Tuberculosis and HIV--Needed: A New Paradigm for the Control and Management of Linked Epidemics

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Medscape General Medicine. 2007;9(3):62. ©2007 Medscape
Posted 09/25/2007

Introduction

Tuberculosis (TB) and human immunodeficiency virus (HIV) disease have been closely entwined since the early years of the HIV/AIDS pandemic. The 2 conditions overlap in their epidemiologic characteristics and clinical manifestations and are both clothed in stigma. They individually carry the risk of creating social, economic, and political instability, which is markedly worsened when they affect a region in concert. The overwhelming burden of disease due to both TB and HIV is borne by resource-limited countries[1] and the hardest hit among these are in sub-Saharan Africa.

In sub-Saharan Africa, the HIV epidemic is accelerating what was already a massive TB epidemic, with the incidence rate of TB increasing from 146 per 100,000 in 1990 to 345 per 100,000 in 2003.[2] Each disease contributes to the morbidity and mortality of the other. TB is now the leading cause of death among persons with HIV disease. HIV increases the risk of reactivation of latent TB infection (LTBI) and progression to active TB disease more than any other known risk factor. In some countries, the percentage of patients with active TB who are coinfected with HIV is now greater than 60%.[2] Even with appropriate management of TB, patients with HIV co-infection have increased mortality as a consequence of HIV-related complications.[3]

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Diagnostic and Clinical Challenges for Resource-limited Settings

The rising number of TB/HIV coinfected patients in sub-Saharan Africa, as well as in other resource-limited areas, has brought with it and intensified the need to identify solutions for diagnostic, therapeutic, and management issues at the interface of both diseases. The recent documentation of multidrug resistant (MDR) and extensively drug resistant (XDR) TB among persons coinfected with HIV and its association with extremely high mortality in South Africa[4] calls for heightened attention to these issues and the urgent need for their solutions. Knowledge and experience in the separate diagnosis and management of TB and HIV is extensive in resource-rich settings and in some resource limited settings. However, knowledge and experience in the diagnosis and management of TB/HIV co-infection is available in resource-rich settings but severely limited in resource-poor settings.

HIV co-infection can complicate the clinical presentation and diagnosis of active TB and limit the sensitivity of the acid-fast bacilli sputum smear, the most widely (and often the only) available TB diagnostic method in resource-limited settings.[5,6] How to overcome this diagnostic obstacle in resource-limited settings is neither known nor well studied. New TB-specific interferon gamma release assays are beginning to be studied in TB-HIV co-infected individuals in resource-limited settings[7,8] as are new rapid mycobacterial culture and drug susceptibility methods that have been developed;[9,10] how and if these tests can be used, and whether their associated cost will be prohibitive in these settings is yet to be determined.

Likewise, the treatment of HIV in the setting of active TB may be complicated by several factors, including additive toxicities of antiretroviral and anti-tuberculous medications, drug interactions, risk of immune reconstitution events, and difficulty in adherence with multiple medications.[11] Successfully overcoming these hurdles in resource limited-settings that often have a dearth of diagnostic testing capabilities and narrow choices of antiretrovirals and anti-tuberculous medications requires creative and inventive solutions. While the coexistence of TB and HIV epidemics creates added challenges, caring for coinfected patients offers opportunities for developing new paradigms to address the co-epidemics. Through innovative operational research, collaborative training, and integrated treatment efforts, these may improve the management and outcome of both diseases.

Current vs Alternative Care and Treatment Paradigms

Although increasing numbers of patients have both conditions, current national TB and HIV programs remain largely separate with varying levels of interaction and communication. This programmatic separation often extends through the entire health care system. While this characteristic is true of developed countries as well, the far greater resources available in developed settings can often compensate for this division and provide adequate care for co-infected patients. In resource-limited countries, however, this separation of programs results in care of co-infected patients that is often fragmented, uncoordinated, and unsuccessful. It is essential, in areas of high HIV prevalence and TB burden, that national TB and HIV programs collaborate and that care for TB/HIV co-infected individuals is integrated at the healthcare delivery level.

Encouragingly, because the leadership of these often separate TB and HIV programs is usually situated within the structure of National Ministries of Health, there is the opportunity for these latter institutions to play a critical role in establishing and strengthening a coordinated approach to both diseases thereby ensuring communication and collaboration between the 2 programs. Rwanda is an excellent example of such collaboration at the central, Ministry of Health level.[12] For effective service integration to take hold in a widespread manner at the healthcare delivery level, collaboration has to first exist at the national level. In some primary care settings, where resources are extremely limited and personnel even more so, TB/HIV collaboration and service integration does occur, but often in an unsupervised, unstructured, and therefore, suboptimal manner.

The figure depicts stylized representations of 2 different paradigms for interactions between HIV and TB programs and service delivery sites: the common current paradigm and a proposed alternative paradigm. The current common paradigm is characterized by separate and distinct programs with little coordination or overlap. The alternate paradigm emphasizes the need for increased communication, collaboration, and integration of services, in an effort to improve the care and treatment of TB/HIV co-infected patients.

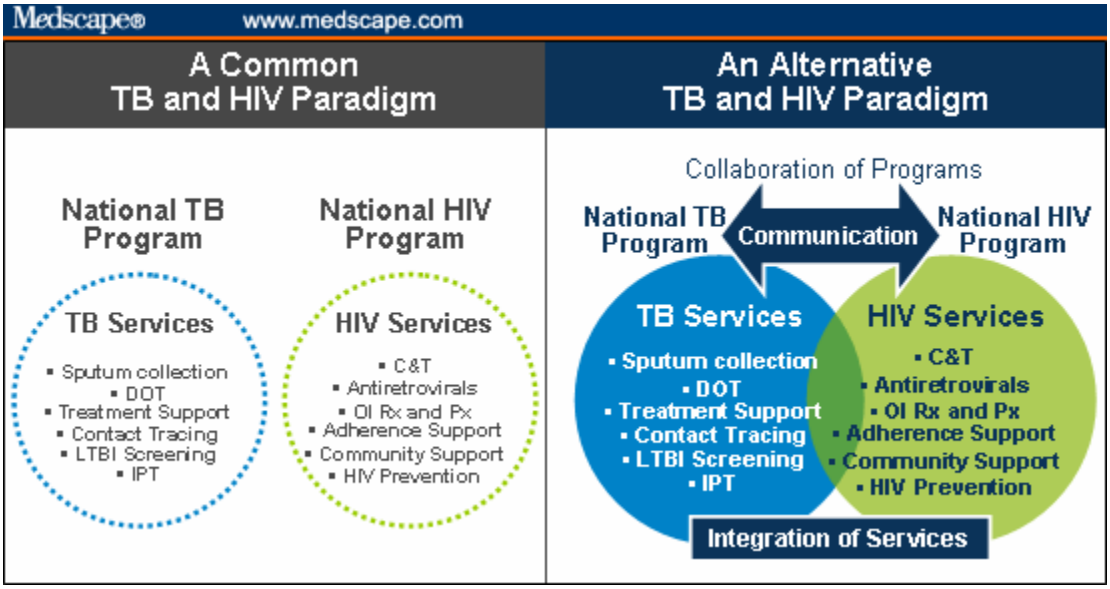

Figure.

Common and alternative TB and HIV program paradigms.

C&T = Counseling and Testing; DOT = Directly Observed Therapy; HIV = Human Immunodeficiency Virus; IPT = Isoniazid (INH) Preventive Therapy; LTBI = Latent Tuberculosis Infection; OI = Opportunistic Infection; Px = Prophylaxis; Rx = Treatment; TB = Tuberculosis

Achieving this alternative paradigm requires assessment of various models of collaboration and integration and their relevance to the specific setting. These models may range from maintenance of separate programs and services with enhanced communication and referral mechanisms between them to programs that partially or fully integrate the services they provide. A variety of models of collaboration and integration will be necessary to suit the diverse characteristics of a range of settings, for example, urban vs. rural, high vs. low TB incidence, high vs. low HIV prevalence. Answers to important question are needed such as: (1) at what level of prevalence of TB/HIV co-infection will integration be of most benefit, (2) how will population density affect the paradigm of collaboration and integration, and (3) how will the cost of

implementing integration influence national decision-making? Ongoing efforts such as those of the National Institutes of Health-sponsored International epidemiologic Databases to Evaluate AIDS (IeDEA) study,[13] the Consortium to Respond Effectively to the AIDS/TB Epidemic (CREATE),[14] and the Zambia and South Africa Tuberculosis and AIDS reduction study (ZAMSTAR) may help answer some of these questions.

Some important progress toward increasing collaboration between HIV and TB programs and integrating services is underway. The World Health Organization (WHO) has formulated recommendations regarding collaboration and integration and has emphasized the importance of addressing TB/HIV co-infection in its new "Stop TB" strategy.[15,16] In Rwanda, screening for TB at enrolment into HIV care and treatment programs and at follow-up visits using simple symptom questionnaires is being implemented.[17] Additionally, some programs, most notably Malawi's, have already begun to adopt the public health-oriented strategies of TB care in newly developed HIV treatment programs.[18] National-level examples such as these can serve as models that other countries can adopt and implement.

Several individual projects assessing the feasibility of various collaborative and integrative efforts at the healthcare delivery level in urban and rural areas have been carried out or are ongoing. In Rwanda, integration of TB and HIV services at a district hospital increased HIV counselling and testing of TB patients and improved TB screening and case detection in HIV-infected individuals enrolled into care.[19] In rural KwaZulu-Natal, once-daily antiretroviral therapy for patients with HIV and TB is successfully being combined with the existing TB directly observed therapy program and is using community-based treatment supporters.[20] In Haiti, combined treatment of both TB and HIV has been shown to be effective both in rural settings using a community-based treatment model[21] and in urban settings using a clinic-based approach.[22] These different experiences in integration of TB and HIV care and treatment are highly encouraging while at the same time their examples highlight the technical, programmatic, staffing and scale-up challenges that remain and demonstrate that although broad program principles of TB/HIV collaboration and integration are essential, specific program components and designs will vary between and even within countries.[23]

Strengthening the Parts to Strengthen the Whole

It is important to acknowledge that it may not be possible to adopt a collaboration strategy in all settings in which HIV and TB epidemics overlap. One major barrier is the current situation that TB programs face, that is, their struggle to cope with rising caseloads driven by the HIV epidemic in the setting of insufficient structural and human resources. The additional responsibilities needed to address TB/HIV co-infection (such as on-site counselling and testing for HIV and effectively addressing issues of TB transmission and infection control) may not be feasible in already overburdened TB programs in certain settings. Similarly, national HIV programs are overwhelmed by current HIV treatment scale-up efforts and by the large number of patients seeking care and treatment. They face enormous challenges, including the need to train clinical staff, establish new laboratory services for patients with HIV and secure an uninterrupted supply of antiretroviral therapy. Finally, national TB and HIV programs in many countries may have limited authority to implement collaborative models of care, either at the national or local level.

Action to overcome these barriers is urgently needed. An infusion of resources to strengthen TB programs, on the same scale as those received by national HIV programs, is critical. These resources could be used to improve TB diagnostic capabilities, especially as they pertain to HIV-infected patients, and to expand the number of trained TB treatment providers and directly observed therapy supporters. As HIV programs establish their care and treatment programs, attention to issues of TB co-infection such as active TB case-finding, must be included, because TB represents one of the most common opportunistic infections that threatens the health of patients with HIV and carries a dangerous risk of transmission of both drug-susceptible and drug-resistant TB to others, particularly those with HIV infection.[4] Lastly, the World Health Organization has advocated the creation of national TB/HIV working groups, which would have the authority to oversee increased collaboration and integration of TB and HIV programs and services at both national and local levels.

New Ways of Delivering Integrated Care With Nontraditional Healthcare Providers

A critically important issue to both TB and HIV programs is the availability of adequately trained healthcare workers who will be able to provide the breadth of care necessary for TB/HIV coinfected patients. Given the limited number of clinical providers currently available in resource-poor settings, it is necessary to evaluate the feasibility of using nonprofessional healthcare workers to serve in auxiliary roles, such as treatment supporters or directly observed therapy workers, which provide support to patients' adherence efforts and monitoring for adverse reactions for TB/HIV coinfected patients.

These healthcare workers can be drawn from community or family members, who are a rich source of support available in many resource-limited settings.[24] The use of these facilitators and a community care model has been shown to be effective for delivering TB therapy in other resource-limited settings[25-27] and may be associated with favorable clinical and virologic outcomes in patients with both TB and HIV disease in need of treatment.[21,28] Efforts are necessary to determine how to effectively and safely adapt these models to serve for the simultaneous treatment of both TB and HIV.

Conclusion

The collaboration between HIV and TB programs and services has been hampered by their separate traditions and practices. TB programs are characterized by firmly established algorithms, standardized measures and outcomes, and are designed to treat large numbers of patients with few resources. On the other hand, HIV care and treatment programs are characterized by a patient-centered approach with rapidly evolving treatment paradigms that necessitate frequent revisions of treatment guidelines, accompanied by the need to intensively monitor for efficacy and toxicity over a patient's lifetime. The nuances, subtleties and added complexities of TB diagnosis and appropriate management, including the treatment of drug-resistant TB, in the context of HIV co-infection must be recognized and incorporated into TB care, as must the need for a large-scale public health approach for the management of HIV in resource-limited settings. Each discipline needs to accommodate the other. For the TB world, HIV should no longer be seen as an intruder and must be accepted as part of the current and future reality. For the HIV world, the accumulated experience acquired over the longer history of TB must be valued and can serve as a source of important lessons. How to best harmonize these 2 approaches is at the core of what needs to be rapidly accomplished to effectively manage and control both TB and HIV. Resources provided by international funding sources encouraging and even requiring such harmonization can contribute to this effort but a new spirit of accommodation and collaboration is also required to greatly benefit patients with TB and HIV and establish a new paradigm for the future.

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Disclosure: Simon J. Tsiouris, MD, MPH, has disclosed no relevant financial relationships.

Disclosure: Neel R. Gandhi, MD, has disclosed no relevant financial relationships.

Disclosure: Wafaa M. El-Sadr, MD, MPH, has disclosed no relevant financial relationships.

Disclosure: Gerald Friedland, MD, has disclosed no relevant financial relationships.