

Laboratory Medicine in Africa: A Barrier to Effective Health Care

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(See the editorial commentary by Bates and Maitland on pages 383–4)

Providing health care in sub-Saharan Africa is a complex problem. Recent reports call for more resources to assist in the prevention and treatment of infectious diseases that affect this population, but policy makers, clinicians, and the public frequently fail to understand that diagnosis is essential to the prevention and treatment of disease. Access to reliable diagnostic testing is severely limited in this region, and misdiagnosis commonly occurs. Understandably, allocation of resources to diagnostic laboratory testing has not been a priority for resource-limited health care systems, but unreliable and inaccurate laboratory diagnostic testing leads to unnecessary expenditures in a region already plagued by resource shortages, promotes the perception that laboratory testing is unhelpful, and compromises patient care. We explore the barriers to implementing consistent testing within this region and illustrate the need for a more comprehensive approach to the diagnosis of infectious diseases, with an emphasis on making laboratory testing a higher priority.

Each year in sub-Saharan Africa, ~12 million people die [1], and, for the majority of individuals, the causes of death are largely uninvestigated. These uninvestigated deaths are generally attributed to infectious diseases [2], most commonly HIV infection, malaria, and tuberculosis, but, in the absence of laboratory confirmation, the accuracy of these estimates remains uncertain. In fact, a recent study from Kenya found that bacterial bloodstream infections diagnosed by blood culture were responsible for 26% of deaths among children [3], which suggests that invasive bacterial infections may be an underappreciated cause of death. With >25 million people with HIV disease in this region [4],

the burden of infectious disease is even more patent. Quality laboratory testing is crucial to confirm clinical diagnoses, conduct accurate infectious disease surveillance, and direct public health care policy. But, in this time of crisis, the current laboratory and health care infrastructures are insufficient to meet these needs and perhaps have been ignored. To date, the vast majority of financial resources from funding organizations have been focused on disease prevention and provision of care, whereas relatively little funding has been allocated to build laboratory capability [5, 6]. Furthermore, because access to reliable diagnostic testing is severely limited or undervalued, misdiagnosis commonly occurs, resulting in inadequate treatment, increased mortality, and an inability to determine the true prevalence of diseases.

Two landmark studies published recently have contributed significantly to our understanding of the etiology of febrile illness in Kenya and Burkina Faso and demonstrate the need for physicians to

consider alternative diagnoses in their clinical practice [3, 7, 8]. However, the laboratory means to identify these infections are routinely unavailable, and investigators frequently neglect the importance of diagnostic testing [9] or fail to emphasize the need for parallel development of laboratory testing for nonresearch purposes [3, 7, 8]. At present, laboratory expenditures are often prohibitive for many countries in this region, where 38% of the population lives on <US\$1 a day and the gross national income per capita is US\$496 [1]. The challenge remains, therefore, to develop affordable and sustainable laboratory infrastructures to support the diagnosis of infectious disease.

Still, the barriers to laboratory testing in sub-Saharan Africa are protean, are unique between and within countries, and extend far beyond economic constraints. Health care policy makers and clinical investigators need to promote rational, cost-effective diagnostic methods for infectious disease, with an emphasis on improving

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Table 1. Inadequacies in laboratory infrastructure in sub-Saharan Africa and potential solutions.

Laboratory infrastructure
Problems
Lack of laboratory consumables
Lack of basic essential equipment
Limited numbers of skilled personnel
Lack of educators and training programs
Inadequate logistical support
De-emphasis of laboratory testing
Insufficient monitoring of test quality
Decentralization of laboratory facilities
No governmental standards for laboratory testing
Potential solutions
Emphasize importance of laboratory testing
Balance the allocation of financial resources
Strengthen the existing health care infrastructure
Routinely monitor test quality
Establish system for laboratory accreditation
Implement laboratory training programs
Encourage partnerships between public and private organizations
Develop affordable, rapid diagnostic tests

the overall health care delivery system. In this article, we demonstrate the need to improve laboratory support; we review the current state of laboratory medicine in sub-Saharan Africa, with a focus on infectious diseases; we explore the barriers to implementing consistent testing; and we discuss potential target areas for building laboratory capacity in the future.

CLINICAL MISDIAGNOSIS

Providing health care in resource-limited settings is admittedly a complex problem, and, for clinics or district hospitals with minimal-to-no laboratory support, diagnoses are often made clinically (e.g., by use of clinical algorithms for malaria and tuberculosis). Reliance on clinical diagnosis is attractive in areas with a high prevalence of disease, incurs no extra cost, and requires no special laboratory equipment or supplies; however, diagnoses based on clinical signs and symptoms can be non-specific, unreliable, and associated with increased mortality [10]. Among 4670 patients admitted to Tanzanian hospitals who received the clinical diagnosis of severe malaria by World Health Organiza-

tion (WHO) criteria, <50% had a blood smear result confirming the presence of *Plasmodium falciparum* [11]. Patients with parasites found on blood smears had better outcomes than did patients without laboratory evidence of malaria, which suggests that other serious illnesses were not considered or were perhaps dismissed in favor of malaria [10–12]. In a retrospective analysis of children at a tertiary referral center in Kumasi, Ghana, 40% of patients who had been given a WHO-defined clinical diagnosis of malaria were confirmed to actually have bacterial sepsis [12]. Clearly, the absence of laboratory support contributes to an overdiagnosis of malaria that leads to a failure to treat or a delay in treatment of alternative life-threatening infections and potentially increases mortality [13]. Clinical overlap between diseases is another common problem that may potentially compromise patient care and that may result in inappropriate antimicrobial therapy [14, 15].

Misdiagnosis occurs with other diseases as well. In Nigeria, the accuracy of clinical diagnoses of typhoid fever, when compared with laboratory culture confirma-

tion, was ~50% [16], and the diagnosis of bacterial meningitis was overlooked in 24% of Kenyan children when a clinical syndromic approach was applied alone [17]. The presumptive diagnosis of tuberculosis can also be nonspecific. One study found evidence of tuberculosis infection in only 52% of 229 patients with suspected tuberculosis in Botswana [18]. In South Africa, a postmortem study of children who were infected with HIV and presented with respiratory difficulty found that the clinical presentation of pulmonary tuberculosis was virtually indistinguishable from respiratory failure caused by *Pneumocystis jiroveci*, cytomegalovirus, bacterial pneumonia, or lymphocytic interstitial pneumonitis [19]. Similarly, in Malawi, a country with a high prevalence of HIV infection, cultures of bone marrow aspirations from adults with severe anemia showed occult infections (mycobacterial and bacterial) to be frequent, treatable causes of anemia [20]. In many cases in sub-Saharan Africa, it appears that diagnosis based on clinical symptoms alone, without the support of basic diagnostic tests, is the rule rather than the exception and leads to inappropriate treatment, increased morbidity, and unnecessary loss of life.

INADEQUATE HEALTH CARE INFRASTRUCTURE

A significant number of obstacles are present that do not involve the clinical laboratory or testing method (table 1). The existing infrastructure is not capable of supporting the routine use of laboratory tests and contributes to a failure to use the few existing laboratory resources. An assessment of district hospitals in Kenya found that, despite the availability of hematological tests, hemoglobin levels were not measured in 15% of children with a clinical history compatible with anemia or malaria [21]. In the same study, review of data for 46 children who presented with fever and stiff neck or with fever and an altered level of consciousness (e.g., seizures, lethargy, or irritability) found that

no lumbar punctures were performed [21]. The inability to collect patient samples results in missed opportunities to perform laboratory tests as an integral part of clinical care. Lack of consumables (e.g., blood vacutainers, lumbar puncture materials, and sterile urine-specimen containers), scarcity of trained personnel, and extreme staff shortages all impact specimen procurement. A central hospital in Kampala, Uganda, generally supports an average of 2 blood culture bottles per ward each week, and EDTA blood collection tubes are reused. Lumbar punctures are sometimes not performed unless the patient or caretaker is willing to purchase the kit materials (authors' personal observations). Staff shortages in which health care workers are often responsible for an overwhelming number of acutely ill patients afford little time to obtain clinical specimens for laboratory testing. In fact, there is a lack of skilled health care professionals at every level, and current efforts in education and training are inadequate [22]. Of 693 technical staff working in 205 Ghanaian laboratories, only 26% were professionally qualified [23]. In many regions of sub-Saharan Africa, attrition of human capital is common and is frequently attributed to death [24] or emigration to better working conditions locally or internationally [25]. Finally, even when laboratory testing and services are available, physicians often perceive them as unreliable and unhelpful, such that they remain underutilized and undervalued [21, 26]. On numerous occasions in Zambia, Uganda, and Ghana, we observed clinical decision-making that occurred in the absence of laboratory confirmation, even when tests were available. Conversely, when tests were performed, clinicians de-emphasized seemingly contradictory laboratory results and elected to proceed with treatment based on clinical judgment alone (authors' personal observations).

Even when specimens are obtained, the health care system places a low priority on laboratory support, and specimen transport can be an obstacle. A courier, pa-

tient's caretaker, or ward personnel may transport the specimen, but none of these strategies guarantees proper delivery, and long delays between collection and testing frequently occur. In many places, none of these options are available or dependable, which leads to underutilization of laboratory services and loss of specimens and/or test results. In Uganda, where the prevalence of tuberculosis is >63,000 [27], the National Tuberculosis Laboratory processes only ~300 specimens per month for the entire country (authors' personal observations). A study designed to target this very problem was conducted in Malawi, where investigators evaluated the use of a bus service and "tuberculosis officers" for transporting sputum specimens to their Central Reference Laboratory [28]. Despite these measures, only 384 (40%) of 964 patients with recurrent smear-positive pulmonary tuberculosis had their specimens arrive at the Central Reference Laboratory.

Further complicating the problem is the decentralization of the health care system, in which governmental, not-for-profit (e.g., missionary or private philanthropic), or commercial (for-profit) organizations often operate independent laboratories. As these nongovernmental institutions are introduced in sub-Saharan Africa to respond to the HIV crisis and its concomitant health care demands, an environment of donor parallelism is created. Despite the lack of data in this area, there is concern that the establishment of plural systems diffuses both existing and incoming resources by creating competition for human capital and financial investments. Health care programs dictated by donor agencies often do not consider broader regional needs or make provisions for overall sustainability. The migration of skilled personnel from the public sector to higher-paying positions within the private and research sectors further weakens the existing infrastructure and exacerbates a quality differential that encourages the increasing use of alternative health care and laboratory sys-

tems. Decentralized systems with fee-for-service laboratory testing and with quality differences in laboratory performance prevent the effective delivery of care to all individuals. A study evaluating the impact of the Bamako Initiative on the delivery of health care in Nigeria demonstrated that people with financial means had a higher probability of accessing laboratory resources and seeking care in private clinics [29]. In Uganda, the decision to send a patient sample to a private or public laboratory varies within the same hospital ward by physician preference, patient socioeconomic status, and laboratory reputation, resulting in ineffective and inefficient health care delivery. The public health care infrastructure, although inadequate, must serve the majority of the population and is progressively destabilized by these competing parallel systems.

LABORATORY CAPABILITY AND DIAGNOSTIC ACCURACY

Depending on the country and location, capabilities of laboratories vary widely. Quality of laboratory facilities, access to utilities (e.g., piped water and constant power supply), availability of laboratory equipment and supplies (e.g., incubator, refrigerator, freezer, microscope, and staining reagents), implementation of standard written operating procedures (including quality-control procedures), and knowledge or skill of supervisors and technical personnel are common variables. Except in the more remote areas, space, electricity, and water are generally present, whereas materials and functioning laboratory equipment are limited, and finding an operational light microscope can be elusive [30]. As of 2000, there was ~1 microscope per 100,000 population in Malawi, with almost one-half of these not in use or in need of repair [30]. Skilled personnel are scarce—in particular, there are few supervisors with technical expertise to monitor the accuracy of test results (au-

thors' personal observations). Thus, for simple tests, quality-controlled and reproducible laboratory testing remains a major challenge, and there are few or no national or regional laboratory guidelines to promote standardization or quality among laboratories.

For sub-Saharan Africa, the WHO has designated malaria microscopic evaluation and hemoglobin, glucose, and HIV testing as essential laboratory services. Nonetheless, the majority of hospitals cannot consistently provide even these basic services in a quality-controlled fashion. After discussing how diagnoses based on clinical symptoms alone may lead to serious medical errors, several studies suggest that an alarming proportion of results of very basic diagnostic tests (e.g., malaria or acid-fast bacilli smear) may be inaccurate, leading to misdiagnosis even when they are included in clinical algorithms. A study in Kololo, Uganda, evaluated 4 glucose-monitoring systems currently in use by both public and private laboratories [31] and found that their accuracy varied greatly, exposing the need for a national quality-control policy for blood glucose testing. In Malawi, 40% of patients given the diagnosis of smear-positive pulmonary tuberculosis in rural or district hospitals had a negative smear result after review at the Central Reference Laboratory [28]. An observed increase in the incidence of typhoid fever in Cameroon led to an investigation of 20 health care facilities, which uncovered poor laboratory performance and erroneous interpretation of the Widal test as probable causes of misdiagnosis [32]. Similarly, the Malaria Control Program in South Africa discovered significant disagreement between laboratories in the microscopic examination of Giemsa-stained thick blood smears, again arguing for the need for quality-control programs [33]. Finally, a recent report from Ghana of the success of a nationwide technician-training program highlighted not only the reality of inaccurate test results but also

the potential for improvement through an organized initiative [23].

Understandably, allocation of resources (human and economic) to diagnostic laboratory testing has not been a priority for resource-limited health care systems, and over-stretched laboratory staff with limited supplies are often reluctant to perform quality control on a routine basis. However, unreliable and inaccurate laboratory diagnostic testing leads to unnecessary expenditures in a region already plagued by resource shortages, promotes the perception that laboratory testing is unhelpful, and compromises patient care. All these factors underscore the need for an external assessment system to monitor laboratory and test performance.

FUTURE DIRECTIONS

Strategic efforts to build laboratory capacity must be pursued urgently by partnerships between public (national and international), private, and commercial sectors to address this health care crisis. The current inequity in funding for laboratory diagnostics must be addressed, and funding organizations should be encouraged to balance the allocation of resources, with greater emphasis on laboratory diagnostics and supportive infrastructure. First, a paradigm shift that acknowledges the critical importance of basic laboratory testing is necessary to impact the perceptions and priority settings of clinicians, health care policy makers, and donor organizations. Second, donor and public efforts should be more unified to address regionally defined needs, with the goal of sustainability. Third, public officials and health care professionals must be made aware of the necessity of laboratory services to differentiate between diseases indistinguishable by clinical syndrome, to direct antimicrobial therapy, and to improve patient care.

In the short term, there should be an increased focus on providing basic laboratory testing by accurate and reproducible methods. Initiatives should be created

to ensure the accurate performance of malaria microscopic evaluation, hemoglobin testing, glucose determination, HIV testing, acid-fast bacilli smear, urinalysis, blood culture, and CSF analysis. In parallel, increased introduction and utilization of new technologies, such as non-culture-based methods (e.g., rapid malaria and HIV tests) for diagnosis of infectious diseases, offer the potential to overcome short-term logistical and educational barriers. These non-culture-based methods may (1) be performed on site in rural primary health care settings, (2) require minimal sample preparation or preservation, (3) be kit based (with reagents resistant to extreme temperatures), and (4) be performed with little technical expertise. Although somewhat costly and perhaps not sustainable in the long term, these approaches would allow more-wide-spread test availability and reproducibility without immediate infrastructure improvement.

In the long term, international donor institutions, scientific investigators, and nongovernmental organizations should partner with the public sector to actively strengthen the existing health care infrastructure. These groups must participate in the local training and education of future health care personnel by demonstrating the role of laboratory diagnostic testing in everyday practice, particularly its use to support or exclude alternative clinical diagnoses (e.g., cerebral malaria vs. bacterial meningitis; enteric fever vs. *Staphylococcus aureus* bacteremia) and to better direct antimicrobial therapy. Improved communication between clinicians and laboratories is essential to change physicians' perceptions and attitudes about the value of diagnostic tests, which, in turn, may lead to improved utilization. For example, many diagnostic procedures, including urinalysis, Gram stain and cell count in CSF samples, hemoglobin testing, microscopic evaluation for malaria, and microscopic evaluation of stool samples, can be performed in areas with limited resources, and their results can have im-

mediate impact on patient care. Finally, to ensure accurate and reproducible diagnostic testing (and thereby secure physicians' confidence in applying laboratory results to their daily practice), private donor and public agencies should assist in laboratory training as well as in the establishment of external quality assessment and accreditation systems. Efforts by the Centers for Disease Control and Prevention and the WHO to develop strategies to address these issues are already underway [34, 35]. Admittedly, strengthening the existing infrastructure in sub-Saharan Africa is a daunting task that may not be politically or financially popular, particularly among government-funded or commercially funded investigators who focus on their research needs alone. Advocacy groups need to encourage donor organizations to incorporate regional and national agendas into their programs and to build within, rather than circumvent, the existing infrastructure, to avoid the creation of redundant parallel systems. Sustainable solutions should be driven by regional and district needs, not by donor agendas.

Policy makers and health care providers must understand that accurate diagnosis is essential to the prevention and treatment of disease in sub-Saharan Africa, and, although the paradigm applied to this region must of necessity be different, it cannot, however, embrace a practice of medicine that routinely involves presumptive diagnosis based on clinical syndrome. No resource-plenty country would actively promote as part of national health care policy the routine use of empiricism without laboratory support in diagnosing disease. Advocacy is necessary to raise public expectation and the minimum standard of acceptable health care services. Building laboratory capacity to provide rapid, accurate, affordable, and reliable diagnostic tests will enable health care workers to deliver more-effective, life-saving treatment, thereby reducing mortality, optimizing the expenditure of health care re-

sources, and improving the quality of health care for this dramatically underserved population.

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