Diagnosis of Tuberculosis: Urgent Need to Strengthen Laboratory Services

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Editor's Note: The presence of this manuscript and the following editorial by the editor-in-chief (*Medical Care on the Brink: The Need for Re-Engineering Healthcare Services*) in the same issue was serendipity. However, the juxtaposition of the two articles was not. In fact, they were arranged as such to provide firsthand information from providers in sub-Saharan Africa who deal with the inadequacies of the healthcare system on the continent on a daily basis. The issue here is their inability to adequately diagnose tuberculosis using just sputum microscopy, especially in those with latent infections, coinfections with HIV, pediatric patients and those with extrapulmonary disease. They correctly state that, beyond microscopy, little is available for the detection of tuberculosis, even in the university referral centers. The reader should be mindful of the fact that this situation exists at the University College Hospital, Ibadan, Nigeria—one of the most distinguished medical institutions on the continent. The resulting impact on drug resistance, treatment failures/reinfections and the "prolonged period of contagious illness" all contribute to the spread of disease and the development of multidrug resistant strains of the bacillus. We support their conclusion that these laboratory services should be upgraded in hospitals at all levels and that regional centers of excellence should be designated. They point out the need for continuing medical education for providers and laboratory technicians as we do. They also stress the interrelationship of tuberculosis and HIV/AIDS with a 40% synchronous infection rate in Nigeria, all in the setting of a disease that is imminently treatable with existing resources that are reasonably priced. In summary, their experience provides real-time justification for the recommendations we make towards the re-engineering of healthcare services in sub-Saharan Africa. Although most governments of developed countries and many aid organizations have offices throughout sub-Saharan Africa, there does not appear to be much attention given to an organized effort at restoration of the medical infrastructure. Hopefully, these two manuscripts will find their way to the decision-makers in this arena.

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Tuberculosis (TB) is of great public health concern globally, and the impact is most felt in developing countries of Asia and Africa, where 95% of cases and 98% of deaths are attributable to the disease. The disease is poverty-driven and the situation is further worsened by absence of rapid diagnostic tools to facilitate early diagnosis of the illness, thus leading to widespread of the disease.

While attention is being focused on the HIV/AIDS pandemic, little is being heard of TB, especially in the areas of laboratory diagnosis despite the fact that the disease is the commonest cause of death in people living with HIV/AIDS.

The importance of a diagnostic laboratory in a TB control program cannot be overemphasized. Smear microscopy, which is the cornerstone of World Health Organization (WHO) 'DOTS' strategy for the treatment of TB, has many drawbacks among which is its inability to detect latent infection and the dependency of its sensitivity on a trained and motivated microscopist. Therefore, there is a need for a more reliable, sensitive and rapid diagnostic test to facilitate early diagnosis of cases and prompt initiation of therapy for a TB control program to have a meaningful impact in the community.

Key words: tuberculosis ■ HIV/AIDS ■ WHO ■ laboratory services

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INTRODUCTION

Diagnosis of TB is undisputed when the causative organism is isolated from the clinical specimen. The extent to which this is achieved depends largely on the diagnostic capacity of the mycobacteriology laboratory.[1]

Rapid and accurate diagnosis of symptomatic patients is a cornerstone of global TB control strategies. Remarkable progress has recently been made

towards upgrading the speed and quality of TB diagnostic services in developed countries, but for most of the world where TB is a large public health burden, these gains are still unrealized.[2] Thus, the primary laboratory tool supporting case detection in the vast majority of cases in disease-endemic countries remains microscopic examination of the stained sputum smear. The shortcomings of microscopic detection method seriously limit the extent and quality of its application, and ultimately, its impact in TB control. First and foremost, it requires equipment that is difficult to maintain in field settings, yields results that depend largely upon the studious attention of a trained and motivated laboratory worker and is notoriously insensitive, especially in the conditions which obtain during the screening program.[3,4]

A previous report shows that less than 20% of the roughly 8 million predicted annual cases of TB are identified as smear-positive.[5] This problem is made more critical by the rising incidence of smear-negative TB cases in countries where HIV infection is prevalent as in sub-Saharan Africa. Slow turnover time for reporting, occasioned by need for duplicate or triplicate sputum examinations, may erode the patient's confidence in laboratory services. Diagnostic delay for TB is considerable, especially in developing countries, resulting in increased morbidity and prolonged transmission. Thus, there is a need for more sensitive, more rapid and more patient-friendly diagnostic tools that will have a significant impact on disease control by abbreviating diagnostic delay.

The control strategy for TB advocated by the World Health Organization (WHO) is DOTS—Directly Observed Therapy Short Course—and this forms the basis of the WHO "Stop TB" campaign program.[6]

DOTS is a six-point strategy based on:

1. Government commitment to TB control
2. A regular supply of drugs, free at the point of delivery to the patient
3. Case finding based on sputum microscopy
4. Therapy administered under direct supervision
5. Training of staff
6. Audit of efficacy of the control program

Sputum microscopy as a case-defining diagnostic tool performs poorly in latent infection and in patients with TB/HIV coinfections. It is also not specific, as both pathogenic and environmental mycobacteria are indistinguishable. Apart from this, it is grossly inadequate for the diagnosis of pediatric cases and extrapulmonary infections.[2]

From the foregoing, accurate case detection is the Achilles heel of the DOTS strategy. The success of any TB control program depends on the ability to detect patients early enough, to institute curative therapy and interrupt the cycle of transmission. The costs generated by the TB diagnostic process are largely borne by the patients. Current low case-detection rates suggest that in many cases, they are not getting their money's worth.[2]

As for laboratory services beyond microscopy, little is available in most disease-endemic countries, even in referral centers. Drug resistance continue to be clinically defined in most areas, and this often leads to repeated treatment failures. The result of this, even where second-line drugs are available, is a prolonged period of contagious illness and opportunity for the spread of multidrug resistant strains (MDR)-TB. A growing appreciation of MDR-TB for global TB control and the development of strategies to combat it (DOTS-plus)[11] highlight the need for simple and inexpensive methods to screen for drug resistance. Similarly, new developments in the treatment of latent infection highlight the difficulty with the only current tool to detect it—tuberculin testing.

To have WHO target case-detection rates, funding to support laboratory capacity strengthening must be top on the agenda of the TB control program, as TB laboratories in many endemic countries operate at far below acceptable standards.[5]

Burden of the Disease

Tuberculosis is a preventable and curable disease. Research studies and clinical trials have shown that the treatment of this disease is not only effective but is also among the most cost-effective ways of prolonging healthy living.[2,7] Globally, there are more cases of TB in the world today than in previous epochs of human history.[7] The problems posed by this disease necessitated the WHO to label it a "global emergency" in 1993. The situation in sub-Saharan Africa is more worrisome. This is as a result of poor environmental living conditions, ignorance, poverty and, most importantly, the HIV/AIDS scourge. The way HIV infection has altered the epidemiology of TB is of great public health importance worldwide. While HIV infection accounts for 8% of new TB cases globally, the situation in disease-endemic countries of sub-Saharan Africa is pathetic, as it accounts for 40% of new cases of TB.[8]

HIV infection is the most potent risk factor for converting latent TB into an active transmissible lesion. As a corollary, active TB infection accelerates the progression of HIV infection into full-blown AIDS. Today, TB is the leading cause of death in persons living with HIV/AIDS worldwide.[9] Nigeria has the second largest number of HIV/AIDS persons in the world[10] whose morbidity and mortality due to TB infection cannot reliably be quantified, especially in the absence of high-quality laboratory services.

Situation on Ground

While TB can be diagnosed within hours in many wealthier industrialized countries with low burden of the disease, the situation in developing countries is pathetic, since diagnosis may take several weeks or months, even in specialized centers. Mycobacteriology laboratories where they exist rely on smear microscopy. Routine culture of acid-fast bacilli (AFB)-positive samples on egg-based media (Lowenstein–Jensen medium) is no longer carried out due to infrastructural decay. This diagnostic dilemma coupled with occasional inconclusive radiological findings poses a big threat to proper management of TB. The unfolding situation may lead to development of further resistant strains, whose incidence has been reported to be on the increase globally.[11]

Strategies and Way Forward

TB diagnosis should be given urgent attention in Nigeria, the most populous country in sub-Saharan Africa. The implementation of DOTS strategy and other control programs in India has been facilitated by upgrading TB laboratory services.[12] The first diagnostic upgrade that most TB laboratories should implement is correctly performed smear microscopy, which includes microscope maintenance and laboratory quality control. Sedimentation with sodium hypochlorite and centrifugation at 4,000 g for 15 minutes has been shown to improve the recovery yield of the organism.[13,14]

Services in TB laboratories should be upgraded, while regional specialist centers should be designated as reference laboratories. Furthermore, a TB laboratory in other specialist hospitals should also be equipped to perform basic tests and possibly carry out surveillance studies on MDR-TB strains.

Laboratory workers, especially technologists and technicians, should be motivated and encouraged. They should be sent to refresher courses to update their knowledge and skills. These are enormous tasks, which require the efforts of donor agencies and private sector participation, as the government at present has many issues to contend with. International collaborations are strongly needed to address the substantial gap that exists in TB research between poor resource countries and the developed world.

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