



In Brief for the 21st Century

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TUBERCULOSIS IN AFRICA OLD SCOURGE, NEW ALLIANCE

It is estimated that 1.86 billion people, one third of the world's population, are infected with the tuberculosis (TB) tubercle.¹ TB kills 8,000 people a day, or almost 3 million people a year. It kills more adults than malaria and it is one of the leading infectious causes of mortality for women globally, surpassing all causes of maternal mortality combined.² Tuberculosis is also the leading killer of HIV-positive individuals, causing over 30 percent of AIDS deaths in Africa.

BACKGROUND

Tuberculosis is not new to sub-Saharan Africa. It was well documented in the 1897 colonial case records of Albert Cook at Mengo Hospital in present day Kampala, Uganda.³ Prior literature suggests that tuberculosis existed in precolonial Africa in several regions. Fragments of the spinal column from Egyptian mummies from 2400 BC show definite pathological signs of tubercular decay. *Mycobacterium tuberculosis* has taken a heavy toll on public health since the time of antiquity and it still does. For a short while, TB was thought to have been conquered in the developed world and was forgotten until the problem of antimicrobial resistance became apparent. But tuberculosis never really disappeared in Africa. Poverty, overcrowding, urban sprawl, malnutrition, civil wars, natural disasters, and refugees and displaced persons all combined to ensure that it remains one of the most important public health threats.

The twin epidemics of HIV/AIDS and tuberculosis are causing chaos not only in Africa, but worldwide. As a result of the recognition of the reemergence of TB, as well as other infectious diseases, and the global threat to be incurred by ignoring their presence, the U.S. Congress in 1997 mandated the U.S. Agency for International Development to revise its health strategy to include a strategic objective reducing the threat of reemerging infectious diseases. USAID's Infectious Diseases Initiative is a direct outcome of that congressional mandate. The initiative has also stimulated



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A patient in a Zimbabwean tuberculosis ward

thinking on how to leverage other donor resources and develop partnerships in support of TB prevention and control activities.

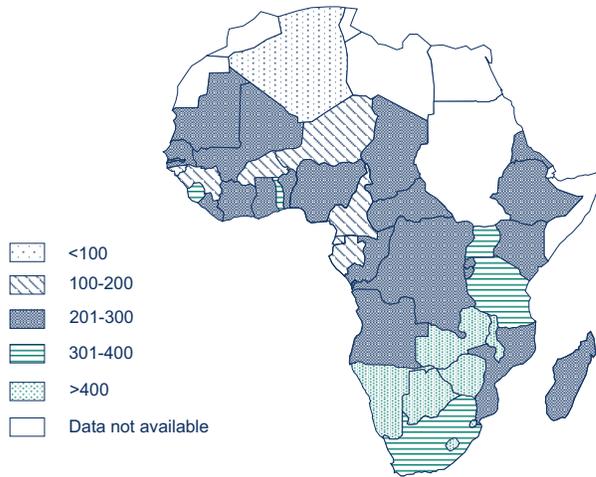
MAGNITUDE OF THE TB PROBLEM

Twenty-two countries account for 80 percent of the world's tuberculosis cases, including eight African countries: Nigeria, South Africa, Ethiopia, the Democratic Republic of Congo, Tanzania, Kenya, Uganda, and Zimbabwe. Other African countries, particularly those in southern Africa, have very high incidence rates, but because their country populations are relatively small, they do not make this list. The map on page two clearly shows the high incidence in southern Africa, intermediate incidence rates in the East African and coastal West African countries, and lower rates in inland West and Central Africa. Overall, sub-Saharan Africa has the highest TB incidence rate per capita (259 per 100,000 in 1997) when compared to other regions worldwide.

The co-infections of TB and HIV have had a devastating impact on national tuberculosis control programs. There are countries in Africa where 50 to 70 percent of TB



Estimated Per Capita Incidence Rates of Tuberculosis in 1997



Source: "Global Burden of Tuberculosis." *Journal of the American Medical Association*, August 18, 1999, Vol. 282, No. 7. Rates are per 100,000.

cases are co-infected with HIV. The staggering numbers are overwhelming country programs already struggling to provide a consistent and reliable anti-TB drug supply. Not only is the drug supply stretched to the limit, but the entire system is beset with problems from accurate diagnosis, to demands on the laboratory, to the need for additional trained personnel to deliver the services.

FINANCIAL BURDEN OF TB

The financial burden of the disease affects men and women equally, but it is particularly problematic if the breadwinner is affected. Even if drugs are provided free, there are travel costs, loss of time from work, and the cost in time and energy of the accompanying person. In a study from urban Zambia, pre-diagnosis costs were substantial.⁴ In seeking diagnosis, patients incurred a mean total cost equivalent to 127 percent of their mean monthly income (US\$59). Nonmedical costs posed sizeable economic constraints. Patients' mean transportation spending represented over one quarter of these costs. More than 90 percent of patients who worked before onset of their illness lost time from work. Patients lost on average 18 workdays before diagnosis. Caregivers incurred costs equivalent to 31 percent of their mean monthly income. All these costs were prior to diagnosis and clearly may deter many patients from presenting their TB-related symptoms to medical facilities.

A study from Burkina Faso looked at the economic costs of illness for rural households.⁵ Time costs amounted to the largest proportion (73 percent) of total household costs. Of the total amount of illness-related time loss to the average household, 45 percent

was due to the fact that healthy household members accompanied their sick kin. Additionally, economic costs vary seasonally; the harvest time, when everyone is needed to bring in the crops, is an inopportune moment to fall ill. Although there is no specific study to cite, it would be reasonable to assume that the financial burden of tuberculosis on women, who are unlikely to control their own funds, would place additional constraints on their decision to seek care.

WOMEN AND TB MORTALITY

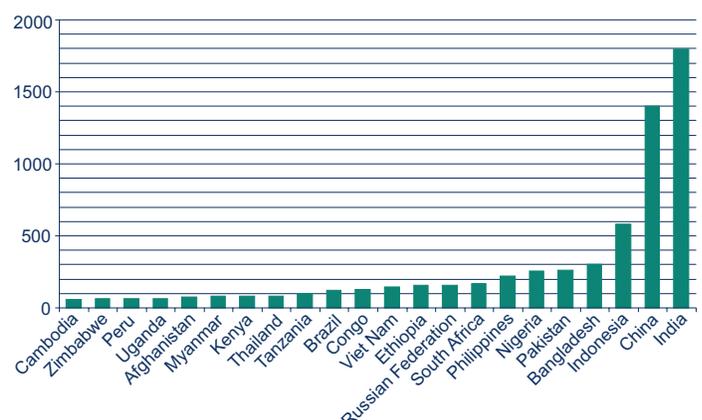
Data presented at a May 1998 meeting co-sponsored by the World Health Organization and the Swedish International Development Cooperation Agency on TB and gender showed unprecedented levels of infection and deaths among women and girls. Over 900 million women are infected with TB worldwide, mainly between the ages of 15-44. Annually, 1 million die, and 2.5 million get sick.

This makes TB one of the leading infectious causes of death among women of reproductive age. Tuberculosis killed more women globally in the reproductive age group (605,000) than all other causes of maternal mortality combined (493,000).⁶ Data from the *WHO World Report 1999* shows that the majority of TB deaths occurred in Asia followed closely by Africa. (See chart page 3.) Fully 70 percent of all female TB deaths occurred in these two regions.

Gender and TB

It is important to distinguish between the terms "sex" and "gender." Gender is used to distinguish those differences between men and women that are socially constructed from those that are biologically given. Case notification rates from countries with a high prevalence of tuberculosis suggest that TB may be less frequent among females. Globally, the ratio of female to male TB cases notified is 1:1.5-2.1. Seventy percent more

Estimated Incidence of TB: Top 22 Countries in 1997



Source: Dye, C., S. Scheele, P. Dolin, V. Pathania, and M.C. Raviglione. "Global Burden of Tuberculosis: Estimated Incidence, Prevalence, and Mortality by Country in 1997." Rates are per 1,000.

smear-positive male than female TB patients are diagnosed and notified to WHO every year.⁷ It is unclear whether the higher prevalence rates in men are due to biological mechanisms placing them at higher risk of developing tuberculosis or to under notification for women, or both.

A recent WHO research workshop on gender and tuberculosis concluded that a combination of biological and social factors is responsible for these differences, and that research within this field is vastly insufficient. One factor thought to play a role is the difference between male and female access to health services. However, a range of social factors such as access to money to pay for health services and transport to reach them and the social stigma of the disease, and cultural factors such as the unstated requirement that women obtain permission from their husbands or other males to seek care could all produce inequalities in access to health services. Few studies have attempted to document the different patterns of health service use among women and men in developing countries.

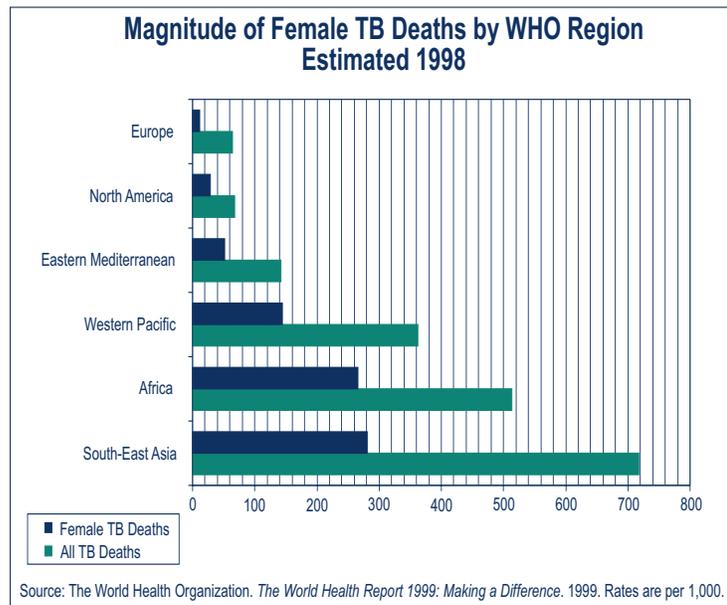
The Impact of Women's Illnesses

The impact of women's illness has consequences not only for themselves but also for their families. A number of studies have shown that women wait longer to report their illness than men.^{8,9} A long-term study in Matlab, Bangladesh, found a strong correlation between maternal survival and child survival to age 10, particularly for girls. A father's death was associated with an increase in child mortality of 6 per 1,000, irrespective of the child's gender. However, increases in child mortality of 50 per 1,000 in sons and 144 per 1,000 in daughters were found to be associated with a mother's death.¹⁰ While there do not appear to be specific studies looking at the impact of TB in women on other household members, it is suggested that younger children are more likely to be infected if their mother has TB than if their father has TB. Tuberculosis in women puts their children at risk for infection, disease, and death. This triple threat demonstrates that detecting and treating tuberculosis in women is absolutely vital to ensure the survival and well being of their children. Clearly, further research in Africa is necessary to understand the nature of the burden of TB not only on women, but also on men.

Tuberculosis and Pregnancy

At various times, pregnancy has been thought to improve, worsen, or have no effect on the prognosis of tuberculosis. Since the advent of anti-tuberculosis chemotherapy, the controversy regarding the impact of pregnancy on the occurrence and prognosis of TB no longer has the same significance. The important lesson

remains that active tuberculosis in pregnant women needs to be diagnosed and treated for the sake of the children as well as for the women. However, the diagnosis is often difficult to make. There is controversy as to whether the form or presentation of tuberculosis changes in pregnancy. A prospective study from London among recent, pregnant immigrants from the Indian sub-continent and Somalia found that 9 of 13 patients had extra-pulmonary tuberculosis with few symptoms.¹¹ HIV co-infection was absent. The median delay between onset of symptoms and diagnosis was



seven weeks (range 2-30). The response to standard treatment was excellent and all patients were cured.

The HIV/AIDS pandemic has certainly added another dimension to the relationship between TB and pregnancy. In some countries, sentinel surveillance shows that one in four pregnant women is HIV positive. Despite this, there are no data on the proportion of these women who are co-infected with TB, or on the proportion with overt tuberculosis. Given that about 50 percent of women in the child bearing age living in sub-Saharan Africa have latent TB infection, and 25 percent are infected with HIV, then at least one in eight pregnant women would be co-infected. Because a co-infected person has at least an 8 percent chance of developing active tuberculosis each year, it is possible that 1 in 100 pregnancies could be complicated by HIV-related tuberculosis.

Not only does HIV infection have a deleterious effect on the course of tuberculosis, there is also evidence that the converse is true and may lead to significant increases in HIV viral load levels.¹² While HIV infection definitely predisposes individuals to the development of active tuberculosis, it is not clear whether pregnancy increases the risk. A study in Kenya indi-



Bob Maddy—World Health Organization

A grandmother caring for the child of her HIV and TB infected granddaughter

cated that recent pregnancy in HIV positive women predisposed them to the development of active tuberculosis, but other studies reveal no such association.^{13, 14} The role of preventative anti-tuberculosis therapy for co-infected women during pregnancy also requires careful consideration. There may be a need for guidelines on screening for tuberculosis during pregnancy, particularly as they relate to developing countries, but little research on the effectiveness and cost-effectiveness of such treatments has been conducted.

THE WHO COMPREHENSIVE TB CONTROL STRATEGY

Tuberculosis continues to spread globally at an alarming rate, despite the existence of a highly cost-effective intervention strategy known as DOTS (directly-observed treatment, short-course). It was developed and field tested in Africa, but is the basis for control worldwide. The DOTS strategy has five key components:

- ◆ Government commitment to sustained TB control activities
- ◆ Case detection by sputum smear microscopy
- ◆ Standardized treatment regimen of six to eight months for at least all sputum smear positive cases, with directly-observed therapy for at least the initial two months
- ◆ A regular, uninterrupted supply of all essential anti-TB drugs

- ◆ A standardized recording and reporting system that allows assessment of treatment of each patient and of the TB control program performance overall

Government commitment is the cornerstone for any sustained TB control and is essential to ensure that the other four components can be implemented. Until the late 1980s, TB was a forgotten disease, but HIV/AIDS and the rise of multidrug-resistant TB (MDR-TB) has forced the world to confront the problem.

The other four technical components of the DOTS strategy are very critical to success. Case detection and diagnosis should be done by sputum smear microscopy. It is not only the most cost-effective method of screening suspected pulmonary TB cases, but the only one able to identify the most infectious cases. Short course chemotherapy refers to a treatment regimen that lasts six to eight months and uses a combination of powerful anti-TB drugs such as rifampicin, isoniazid, streptomycin, and ethambutol. Standardized treatment regimens are based on whether a patient is newly diagnosed or previously treated. An essential component in the strategy is direct observation of treatment—watching patients taking their medicines—and is essential at least during the initial two-month intensive phase of treatment. Lack of adherence to the drug regimen is a major problem of any TB program, but patients should not be expected to bear the sole responsibility for completing treatment. A range of support services is required to ensure that patients complete their treatment. Of course, there is no program without a steady and reliable system for the supply of drugs. And lastly, a recording and reporting system must evaluate patient as well as program progress.

Completing standard TB therapy requires commitment, but even resource poor African countries have shown that DOTS can work. Nonetheless, only 32 percent of African countries (15 of 47) have fully implemented the DOTS strategy.

DELIVERY OF TB SERVICES TO THE COMMUNITY

Access to effective tuberculosis care is not readily available in sub-Saharan Africa. Government health services reach only a small proportion of the population due to inadequate health service infrastructure, insufficient decentralization, and human and financial resource requirements that exceed national capabilities. If health facilities cover less than half of a population, the WHO DOTS strategy will be more difficult to implement. It particularly affects a patient's ability to adhere to a long treatment schedule. There is an immediate need to evaluate community contributions to tuberculosis care in sub-Saharan Africa, where the HIV-fuelled TB epidemic is outstripping the ability of health services to cope.

Nine district-based projects in seven countries (Botswana, Kenya, Malawi, Namibia, South Africa,

Uganda, and Zambia) are testing different community approaches to determine how well they are able to support the delivery of TB drugs and to directly observe treatment of patients.¹⁵ All the studies will assess ways to identify and mobilize appropriate community organization; methods to train and supervise community members; strategies to develop and introduce recording and reporting systems; how to distribute anti-tuberculosis drugs and prevent their potential abuse, particularly of rifampicin; and the linkages necessary to general health services. The ongoing district-based projects are at various points of implementation but encouraging provisional results are emerging from some sufficiently advanced studies. TB treatments delivered by community workers consistently produce higher cure and treatment completion rates when compared to those of health facilities. Providing care that is convenient and accessible to tuberculosis patients is essential to ensure successful treatment and cure. Community delivery of TB services benefits not only those co-infected with TB and HIV, but also those with active TB alone. It is a win/win situation for patients and the community.

PREVENTION AND THE ROLE OF PREVENTIVE THERAPY

To prevent the spread of tuberculosis in communities, you have to identify and completely treat active (infectious) cases of tuberculosis. In communities where there is high prevalence of TB and HIV, there is an even greater need to identify and treat these cases. Since TB is the most common opportunistic infection in HIV positive individuals in Africa, many researchers have argued for the role of preventive isoniazid (INH) chemotherapy. It is well known that a majority of the population in sub-Saharan Africa has come in contact with the TB bacterium and have latent infections. Rather than wait passively for the TB to be activated, many have argued forcefully for the need to prevent infection. Protocols are being developed where, as part of the prevention and care continuum, voluntary counseling and testing centers offer a comprehensive package of HIV/AIDS/STD/TB prevention, care, and support at the district level. Specific components would vary but could include the following:

- ◆ Increase access to voluntary HIV counseling and rapid HIV testing
- ◆ Improve TB case finding, treatment completion, and cure rates among people living with HIV/AIDS
- ◆ Provide access to sustainable INH preventive chemotherapy and co-trimoxazole prophylaxis for people living with HIV/AIDS, taking into account feasibility and cost-effectiveness

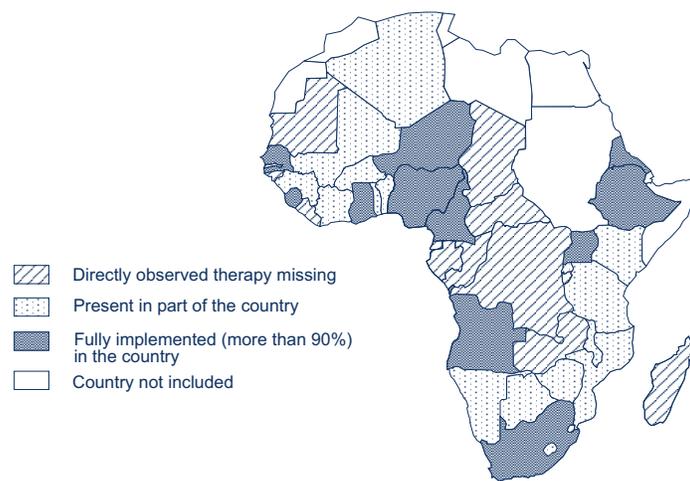
- ◆ Develop and advance comprehensive HIV/AIDS/STD/TB care and referral to ensure continuity of care for people living with HIV/AIDS

This type of package not only provides comprehensive care to those infected, but encourages others in the community to come forward for testing as options for care and support become more visible.

REFUGEES IN AFRICA AND TUBERCULOSIS

The United Nations High Commission for Refugees estimates that there are 21.4 million refugees in the world*; 29 percent (6.2 million) are found in Africa. Of the 10 major refugee populations around the world, five African countries have the largest numbers of their

Summary of DOT* Distribution in African Regions



Source: Global Tuberculosis Control, WHO Report 1999
*Directly Observed Therapy, one of five components of the DOTS Strategy.

citizens in adjacent host countries: Somalia (525,000), Burundi (517,000), Liberia (487,000), Sudan (351,000), and Sierra Leone (328,000). Tuberculosis is well recognized as a health problem among refugee populations. The crowded living conditions, coupled with the underlying poor nutritional status of refugee populations, may fuel the spread of the disease. Although usually not a leading cause of mortality during the emergency phase, TB often emerges as a critical problem once measles and diarrheal diseases have been adequately controlled. In Somali refugee camps in 1985, 26 percent of adult deaths were attributed to tuberculosis. In eastern Sudan, two refugee camps reported that between 38 and 50 percent of all deaths were caused by TB during the 9 to 10 month period after the camps opened.¹⁶

The decision whether to start treatment in refugee camps needs to incorporate factors including the

* Refugees (11.5 million), returnees (1.9 million), asylum seekers (1.3 million), and internally displaced persons (6.7 million).

uncertain duration of stay, frequent changes of camp locations, ease of mobility of the refugees, camp organization, personnel with TB expertise, and management capability to supervise therapy and follow-up with nonadherent patients. Consideration must also be given to the consequences on host countries of *not* controlling TB in the refugee population. If refugees easily mingle with the host population, nontreatment could place nationals at increased risk. Before any TB control program is instituted, a clear policy covering case definition, case finding, treatment regimen, and supervision of chemotherapy must be agreed on by all parties providing health services to the refugees.

The selection of a first-line chemotherapy regimen should generally be consistent with the national policy of the host country ministry of health and internationally accepted guidelines. The WHO TB control strategy in refugee situations is the same DOTS strategy outlined above.¹⁷ There is still some controversy as to whether TB patients in refugee situations should be routinely offered voluntary counseling and testing services for HIV. A successful TB control program depends on good management, close supervision, and the cooperation of the refugee community. To ensure success, a community education program must be established to educate the population about TB, dispel any myths, and ensure adherence to the treatment.

CHALLENGES FOR EFFECTIVE TB PREVENTION AND CONTROL IN AFRICA

MultiDrug-Resistant TB

MDR-TB, while more of a problem in other parts of the world, is starting to occur in African countries. MDR-TB is caused by inconsistent or partial treatment of cases due to a variety of factors such as poor adherence to treatments, use of improper drugs, and an unreliable drug supply system. From a public health perspective, poorly supervised and incomplete treatment of TB is worse than no treatment at all; if TB cure rates are below 70 percent, transmission continues and drug resistance starts to increase. And MDR-TB is more difficult and more expensive to treat. Paradoxically, MDR-TB has been more of a problem in developed countries. In Africa, the problem has been an overall lack of anti-tuberculosis drugs, preventing the start of treatment. Of course, the cost in terms of mortality is high. The DOTS strategy is particularly important for Africa, for if it is implemented correctly, it can prevent the development of MDR-TB.

There also needs to be a quality assurance element in the program that reviews the microscopy work in a country's laboratory network. A central lab needs to confirm a certain percentage of the diagnoses. Health centers and district labs also need a place to refer suspected resistant organisms for further evaluation.



A nurse with patients in a Zimbabwe tuberculosis ward

Bob Maddy—World Health Organization

Beliefs and Health-Seeking Behavior

One study in Uasin Gishu, Kenya, showed that women and men share many beliefs concerning the causes of TB and health-seeking behavior.¹⁸ TB treatment is considered long and difficult, so health-seeking behavior was put off for several months to a year. Prolonged self-treatment and consultation with traditional healers, as well as the social stigma attached to the disease, increased a patient's delay in seeking treatment. Many felt that TB was not completely curable. The community's attitude towards TB was to avoid contact not only with the patient, but also the patient's family.

The Stigma Of TB

Stigmatization of TB patients is almost universal, but especially affects women. The research is most telling from Asia. Studies from Sialkot, Pakistan, show how tuberculosis affects women.¹⁹ For unmarried girls, marriage engagements might be broken. Parents might delay treatment for marriageable girls. Married women often tried to hide their illness for fear of desertion, rejection, or blame for developing the disease. Divorce was another indirect consequence of tuberculosis.

Adherence

Poor compliance with drug therapy is the single most important cause of treatment failure in TB programs. Research studies show conflicting evidence between males and females regarding adherence to treatment. A study from Ghana found that defaulting on treatment was significantly higher in men than women. Cost may have been more of a barrier for men since women in that part of Ghana are active traders and have control over their own income. In the Philippines, reasons for defaulting were different for men and women. There was a high default rate among pregnant/lactating women

because they feared the medicine would cause miscarriage or harm the baby. On the other hand, men, once their symptoms had abated, stopped treatment because they found it too hard to give up alcohol. Abstaining from drinking marks a man as seriously ill.

Accessibility

Several studies suggest that women face more barriers to obtaining opportune TB treatment than men. Studies in Nepal comparing active case finding to passive case finding (self referral) of patients to the existing services showed that a higher proportion of women were undiagnosed in the community.²⁰ Active case finding showed the male to female ratio was very close (1.2:1) while passive case finding found the male to female ratio of 1.6:1. This suggests that in TB programs that rely on self referral, as most programs do, under-diagnosis of tuberculosis in women may occur.

STOP TB INITIATIVE

The STOP TB Initiative is a global partnership of public, private, and nongovernmental organizations for action against one of the world's most devastating diseases. STOP TB's mission is to ensure that every TB patient has access to TB treatment and cure; protect vulnerable populations, especially children, from TB and multidrug-resistant TB; and reduce the social and economic toll that TB exacts on families and communities. One of STOP TB's specific objectives is to reach the global TB control target by 2005, and then sustain its achievement. STOP TB is coordinated by WHO but is supported by many partners such as the International Union Against TB and Lung Disease, the Royal Netherlands TB Association, the Centers for Disease Control and Prevention, the American Lung Association, and USAID.

As a result of the Ministerial Conference on TB and Sustainable Development sponsored by STOP TB March 22-24, 2000, ministers of health, finance, and development planning from 20 of the highest burden countries in the world endorsed a declaration to take action on stopping TB worldwide. The 20 countries unanimously committed themselves to meet the following objective by 2005: expanding coverage of the DOTS strategy to provide for at least 70 percent detection of all infectious cases by the year 2005. To implement this objective, the following will need to be put in place:

- ◆ A global partnership agreement to STOP TB—the framework for action that will operationalize the declarations made during the conference
- ◆ A Global Fund for Tuberculosis to mobilize and invest new, additional resources to support these activities
- ◆ Accelerated research into the development of new tools, including diagnostics, drugs, and vaccines

ROLE OF USAID MISSIONS REGARDING TUBERCULOSIS

The **USAID Infectious Disease (ID) Initiative** is a 10-year congressionally mandated strategy aimed at reducing the global threat of infectious diseases. The ID Initiative focuses on antimicrobial resistance, surveillance, malaria, tuberculosis, and other infectious diseases of public health importance. Since 1998, \$194 million has been allocated to the ID Initiative, with Africa Bureau receiving \$49 million of these funds to implement infectious disease activities. It is now time to focus on tuberculosis and gear up activities to contain this threat.

As part of the U.S. response to the AIDS crisis, the **Leadership and Investment in Fighting an Epidemic (LIFE) Initiative** was developed in July 1999 to address the global AIDS pandemic. The initiative will address four key program elements critical to fighting the pandemic: primary prevention, improving community and home based care and treatment, caring for children affected by AIDS, and capacity and infrastructure development. Under the LIFE care and support component, voluntary counseling and testing, active case diagnosis and tuberculosis treatment, INH preventive chemotherapy, and community delivery of TB services will play prominent roles in improving the quality of life for HIV positive patients and their families.

As missions prepare to receive either LIFE or ID funds, the task ahead may appear daunting. It is clear that USAID missions must explore those areas for which it has a comparative advantage. Each country has its unique constraints but USAID's strengths lie in policy dialogue and consensus building, monitoring and supervision, and collaboration with and support to NGOs at the community level. Areas that might need strengthening in national TB programs are recording and reporting systems crucial in determining individual patient progress towards cure or treatment completion, and looking at ways to improve community delivery of TB services. This would involve looking at community organizations, NGOs, traditional healers, or community health workers who could deliver TB treatment closer to the patient.

There are specific steps that bilateral and regional programs can undertake now to address the deadly alliance of TB and HIV/AIDS:

- ◆ Initiate dialogue with the National Tuberculosis Program (NTP) to determine the status of the twin epidemics—TB and HIV/AIDS—and to ensure that the TB-HIV/AIDS link is on the policy agenda with host governments, NGOs, and USAID partners
- ◆ Determine if DOTS therapy is offered in pilot projects or has been scaled up nationally



- ◆ Identify and explore those areas in which USAID has a comparative advantage, which could assist the NTP to expand the coverage area of DOTS, or to strengthen certain components of the program
- ◆ Assist the NTP to establish more effective links to the national HIV/AIDS program and work with both programs to develop a care and support component that has a dual approach, addressing both community delivery treatment programs and prevention

The twin epidemics of tuberculosis and HIV/AIDS in Africa are so overwhelming that it is easy to think that little can be accomplished against so deadly an alliance. The solution lies in building partnerships between and across people, programs, agencies, and governments. If we each play our role and are unwilling to accept defeat, even the mightiest alliance can be overturned.

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ENDNOTES

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