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International Tuberculosis Laboratory Consulting

Edward Desmond, Ph.D.[1] and Christopher R. Peter, Ph.D.,[2] [1]Microbial Diseases Laboratory, Division of Communicable Disease Control, California Department of Health, Richmond, CA and [2]2450 Grafton St., El Cajon, CA

Abstract

Improving tuberculosis (TB) laboratory test capacity internationally is essential to combat the increasing prevalence of drug-resistant TB in many countries throughout the world, which poses a direct public health threat to the United States. Microbiologists from the U.S. who plan to serve as consultants to assist in improving TB laboratories in resource-challenged countries should prepare for such work using available resources that are readily available from the Centers for Disease Control and Prevention, as well as the Global Laboratory Initiative of the World Health Organization (WHO). Identifying and networking with potential collaborators in various countries can help ensure success. Consultants should also become familiar with WHO-recommended TB laboratory test methods, available training programs, and tools for laboratory accreditation.

The Need for International TB Laboratory Consultations

Because drug-resistant TB is increasing worldwide, the need for laboratories to detect the drug-resistant form of the disease is increasing. This presents a challenge to the laboratory community that will be difficult to meet. This article describes the need for help from skilled microbiologists and outlines some of the skills and knowledge needed to develop the necessary infrastructure while avoiding pitfalls and mistakes.

In 2012, there were 9,954 reported cases of TB in the United States, dipping below the 10,000 mark for the first time since case numbers began being formally reported more than 60 years ago (1). The prevalence of multidrug-resistant (MDR) TB (defined as resistance to the two most effective drugs, isoniazid and rifampin) remained stable at 1.1%. However, other developments suggest that TB will continue to be a threat to public health in the U.S., and perhaps an increasing threat. In 2012, 63.1% of TB cases in the U.S. occurred in foreign-born individuals, up from 29% in 1993. The most prevalent countries of origin for foreign-born TB cases were Mexico, the Philippines, India, Vietnam, and China, where the prevalence of multidrug resistance is 1.8%, 5.6%, 4.3%, 3.7%, and 6.4%, respectively (2). Worldwide, the prevalence of MDR TB in new, untreated TB patients increased from 2.9% in 2005 to 5.7% in 2012 (2), and the prevalence of MDR TB in patients being re-treated after an initial treatment failure increased from 3.6% in 2005 to 8.9% in 2012. Thus, with foreign-born cases making up an increasing proportion of U.S. TB cases and with MDR-TB increasing worldwide and in the countries that are the source of immigration to the U.S., it seems inevitable that the problem of drug-resistant TB in the U.S. will increase.

In April 1993, the World Health Organization (WHO), recognizing the increased prevalence of TB worldwide, declared the disease to be a global emergency and predicted that TB would claim more than 30 million lives over the next decade unless action was taken. Similarly, in 2005, TB was declared an emergency in Africa, where the rate had doubled in 15 years, with the disease killing 1,500 people per day. WHO responded to this emergency by creating the Directly Observed Therapy, Short Course (DOTS) program, consisting of government commitment,

Corresponding Author: Edward Desmond, Ph.D., Microbial Diseases Laboratory, Division of Communicable Disease Control, Center for Infectious Diseases, California Dept. of Public Health, 850 Marina Bay Parkway, Room E164, Richmond, CA 94804. Tel.: 510-412-3781. E-mail: ed.desmond@cdph.ca.gov

case detection by smear microscopy, standardized treatment regimens, regular drug supply, and a standardized recording and reporting system. In 1995, WHO developed a promotion strategy for DOTS, and in the intervening years, the DOTS strategy has led to successful treatment of tens of millions of people and has saved millions of lives. However, with the DOTS strategy of case detection by acid-fast microscopy and the use of standard treatment regimens, patients with drug-resistant disease were not recognized, and many were treated with inadequate regimens. While standardized treatment regimens initially led to reductions in drug resistance, it can be argued that relying on acid-fast microscopy for diagnosis without drug susceptibility testing failed to prevent the increases in drug-resistant TB.

WHO now calls for "quality-assured bacteriology" rather than the use of acid-fast microscopy as the laboratory component of the DOTS strategy. It calls for introduction of culture and drug susceptibility testing, in a phased manner, along with acid-fast microscopy (3). Molecular methods have also been recommended for the detection of drug-resistant TB (4). However, serious obstacles remain before detection, treatment, and control of drug-resistant TB can be accomplished (5). The most challenging obstacles are the paucity of educated, trained, and skilled laboratory staff; poor quality management; and a lack of laboratory infrastructure in countries that have a high incidence of TB (6-8).

Plan to Combat XDR TB in the U.S.

In response to the threat of drug-resistant TB, the U.S. Centers for Disease Control and Prevention (CDC) convened a Federal Tuberculosis Task Force, which in 2009 published a Plan to Combat Extensively Drug-Resistant Tuberculosis (9). Extensively drug-resistant (XDR) TB is defined as infecting TB bacilli that are resistant to isoniazid, rifampin, at least one fluoroquinolone drug (for example, ofloxacin), and at least one injectable drug (amikacin, kanamycin, or capreomycin). Earlier, international attention had been riveted on an outbreak of XDR-TB in Tugela Ferry, South Africa. There, 53 patients, mostly HIV positive, contracted XDR-TB, and all but one died of the disease, on average within 16 days of presenting for medical attention. Some of those who died were hospital staff (10). The CDC plan (9) to combat XDR-TB in the United States included the following:

- Objective 1.1: increase awareness of the need to develop the necessary capacity and capabilities for the laboratory diagnosis of TB.
- Objective 5.2: develop integrated TB laboratory systems in high-burden countries and countries with limited resources.
- Action step 9.1.1: strengthen TB laboratory capacity to detect AFB smear-negative TB through support of global efforts to increase culture capacity in TB laboratories.
- Action step 12.1.3: support the Stop TB Partnership's Global Laboratory Initiative (GLI).
- Objective 23.2: increase capacity to perform sustained drug susceptibility testing on a routine basis (international).

Challenges to Improving TB Laboratories in Countries with a High Burden of TB

This Federal task force report clarifies that work to help control TB internationally is a priority for helping control TB in the U.S. The U.S. has a significantly large group of microbiologists who have expertise in quality management systems and mycobacteriology. However, U.S. microbiologists may lack awareness of some challenges they may encounter when invited to assist with improvement of TB laboratory practices in non-U.S. settings, particularly in resource-challenged countries (6-8).

Laboratory personnel shortages are common in countries with a high burden of TB. The causes include a lack of academic programs at universities to train a sufficient number of students in laboratory sciences. Low salaries that do not provide a living wage, particularly in government-operated laboratories, can be another obstacle to hiring qualified personnel. Training opportunities for laboratory personnel may be minimal and only provided to supervisors who do little hands-on laboratory work. Quality management systems may not be established or maintained.

Adequate laboratory infrastructure and functioning equipment are frequently unavailable. Electricity and water supplies may be intermittent, causing work disruptions and preventing proper storage of perishable supplies and reagents. Equipment maintenance may not be done because of a lack of technically qualified service personnel and replacement parts. Supply shortages may occur due to inadequate budgets, inefficient purchasing systems, and transportation problems. Once a consultant becomes familiar with the issues faced in a developing country, solutions typically require many steps over a long period.

Helpful Resources for TB Laboratory Consultants

Fortunately, there are a number of effective tools and resources consultants can use to help improve TB laboratory services in resource-constrained countries. Among them are the documents found on the WHO/GLI website (8) shown in Table 1 below.

A particularly valuable resource among those listed above is the GLI stepwise process towards laboratory accreditation (12). The process is a tool for the stepwise implementation of a quality management system in TB laboratories to prepare for International Organization for Standardization (ISO) 15189 accreditation (13). For every task in each step, the tool includes a brief description of what needs to be done, why and how it should be done, and who should do it. Links are provided for reference documents, procedures, and sample templates as resources. The tool is based on the Clinical Laboratory Standards Institute's 12 quality system essentials (14) and is to be completed in the phases shown in Table 2.

To facilitate completion of the tasks required for each phase of the GLI stepwise process, a roadmap tool is included. The roadmap guides the user through an easy-to-follow sequence of tasks, beginning with the initial step of creating a commitment among staff and key personnel to work toward laboratory accreditation. Checklists are also provided to keep track of progress.