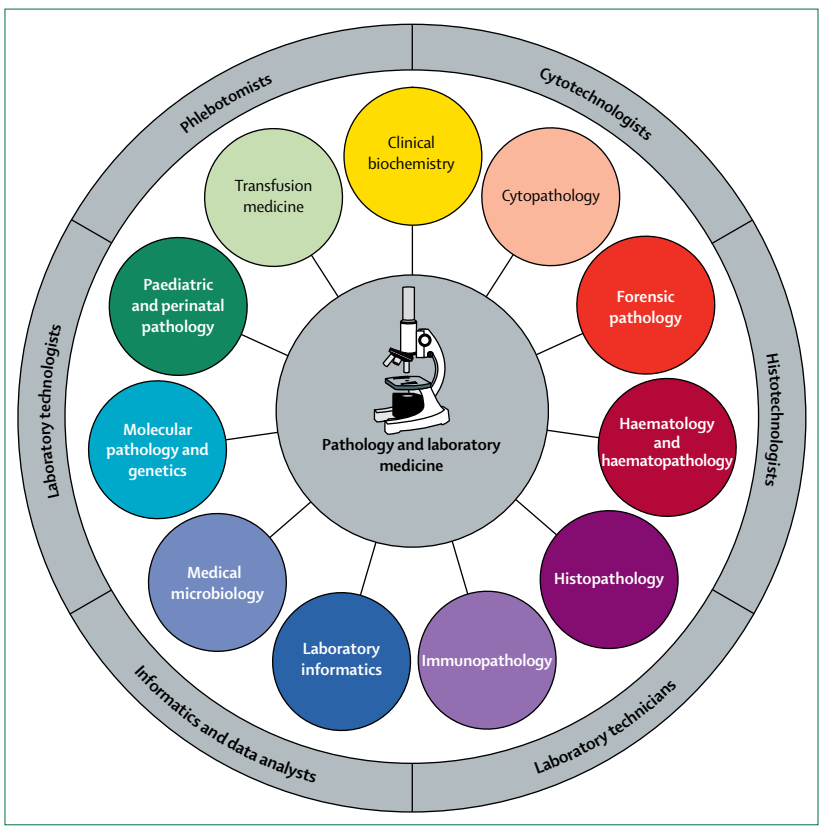

Figure 2: **The organisation and integrated structure of pathology and laboratory medicine (PALM)**
PALM is a highly complex and integrated set of medical and technical subdisciplines that must function as a coordinated team to provide the scope of services needed for contemporary health care.

cancer, making screening programmes for this disease a high public health priority.[31] Although primary detection of human papilloma virus (HPV) might be a more cost-effective option than cytology (pap smears), reduction of cervical cancer incidence, prevalence, and mortality has, so far, only been possible by use of population-based cervical cancer screening using cervical cytology in pathology laboratories.[32–34] Furthermore, although there are strengths and weaknesses in any single approach to cervical cancer screening, and the best approach varies by patient age, a crucial component for successful testing is the establishment of quality control programmes to assure accuracy of diagnosis, whether the approach is based on cytopathology, HPV testing, or co-testing.[35–37] Such quality control oversight requires appropriate expertise in PALM. Additionally, where resources are available, patients who have positive screening tests are typically referred for colposcopy with biopsy of suspicious lesions, which also requires access to anatomical pathology services.

Screening programmes for colorectal cancer, although not yet common in LMICs, are becoming more widespread in upper-middle-income countries and share similarities with cervical cancer screening programmes. There are several laboratory tests that can be used for primary colorectal cancer screening, such as faecal occult blood testing[38,39] or detection of tumour DNA,[40,41] with patients who have had positive screening tests being referred for colonoscopy and biopsy of suspicious lesions.[42] These tests are integrated into comprehensive colorectal cancer prevention programmes, which require access to laboratory testing for initial screening, anatomical pathology for interpretation of biopsy results, and, when necessary, assessment of resection specimens for tumour grading and staging. Data derived from examinations of tissue specimens and cancer staging are crucial for patient care and for populating datasets, such as cancer registries.[43,44] Screening programmes for breast cancer are also becoming more common in upper-middle-income countries.

Molecular diagnostic testing is now used extensively for diagnosis of cancer, guiding treatment, detection of residual disease, and (as in the examples noted previously) screening for some types of cancer. However, there are new molecular tests that can be used to screen for disease and can bypass traditional cancer screening methods, giving health-care systems the potential to more rapidly begin and scale up cancer screening programmes at the population level. One such example is the use of detection of Epstein-Barr virus DNA in plasma to screen for nasopharyngeal carcinoma in an endemic region.[45] It is probable that such molecular techniques will become more common, replacing traditional cancer screening methods for several types of cancer. Because the development, introduction, and use of these tests requires technology and expertise that is not present in many LMICs, the gap between what should be available to populations in these countries and what is actually available will only continue to grow as we approach 2030. However, to fully understand how large this gap is and how fast it will grow, more studies are needed to overcome the current paucity of data about these issues.

Global health security

PALM plays a central role in communicable disease surveillance and global health security, especially for detection of emerging epidemics, identification and monitoring of antimicrobial resistance, and documentation of infection rates in populations.[46,47] Experience has shown the need for accurate detection and monitoring of disease outbreaks, such as the rapid spread of West Nile virus across the USA during 1999–2010,[48] the Ebola virus outbreak during 2014–15 in West Africa,[49,50] and the more recent emergence of Zika virus infection in Central and South America.[51] Prompt and effective responses to outbreaks such as these require access to high-quality rapid laboratory testing. This, in turn, requires continuously functioning PALM systems that operate within larger health-care systems to facilitate patient management when PALM test results become available. Because most patients present to

primary care clinics or district hospitals when ill, particularly at the onset of an outbreak, the most practical and rapid means for disease detection is to have functional laboratories in these clinical settings. This notion was the basis of a programme started in 1999 in the USA called the Laboratory Response Network (LRN).[52] The LRN is a three-tier network composed of sentinel laboratories, the several thousand hospital-based laboratories in the USA that are on the front line of diagnostic testing, reference laboratories that are primarily local and state public health laboratories with more specialised diagnostic testing, and national laboratories with the resources to handle highly infectious agents safely and the diagnostic capacity to identify these agents.[52] Because of their proximity to patients, sentinel laboratories almost certainly will be the first to admit patients with emerging infections or exposures to toxic agents and, with appropriate systems in place, the LRN allows for rapid assignment of specimens to the appropriate level of testing. The conceptual basis for such a system relies entirely on a network of clinical laboratories providing testing for routine patient care.

Similarly, clinical microbiology laboratories doing routine cultures and antimicrobial susceptibility testing are crucial for monitoring patterns of antimicrobial susceptibility and resistance,[53–56] identifying emerging patterns of infection, such as changes in causative pathogens of bacteraemia and fungaemia through time, and for isolating pathogens for traditional and molecular epidemiology to identify outbreaks, such as the identification of a global outbreak of *Mycobacterium chimaera* in patients after surgery.[57] As with global health security, leveraging resources already in place for routine patient care is the most practical method for creating networks with access to both the microbial isolates and the information needed to continuously monitor changes in the ecosystem of infection. This network includes not only functional laboratories at primary, secondary, and tertiary levels of care, but also systems that link and coordinate activities at all levels (expanded upon in the second paper of this Series).

Disease registries

Disease registries facilitate storage of information about patients with specific diseases, usually for chronic diseases, such as cancer. Cancer registries vary in their complexity and function, but most capture detailed clinical information about patient demographics, diagnosis and staging, treatment, and outcomes. Not surprisingly, histopathology and surgical pathology generate much of the data used to populate cancer registries, particularly with information derived from cancer screening programmes (as described previously), diagnosis of biopsy and resection specimens, and pathological staging of cancer cases.[43,44] As global efforts accelerate to prevent, diagnose, and treat cancer, PALM will have an increasingly important role in LMICs to generate timely and accurate data for cancer registries. In the absence of such data, it is impossible for governments to develop coherent cost-effective strategies for cancer control.

Other types of registries play a similarly important role in disease surveillance and development of public policy.[58–60] The Diabetes Collaborative Registry, for example, uses a data collection form that requires access to 31 different laboratory test results, including information on lipid measurements, routine clinical chemistry test, and haematology tests.[57,58] Because disease registries collect large amounts of data through time, they play a unique role in supporting investigations that are used to develop evidence for treatment and prognosis. As such, these registries are central to both clinical research and patient care, and without access to data provided by PALM services, these roles would be severely compromised. For LMICs, it is crucial that disease registries be established and used to develop public policy and guide allocation of often scant resources.

Autopsy and medicolegal systems

Identifying an accurate cause and manner of death is crucial to public health policy development, to treatment-related research programmes, and to education of clinicians. This process of identification remains a challenge in many settings. Autopsies continue to play

Panel 2: Pathology and laboratory medicine (PALM) testing guides personalised medicine

Our growing understanding of disease processes has led to the emergence of a personalised health agenda, in which biology-informed precision medicine drives identification of different disease subtypes that can be targeted by more specific therapeutic interventions. Establishing an effective precision medicine ecosystem requires a robust PALM system that is capable of delivering accurate and timely diagnostic approaches for clinical application. In addition to traditional pathology interpretations and laboratory tests, detection and quantification of new biomarkers not only guides therapy, but also has prognostic implications. For example, patients with breast cancer who overexpress HER2/NEU (receptor tyrosine-protein kinase erbB-2) usually benefit from targeted therapy using drugs such as trastuzumab, but in the absence of that therapy they have a worse prognosis compared with patients who do not express the biomarker.[19] Accurate detection and quantification of biomarkers, such as HER2/NEU, requires careful monitoring and quality control of specimen acquisition and processing, selection and performance of biomarker tests, and interpretation of results.[20] Pathological examination of tissue, including cancer staging and incorporation of reporting appropriate biomarkers, plays a crucial role in initiating and monitoring response to treatment and prognosis.[21,22]

Panel 3: Ethiopian national transfusion services—a model for implementing a new pathology and laboratory medicine (PALM) service

Access to a safe and adequate blood supply is one of the fundamental requirements in health-care systems that provide surgery, trauma care, and cancer care. Blood safety is ensured through systems that: screen donors for risk factors and test donated blood for infectious diseases, such as viral hepatitis, HIV, and other agents that are endemic to specific regions (eg, Chagas disease in South America); select donors to mitigate risks of transfusion reactions, such as transfusion-related acute lung injury; and have the ability to do blood typing that is needed to guide therapy and reduce the risk of transfusion reactions caused by the many blood types that occur naturally or are acquired through transfusion.[26] Transfusion service capacity is ensured by having a sustainable blood supply supported through a system that includes pools of donors who can be called upon to donate as needed, a network of blood donation centres that collect blood and transfer donated units to testing facilities, processing and testing facilities, and a procedure to distribute blood to hospitals and clinics.

Many low-income and middle-income countries either do not have national transfusion services or have ineffective services that cannot provide access to a safe and adequate blood supply.[27] Additionally, most of these services are located in urban areas and, therefore, are unavailable to patients in rural areas.[27] Providing access to transfusion services on a national basis where they did not previously exist is challenging, but can be done through partnerships of ministries of health, hospitals and clinics in a health-care system, and PALM expertise. As an example, in 2005 the Ethiopian Federal Ministry of Health developed a national strategy to create a national blood transfusion service that was based on the following key principles:[28]

- Establishment of nationally coordinated blood transfusion services.
- Recruitment and retention of voluntary non-remunerated blood donors and blood collection.
- Testing of blood and blood products for transfusion-transmissible infections and appropriate blood grouping and compatibility.
- Promotion of appropriate use of blood and blood products in a safe manner.
- Comprehensive quality management system to cover the entire transfusion process.
- Establishment of data management and monitoring and evaluation system for the service.
- Collaboration with national and international partners supporting the service.

This strategy was implemented over the subsequent years, and by 2014 the following achievements had occurred:[29]

- The national blood transfusion service was granted autonomy status under the ministry of health.
- Number of functional blood banks increased from 12 to 25, each covering hospitals within a radius of 100 km.
- Number of hospitals accessing safe blood and blood products increased from 48% in 2012 to over 90% in 2014.
- Number of active mobile blood collection teams increased from four in 2012 to 31 in 2014.
- Total number of units of blood collected increased from 24 000 units per year in 2004 to 95 466 units per year in 2013.
- Proportion of voluntary blood donations increased from 10% of all blood collections in 2012 to 92·1% in 2014, achieving the WHO regional target of 80% voluntary blood donation.
- HIV prevalence among blood donors dropped from 3·5% in 2004 to 0·78% in 2014.

By 2017, the percentage of voluntary blood donation in Ethiopia had further increased to over 98% of all blood collections.[30] Although challenges remain for this system, it provides a good example of what can be achieved through development of national policy and strategy and an effective implementation.[30]

an important role in hospitals in LMICs, in which they help with clinic-pathological correlations and in assessing cancer mortality patterns.[61,62] The evidence continues to show that, in the absence of autopsy, death certification is inaccurate,[63] even when other diagnostic modalities are readily available.[64] This is particularly true for deaths outside hospitals, which fall under the jurisdiction of the medicolegal system, in which the involvement of pathologists has been shown to improve the accuracy of death certification.[65] Global deaths due to traumatic injuries are expected to remain one of the top 20 causes of mortality, and autopsies used within a functioning medical-legal system are necessary to document the types and extents of injuries, collect specimens for toxicology testing, and detect underlying medical conditions that were contributing factors.

Causes of inadequate access to PALM services in LMICs

The shortage of access to PALM services in LMICs has many causes, some that are generalisable across countries and regions and others that are specific at national or local levels. We identified four key barriers to PALM services in LMICs: insufficient human resources, inadequate education and training, inadequate infrastructure, and insufficient quality, standards, and accreditation. These four major barriers, in addition to being generalisable and, thus, amenable to scalable solutions, are foundational. Without solving these four barriers, any solutions that are developed for overcoming other barriers are unlikely to have any long-term positive effect.

Insufficient human resources and workforce capacity

The available information regarding global workforce capacity in pathology is confounded by a scarcity of systematic data collection (with the exception of a few high-income countries, including the USA, UK, and Canada) and by the large, diverse group of medical and doctoral professionals who are often considered to be pathologists—despite the fact that the term should refer only to physicians with specialty training in one of the subdisciplines of pathology (figure 2). Most of the workforce data on PALM come from a few publications, which we have supplemented by doing a workforce survey as described in detail in the appendix.[66–70] Despite the scarcity of data, it is clear that, for much of the world, access to PALM services is severely restricted by insufficient workforce capacity (figure 3). The best data available for LMICs are from sub-Saharan Africa, with only scarce data existing for LMICs in most other regions of the world.[66–70] In sub-Saharan Africa, the number of anatomic pathologists is approximately one per 1 000 000 patients, a ratio roughly 50 times less than that of high-income countries.[66] In China, it is estimated that there are only 10 250 anatomical pathologists, or one per 134 517 population (unpublished data, Chinese Society of Pathology, 2015). To have approximately the same ratio of

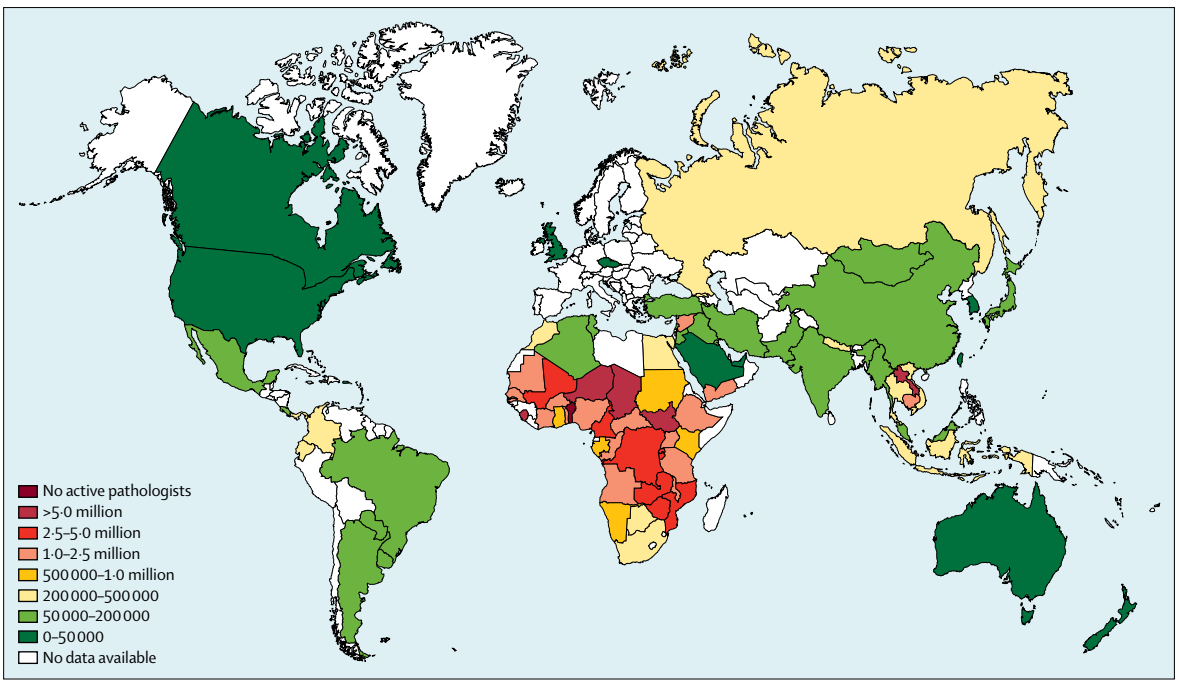

Figure 3: **Global workforce capacity in pathology and laboratory medicine (PALM)**
Data derived from previous studies[66–70] and the survey data shown in the appendix.

See Online for appendix

anatomical pathologists per population as the USA or UK, China would need an estimated additional 70 000 of these professionals. As with health care in general, workforce capacity is the single greatest challenge to providing access to PALM as part of universal health coverage.

Inadequate education and training

In any medical system, competent professionals are key to the delivery of high-quality health-care services. Most high-income countries have rigorous standards for medical education, postgraduate training, board certification, credentialing, privileging, and maintenance of competency and certification.[71–74] In sharp contrast, with a few notable exceptions,[75] most LMICs either do not have systems or have inadequate ones to assure the quality of education of students, of training of postgraduates, or of professional competence of practitioners. This insufficient overall capacity for medical and science education and training in LMICs results in low numbers of physicians and scientists entering the workforce.[76] Because few graduating medical or doctoral students pursue careers in PALM in these countries, a shortage of pathologists and laboratory professionals is a constant reality in almost all LMICs.

In addition to low total number of pathologists, the insufficient expansion of the global pathology workforce is of concern. In 2015, there were only 13 286 pathologists practising in the USA, or 1·5% of the physician workforce.[77] However, from 2013 to 2017, the percentage of medical school graduates entering postgraduate training in PALM in the USA decreased slightly from 2·2 to 2·1%.[78] Other high-income countries have reported similar percentages, such as Canada[79] (2·5% in 2016), the UK[80] (1·7% in 2015), and Taiwan[70] (1·8% in 2008). Moreover, the number of US pathologists involved in teaching, and thus training future pathologists and helping to grow the workforce, was only 289 during 2013 compared with 755 for paediatrics, 1217 for internal medicine, and 1608 for family medicine.[77] The situation in LMICs is even more challenging. In 2013, there were only 168 medical schools in the 47 countries in sub-Saharan Africa, with 24 countries having only a single medical school and 11 countries having none.[81] Most medical schools in LMICs graduate few medical students every year and, because only a few of these students go on to receive postgraduate training in PALM, the pathology workforce grows very slowly, if at all.[82] At these rates of education and training in sub-Saharan Africa, it might take more than 400 years to match the pathologists-to-population ratio of this region to that of the USA or UK. Additionally, because each LMIC has unique populations and challenges, it is unlikely that a single model for increasing human resources capacity can be used globally. Models developed for high-income countries can provide a starting point but need to be modified to fit local circumstances to succeed.[83]

Rapid progression of medical knowledge in diagnosis and treatment is driving an increased need for continuing professional development to maintain clinical competence and for ensuring access to training for skill enhancement. However, most LMICs have insufficient

capacity for both continuing professional development and skill enhancement.[84,85] Reasons for this low capacity include small numbers of academic medical centres, many of which have few faculty members, a dearth of systems for tracking continuing professional development and recertification systems, inadequate professional networking systems, and insufficient financial support for these activities.[85] Because of the very low number of practitioners, time devoted to continuing professional development or skill enhancement can negatively affect the delivery of services and, on a personal level, can lead to reduced income when time is taken away from practice. Additionally, with inadequate overall health-care delivery systems, pathologists and laboratory professionals in LMICs do not work in an environment that promotes a need for continuing professional development, skill enhancement, or development of performance indicators to improve quality.

Many LMICs have insufficient ability to train the other types of personnel that are crucial for providing PALM services. Many countries do not have training programmes for medical laboratory scientists (also known as medical technologists) or for biomedical engineers needed to help maintain and support diagnostic laboratories.[66] Moreover, we found few, if any, examples of LMICs that have successfully developed integrated educational systems in which, for example, the number of pathologists being trained is aligned with training of the histotechnologists and cytotechnologists who are needed to support pathologists in providing PALM services. There is an urgent need to develop such integrated education and training programmes as part of national PALM strategic plans, particularly because developing new programmes and curricula is complex, education infrastructure needs to be developed, faculty need to be recruited, and the time needed to develop these programmes is typically 1–2 years, if not longer, where resources are limited and there is not a precedent for such development.

Inadequate infrastructure

Most LMICs have inadequate infrastructure to support PALM services.[86,87] This framework includes physical laboratory infrastructure, technical support for instrumentation, supply chains, information technology, and integrated systems needed to provide quality pre-analytical, analytical, and post-analytical phases of testing. Contemporary laboratories require sufficient space, lighting, stable electrical supply, and clean water. Additionally, laboratory instrumentation that can be used in different environments, with adequate technical support for repair and maintenance, is needed. Supply chains are required for all laboratory instruments and basic laboratory supplies, including cold supply chains for many reagents. Information technology increasingly is important, as paper-based systems are inefficient and too prone to error for high-volume laboratories or for patients living in rural areas, with no practicable means of maintaining paper health records. Although the state of laboratories in many LMICs is characterised by restricted scope and low quality, focused efforts have shown that these shortcomings can be addressed, at least in part, in a short timeframe.[88]

Insufficient quality, standards, and accreditation

PALM services are highly technical and, therefore, require rigorous programmes to assure the accuracy and reproducibility of test results between laboratories and through time. In high-income countries, PALM services are highly regulated, a process typically driven by national governments with participation by professional societies in regulation development, implementation, and updating.[89,90] By contrast, access to systems for assuring laboratory quality standards and accreditation in LMICs varies widely between regions and countries, with few LMICs having a regulatory mandate for such systems or having the necessary structures in place to verify compliance with these regulations. In analyses of 954 clinical laboratories in Kampala, Uganda, only 45 (5%) of those met or surpassed minimal standards for quality, as defined by the WHO Regional Office for Africa.[91] The other laboratories provided low-volume and low-quality services.[92] Certain countries, such as Thailand, Malaysia, and Kenya, have developed in-country standards and systems of accreditation, but these are rare exceptions in LMICs.[93–95] Although there might be some benefits in development of in-country systems, many LMICs do not have the expertise or resources to achieve such development and a patchwork of national systems will confound efforts to develop external quality assurance programmes.[96] This difficulty will negatively affect the ability of manufacturers of test platforms to meet accreditation requirements, making the implementation of much-needed quality systems more difficult to achieve.

International programmes for PALM quality and accreditation have a cost associated with them and, therefore, are unaffordable in many LMICs.[97–100] Where these international programmes have been subsidised and supported by external development initiatives, they have been successful, but there is little experience with their use in the absence of such support. In addition to the cost of these programmes, their successful ongoing implementation and sustainability requires access to expertise and resources that are frequently unavailable in LMICs. Even where international programmes might be affordable, inadequate (or an absence of) systems for assuring compliance with these standards and accreditation almost certainly means that, as has been observed in the example from Uganda, only a few laboratories will comply voluntarily.

The consequence: inequitable access

The four key barriers described in this Series paper result in PALM services that all too frequently are severely inadequate in scope and capacity in most LMICs. This situation leads to access that is inequitably distributed:

access is most restricted in rural areas, where PALM capacity is at its lowest, and for patients in urban areas who cannot afford the cost of using PALM services because of inadequate financing systems. As inequitable access is associated with poorer health outcomes,[101] finding affordable and scalable solutions to the barriers outlined in this Series paper is essential to help drive public health policy and resource allocation in LMICs. Scarcity of access to high-quality PALM services means that providers are forced to care for patients without guidance from crucial diagnostic tools that are needed in contemporary medical care. This practice results in substandard care, with inevitable and unnecessarily prolonged suffering for patients. Additionally, there is an economic impact resulting from substandard care, with resources wasted on the wrong disease (eg, staff time, misallocation of drugs and other therapies) and lost economic output from the patient and members of the family, who frequently have to take time off work to cope with changing circumstances. The net effect can undermine the entire health-care system.

Conclusion

In this Series paper, we have provided an overview of modern PALM services and described how they fit into contemporary health-care systems, how access to such services is inadequate in many LMICs, and the four key barriers to such access. The second paper in this Series will propose solutions to the four specific barriers and will describe a PALM package for LMICs that integrates PALM services into national health systems. In the third paper, emphasis will be given to the need for national strategic planning for PALM services that can align system integration with capacity building and partnerships. Such planning can incentivise governments and other donors to invest in capacity building.[102] This third paper will also address two crucial issues for mobilising and enabling the support needed to implement our solutions: appropriate financing and defining the economic value of PALM[103] and advocacy, with particular emphasis on the need for PALM leadership. Lastly, the third paper will propose eight key recommendations to address the barriers identified in this *Lancet* Series and issue a call to action for a Global Alliance to ensure the effective provision of PALM services in resource-limited settings.

We have not tried to prioritise the four key barriers or their solutions, because both barriers and solutions are interdependent; none of the barriers can be solved in isolation without at least partly addressing the others. More importantly, their impact on effective PALM delivery varies substantially from region to region—and can change over time. We also do not want to create the erroneous impression that efforts to increase and improve PALM capacity in LMICs can be achieved by fixing only part of the problem. We place particular emphasis in the third paper of this Series on the issues of advocacy and financing, because those two issues must be addressed for effective and sustainable capacity building programmes to emerge and be successful.

Given the number of gaps that exist in health-care systems generally, and the fact that the resources with which to address those gaps are finite, why is it a priority to improve PALM? The answer lies, in part, in the fact that rates of NCDs in LMICs are increasing greatly. As we have highlighted in this Series paper, coping successfully with this increasing challenge will require competent PALM systems. If progress on improving such PALM systems is not introduced immediately, then the resulting burden of ill health and economic disruption will be much larger than could have been otherwise. Additionally, accurate and timely diagnosis underpins more specific treatments rather than empirical treatments, thus helping with stewardship of resources. Otherwise, resources and efforts invested in non-PALM parts of the health-care system will be wasted. Lastly, future prevention and management of the increasing number of epidemics (such as Ebola) and of the secondary issues that can undermine entire efforts of disease prevention and control (such as development of antimicrobial drug resistance), requires a competent PALM system to be in place now. Accordingly, we believe that immediate investments in PALM represent the most effective approach to deliver health-care benefits across low-income and middle-income health systems.

Contributors

All authors assisted with initial literature search, participated in design of the Series and first paper, and assisted with the design and analysis of the workforce survey. MLW drafted the figures and wrote the initial draft of several sections. KAF coordinated initial drafts with the other two papers in the Series. MLW and KAF provided overall coordination of writing and revisions. MAK wrote the introduction and assisted in initial drafts of several sections. LML assisted in initial drafts of several sections. NL and KR wrote the clinical vignette and assisted in initial drafts of several sections. MK, LML, NL, and KR provided overall review and critique during the writing process.

Declaration of interests

We declare no competing interests.

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