Special Article

CONTROLLING TUBERCULOSIS IN INDIA

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ABSTRACT

Background Tuberculosis kills nearly 500,000 people in India each year. Until recently, less than half of patients with tuberculosis received an accurate diagnosis, and less than half of those received effective treatment.

Methods We analyzed the effects of new policies introduced in 1993 that have resulted in increased resources, improved laboratory-based diagnosis, direct observation of treatment, and the use of standardized antituberculosis regimens and reporting methods.

Results By September 2001, more than 200,000 health workers had been trained, and 436 million people (more than 40 percent of the entire population) had access to services. About 3.4 million patients had been evaluated for tuberculosis, and nearly 800,000 had received treatment, with a success rate greater than 80 percent. More than half of all those treated in the past 8 years were treated in the past 12 months.

Conclusions India's tuberculosis-control program has been successful in improving access to care, the quality of diagnosis, and the likelihood of successful treatment. We estimate that the improved program has prevented 200,000 deaths, with indirect savings of more than $400 million — more than eight times the cost of implementation. It will be a substantial challenge to sustain and expand the program, given the country's level of economic development, limited primary health care system, and large and mostly unregulated private health care system, as well as the dual threats of the human immunodeficiency virus and multidrug-resistant tuberculosis. (N Engl J Med 2002;347:1420-5.)

INDIA is in a unique position with respect to the global tuberculosis epidemic. Pioneering studies in India demonstrated the effectiveness of ambulatory treatment of tuberculosis,[1] the necessity and feasibility of direct observation of treatment,[2] the efficacy of intermittent treatment with antituberculosis drugs,[3] and the feasibility of case detection by sputum-smear microscopy in primary health care institutions.[4] However, tuberculosis remains the leading infectious cause of death in India, killing close to 500,000 people a year. India has far more cases of tuberculosis than any other country in the world — about 2 million new cases each year[5] — and accounts for nearly one third of prevalent cases globally. A director-general of the World Health Organization once remarked, "The whole world benefits from the fruits of Indian [tuberculosis] research — the whole world, except India."[6]

In the past few years, there has been remarkable progress in diagnosing and treating tuberculosis in India. This public health success story has important implications for tuberculosis control and potentially for other diseases, such as the acquired immunodeficiency syndrome. We describe the first eight years of program implementation, including the past three years, during which the program has been implemented on a large scale.

METHODS

The Revised National Tuberculosis Control Program

A comprehensive review of the tuberculosis program in India in 1992 found that less than half of patients with tuberculosis received an accurate diagnosis and that less than half of those were effectively treated. Laboratory services were underutilized, treatment regimens were unnecessarily complicated, drug shortages were common, and completion of treatment was not systematically assessed.

In response, a pilot project using the World Health Organization (WHO)–recommended strategy of directly observed treatment, short-course (DOTS),[7] the Revised National Tuberculosis Control Program, was begun in 1993. Diagnosis is primarily by sputum microscopy, treatment is directly observed, and standardized regimens and methods of recording and reporting are used. For diagnosis, physicians are trained to ask all patients attending health care facilities if they have had a cough for three weeks or more. Those with a cough undergo three sputum-smear examinations over a two-day period. If two or three of the smears are positive for acid-fast bacilli, antituberculosis treatment is initiated. If all three smears are negative, one to two weeks of broad-spectrum antibiotics (e.g., trimethoprim–sulfamethoxazole) are prescribed. If only one of the three smears is positive or if symptoms persist after the administration of broad-spectrum antibiotics, a chest radiograph is obtained, usually at a larger health center, and the patient is evaluated.

On the basis of their clinical features (Table 1), patients are given one of three categories of treatment, and treatment is based on the category to which a patient belongs. All treatment is given three times weekly (Table 2). Patients who have not previously been treated who have new sputum smears positive for acid-fast

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TABLE 1. DEFINITIONS OF OUTCOMES.*

Cured†	A patient who initially had a positive sputum smear for acid-fast bacilli has completed treatment and has a negative sputum smear in the last month of treatment and on at least one previous occasion.
Defaulted	A patient whose treatment was interrupted for two or more consecutive months.
Died	A patient who died from any cause during the course of treatment.
Transferred out	A patient who has been transferred to another recording and reporting unit and for whom the treatment outcome is not known.
Treatment complete†	A patient who has completed treatment but who does not meet the criteria to be classified as cured or as having treatment failure.
Treatment failed	A patient who has a sputum smear positive for acid-fast bacilli after five or more months of treatment or a patient whose initial sputum smear was negative and who has a sputum smear positive for acid-fast bacilli after two or more months of treatment.

*Definitions are from the World Health Organization.[7]

†Treatment success is the sum of patients who are cured and those who have completed treatment.

bacilli and seriously ill patients with negative sputum smears (category 1) are treated with four drugs (isoniazid, rifampin, pyrazinamide, and ethambutol) for two months and then with two drugs (isoniazid and rifampin) for four months. Previously treated patients (category 2) receive these four drugs plus streptomycin for two months, then the first four drugs for one month, then three drugs (isoniazid, rifampin, and ethambutol) for five months. Patients in categories 1 and 2 whose smears are positive for acid-fast bacilli at the end of the intensive phase of treatment (the first two or three months in categories 1 and 2, respectively) receive another month of intensive-phase treatment. Patients in category 3 are those whose smears are negative for acid-fast bacilli, who have abnormal radiographs, and who are not seriously ill, including those with extrapulmonary tuberculosis. These patients receive the same treatment as those in category 1, except that ethambutol is omitted. Every dose of medication in the initial phase is directly observed, either by a health worker or by a community member who is not a family member. In the four-to-five-month continuation phase, when the bacterial load is far lower, at least the first of each of the thrice-weekly doses is directly observed. Medications for both phases of treatment are kept in an individual box containing the entire course of treatment for a single patient. Diagnosis and treatment are free of charge to the patient. Recording and reporting are performed according to WHO recommendations, with the progress and outcome of every patient recorded and reported quarterly.[8]

Policy and Finance

Policy direction and supervision, drugs, and microscopes are provided by the central government. State governments hire the gen-

TABLE 2. REGIMENS USED IN THE REVISED NATIONAL TUBERCULOSIS CONTROL PROGRAM IN INDIA, 1993 TO 2001.*

CLINICAL FEATURES	REGIMEN†
Category 1	
Positive sputum smear Negative sputum smear, patient seriously ill Patient has extrapulmonary tuberculosis and is seriously ill	Isoniazid, rifampin, pyrazinamide, and ethambutol for 2 mo, followed by isoniazid and rifampin for 4 mo
Category 2	
Positive sputum smear, patient relapsed Positive sputum smear, treatment failed Positive sputum smear, patient treated after default	Isoniazid, rifampin, pyrazinamide, ethambutol, and streptomycin for 2 mo, followed by isoniazid, rifampin, pyrazinamide, and ethambutol for 1 mo, followed by isoniazid, rifampin, and ethambutol for 5 mo
Category 3	
Negative sputum smear, abnormal radiograph, patient is not seriously ill Patient has extrapulmonary tuberculosis, but is not seriously ill	Isoniazid, rifampin, and pyrazinamide for 2 mo, followed by isoniazid and rifampin for 4 mo

*A negative sputum smear with pulmonary tuberculosis was defined as at least three new sputum smears negative for acid-fast bacilli; radiographic abnormalities consistent with active pulmonary tuberculosis; no response to a course of broad-spectrum antibiotics; and decision by a clinician to treat with a full course of antituberculosis chemotherapy. A positive sputum smear was defined as two or more new sputum smears positive for acid-fast bacilli; or one new sputum smear positive for acid-fast bacilli plus radiographic abnormalities consistent with active pulmonary tuberculosis, as determined by a clinician; or one new sputum smear positive for acid-fast bacilli plus sputum culture positive for *Mycobacterium tuberculosis*. Relapse was defined by the diagnosis of bacteriologically positive tuberculosis (acid-fast bacillus smear or *M. tuberculosis* culture) in a patient previously treated for tuberculosis who has been declared cured or as having completed treatment.

†All drugs are administered three times weekly. The doses are as follows: isoniazid, 600 mg; rifampin, 450 mg; pyrazinamide, 1500 mg; ethambutol, 1200 mg; and streptomycin, 750 mg. Patients who weigh more than 60 kg receive an additional 150 mg of rifampin in each dose. Patients more than 50 years old and those weighing less than 30 kg receive 500 mg of streptomycin. Patients in categories 1 and 2 who have a sputum smear positive for acid-fast bacilli at the end of the initial intensive phase of treatment (the first two or three months) receive an additional month of intensive-phase treatment.

eral health staff as well as the specialized staff of the district tuberculosis centers, clinics, and hospitals. In rural areas, India has an established health infrastructure, with a large health center for each 100,000 people, a smaller clinic for each 30,000 people, and a health post staffed by paramedical staff for every 5000 people.

Financial assistance for implementation has been provided by the World Bank and the Danish and United Kingdom aid agencies. Funds are provided to the government of India, which sends them to district and state tuberculosis-control societies. These societies are registered charities; the officers are government officials, and the members include private physicians, representatives of community organizations, and others. These societies, each of which serves an average population of about 2 million, hire contractual staff, purchase necessary items, and perform other functions more efficiently than they are performed by the usual government procedures.

Implementation and Supervision

After a decision has been made to begin the program in a district, the district forms a society and prepares a plan for implementation of the project, based on detailed guidelines and assistance, as required, from the central and state governments. The state must ensure posting of a full-time doctor as the district tuberculosis-control officer. This officer is trained for 10 to 12 days at a central institution with the use of standard modules and field visits. The society hires one treatment supervisor and one laboratory supervisor for each tuberculosis unit; tuberculosis units have an average population of 500,000. Additional staff are provided for difficult mountain, urban slum, and tribal areas. A doctor from the regular health service at the tuberculosis unit is in charge of tuberculosis-control activities. The district, with support from the state, is required to train at least 80 percent of the doctors and laboratory technicians and at least 50 percent of the paraprofessional health staff, using modules designed for each category of staff. Microscopy centers and drug-storage areas are refurbished according to standard architectural drawings. When the district has met the predefined criteria, it is appraised by a joint committee consisting of central, state, and district government staff. This committee identifies any deficiencies; after the district rectifies these, as certified by the state government, the central government sends antituberculosis drugs and the district begins service delivery. Each quarter, every tuberculosis unit submits standardized reports on case detection, treatment outcomes, and program logistics. The district sends these reports on to the state and central governments.

There are several levels of support, monitoring, and supervision. Staff from the state and central governments and the WHO make site visits, particularly to districts that are preparing slowly or performing poorly, to identify problems and facilitate improvements. Laboratory supervisors provide quality control of sputum microscopy, and treatment supervisors monitor the quality of observation of treatment and the accuracy of recording and reporting. Starting in 1999, in concert with the central and state governments of India, the WHO hired, trained, and deployed doctors to act as consultants to central, state, and local governments. Each consultant undergoes intensive training and covers a population of 10 million to 40 million. The consultant is provided with a four-wheel-drive vehicle, laptop computer, mobile telephone, and Internet access. The central government and some state governments provide detailed feedback each quarter on the comparative performance of all states and districts.

RESULTS

Program Expansion, Case Detection, and Treatment Outcomes

The pilot programs began on October 2, 1993. Eight years later, delivery of service had begun in 211 districts of 19 states, covering 436 million people (43 percent of the entire population). Nearly 200,000 health staff had been trained (Table 3). More than 3000 laboratories had been provided with electricity and water connections, new binocular microscopes, and reagents.

On an average day during 2001, there were nearly 300,000 adult outpatient visits to facilities covered by the program, more than 5000 patients were examined for tuberculosis (involving more than 20,000 microscopical examinations for acid-fast bacilli), and more than 1300 patients were started on treatment. By September 2001, about 3.4 million symptomatic patients had been assessed for tuberculosis, and in the case of nearly 800,000, treatment had been started in the past 12 months. More than 200,000 patients were receiving treatment at any one time. Of the patients in whom pulmonary tuberculosis was diagnosed, 55 percent were documented to have sputum smears positive for acid-fast bacilli, as compared with less than 25 percent in the previous program. Since 1998, less than 5 percent of the districts have had an unusually low proportion (less than 45 percent) of laboratory-confirmed cases, suggesting a poor quality of diagnosis.

Patient outcomes are reported one year after the start of treatment (Table 4). Eighty-three percent of 666,037 patients due for evaluation were successful-

TABLE 3. ACTIVITIES UNDERTAKEN TO PREPARE FOR IMPLEMENTATION OF THE REVISED NATIONAL TUBERCULOSIS CONTROL PROGRAM IN INDIA, 1993 TO 2001.

ACTIVITY	NUMBER
Microscopy laboratories upgraded	≈3,000
Contractual treatment and laboratory supervisors hired	>1,500
State- and district-level societies formed as registered charities	>200
Policy and training booklets printed	>1 million
Treatment cards and forms printed locally	>7 million
Binocular microscopes procured through international competitive bidding	>4,000
Antituberculosis tablets procured through international competitive bidding	>500 million
Four-wheel-drive vehicles procured	200
Motorcycles procured	636
Personnel trained	
State and district tuberculosis officers and tuberculosis-unit medical officers	1,255
Treatment supervisors	825
Laboratory supervisors	832
Laboratory technicians	6,187
Medical officers	22,735
Allied health workers	98,054
Multipurpose health supervisors	10,277
Child-survival workers or equivalent	47,469
Midwives	7,250
Community volunteers	5,863
Total trained	200,747

TABLE 4. OUTCOMES OF PATIENTS TREATED IN THE REVISED NATIONAL TUBERCULOSIS PROGRAM IN INDIA, 1993 THROUGH 2001.

PATIENT FEATURES	NO. OF PATIENTS EVALUATED*	TREATMENT SUCCESSFUL†	DIED	TREATMENT FAILED	DEFAULTED	TRANSFERRED OUT
			number (percent)			
New, positive sputum smear	261,077	217,862 (83.4)	11,530 (4.4)	7,611 (2.9)	22,103 (8.5)	1971 (0.8)
New, negative sputum smear	208,767	178,284 (85.4)	7,433 (3.6)	2,466 (1.2)	19,240 (9.2)	1344 (0.6)
Extrapulmonary tuberculosis	76,785	69,746 (90.8)	1,474 (1.9)	177 (0.2)	4,936 (6.4)	452 (0.6)
Relapsed	34,793	25,516 (73.3)	2,322 (6.7)	1,987 (5.7)	4,536 (13.0)	432 (1.2)
Other retreatment	84,615	59,577 (70.4)	5,940 (7.0)	4,416 (5.2)	13,854 (16.4)	828 (1.0)
Total	666,037	550,985 (82.7)	28,699 (4.3)	16,657 (2.5)	64,669 (9.7)	5027 (0.8)

*Data are for patients whose outcomes were reported through September 2002, including all cohorts of patients registered up to June 30, 2001. Patients evaluated represent 99.85 percent of all patients registered. Patients registered but not evaluated include those registered in error (i.e., duplicate registrations, diagnoses of something other than tuberculosis, and clerical errors), as well as those whose outcomes were never reported.

†Among the 217,862 patients with a new, positive sputum smear who were successfully treated, 214,033 (82.0 percent of those evaluated) met the definition for cure. Among the 25,516 relapsed patients who were successfully treated, 24,413 (70.2 percent of those evaluated) met the definition for cure.

ly treated. Approximately 20 percent of districts had treatment success rates of less than 80 percent, but only 5 percent had treatment success rates of less than 70 percent. For previously treated patients, the rate of treatment success was 71 percent. For patients in whom treatment had previously failed, the risk of failure of the retreatment regimen was higher than for patients who had previously had a relapse, those who had discontinued treatment prematurely, or other patients undergoing retreatment (the failure rates were 12.9 percent, 5.7 percent, 5.3 percent, and 2.2 percent, respectively; $P<0.001$). There have been more than 250,000 supervisory visits, half to patients' homes and half to health care facilities.

Challenges

India has faced several challenges in implementing this program. First, the general health service often does not function optimally. Although the per capita number of adult visits to health care facilities varies by a factor of more than 50 between the least and the most functional states, the number of visits per capita does not appear to correlate closely with case-detection rates. This suggests that patients with tuberculosis can be identified and treated even in a relatively dysfunctional health care system.

Second, a large and mostly unregulated private sector provides a substantial proportion of outpatient care, and this care is of inconsistent quality.[9] In areas where the Revised National Tuberculosis Control Program is in operation, about 50 to 60 percent of patients are treated by the program.

Third, the level of socioeconomic development can have a major effect on program performance. For example, many areas lack a regular supply of electricity. Drought and economic hardships sometimes cause large-scale migration, greatly reducing the rates of treatment completion and cure.

Fourth, as identified by the World Bank,[10] the role and effectiveness of the state also pose a challenge. Potential problems include pressure to hire, purchase, and fund activities, as well as requests for unofficial payments to health staff, which could undermine the principle of free care. The accuracy of reporting is regularly monitored. The DOTS information system is simple to maintain but very difficult to falsify convincingly. Intensive supervision has identified falsification as a significant problem in less than 5 percent of districts, primarily in two states.

Fifth, ensuring the quality of drugs is difficult. The drugs are packaged in blister strips, the strips are packaged in pouches, and the pouches are packaged in boxes, one box per patient. The quality of the packaging has been variable. Creating and verifying appropriate and unambiguous specifications for packaging have sometimes been difficult. Ethambutol, which is hygroscopic, sometimes degrades in flooded areas and other areas of high humidity. Medicines or packaging materials that appear to be of poor quality may undermine confidence in the program, even if the medicines are of acceptable bioequivalence. Because of concern about quality, shelf-life, and bioavailability, fixed-dose combinations of antituberculosis drugs have not been used.

A sixth challenge is establishing patient-friendly services, with the patient as the "VIP" of the program. This approach sometimes contrasts with long-standing patterns in Indian society and in its health care

system. The program's goal is that no patient should have to pay for transportation or lose wages to participate, but many patients still face substantial barriers to care.

DISCUSSION

The Indian tuberculosis-control program is now one of the largest public health programs in the world. The program has been remarkably successful, although it still faces many challenges. Direct health benefits to date include the treatment of 1.4 million patients with tuberculosis, prevention of more than 200,000 deaths,[11] with reduction in the prevalence of tuberculosis in some areas, and prevention of the spread of tuberculosis. On the assumption that half of the cured patients would not have been cured by the previous program and that half of these were infectious for an average of one year, during which time each of them would have infected an average of one other person per month, the program has prevented more than 2 million tuberculosis infections and therefore more than 200,000 secondary cases. The indirect benefits depend on the economic effect of deaths, which account for about 90 percent of the indirect costs. More than 200,000 deaths have been averted. Even with the conservative estimates that only 25 percent of those who died would have been employed and that they would have worked for an average of 20 years, earning $400 per year, the reduction in deaths had indirect economic benefits of more than $400 million — more than eight times the incremental costs.

The total project expenditure for all incremental efforts during these eight years was approximately $50 million. Much of this expenditure was for one-time investment in infrastructure and capacity. The ongoing yearly project costs are approximately $0.05 per capita.[12] At current rates of case detection and treatment, these costs correspond to less than $40 per patient treated, less than $50 per patient cured, and less than $200 per life saved.

In addition to the challenges explained above, drug resistance is a threat. Drug resistance results from the inappropriate prescription or use of drugs, and it reflects poor program performance. Drug resistance presumably accounts, at least in part, for the higher failure rates among patients who are treated a second time. In several areas, from 1 percent to 3.4 percent of new patients have multidrug-resistant tuberculosis.[13] These percentages are higher than those in many countries but much lower than those in the "hot spots" of New York City[14] in the early 1990s (7 percent) and of areas of Russia[15] more recently (10 to 15 percent). However, if even 2 percent of new patients in India have multidrug-resistant tuberculosis, this represents some 20,000 new infectious cases every year. The financial and human resources required to treat 1 patient with multidrug-resistant tuberculosis are greater than those required to treat 100 other patients. More than 1 million new patients with tuberculosis still do not have access to the basic program package in India.

The human immunodeficiency virus (HIV) epidemic may undermine tuberculosis control in India. There are an estimated 4 million HIV-infected people in India,[16] about half of whom are also infected with *Mycobacterium tuberculosis.* Active tuberculosis will develop in about 7 percent of coinfected persons each year,[17] producing 140,000 cases of tuberculosis each year from reactivation disease alone. Thus, given the experience in other countries that 30 to 60 percent of cases of tuberculosis in HIV-infected persons arise from recent infection,[18-20] approximately 200,000 additional new cases will occur each year, representing a 10 percent increase in cases, even at the current relatively low rate of HIV infection.

Lessons for other programs include the use of well-tested modules for standardized training, the application of strict criteria before allowing an area to begin services, intensive monitoring of and feedback on quarterly reports, and on-site supervision by specialized staff both from the program (contractual supervisors) and from outside the program (WHO consultants). The information system, which requires evaluation during and at the end of treatment of every patient, has also been critical. Tuberculosis control is a management problem; the disease itself is nearly 100 percent curable with interventions that are inexpensive and relatively simple. This program has shown that, with careful management, it is possible to provide high-quality treatment to large numbers of patients, even in the context of a suboptimally functioning health care system.

Sustaining this program in India will require continued financial support, particularly for drugs and contractual supervisors, as well as continued and intensified supervision and monitoring. The creation and equipping of small laboratories and the initial training of large numbers of health workers should have long-term benefits. If the prevalence of HIV does not further increase substantially, a large decrease in the prevalence and a smaller decrease in the incidence of tuberculosis will facilitate continuation of the program.

Effective diagnosis and treatment do not necessarily lead to a rapid reduction of the incidence of tuberculosis. An effective program in Peru has been documented to reduce the incidence of tuberculosis by 7 percent or more per year.[21] However, the rate of decline in the incidence of tuberculosis will be affected by the proportion of cases resulting from recent transmission, as well as by other factors. It will be at least several years before the Indian program can be expected to have a discernible effect on disease incidence.

Further expansion to cover the entire country is under way, with plans to cover 80 percent of the country by 2004. Coverage of the entire country will require training of 20,000 more doctors and more than 100,000 allied health staff, improvements in more than 6000 laboratories, and the medications to treat more than 1 million patients per year. Given the success of the program to date, expansion on this scale appears to be possible, but it is far from assured. Continued high-level commitment and technical rigor from the central and state governments of India and assistance from international organizations will be essential.

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REFERENCES

1. Tuberculosis Chemotherapy Centre. A concurrent comparison of home and sanatorium treatment of pulmonary tuberculosis in south India. Bull World Health Organ 1959;21:51-144.
2. Fox W. Self-administration of medicaments: a review of published work and a study of the problems. Bull Int Union Tuberc 1962;32:307-31.
3. Tuberculosis Chemotherapy Centre. A concurrent comparison of intermittent (twice-weekly) isoniazid plus streptomycin and daily isoniazid plus PAS in the domiciliary treatment of pulmonary tuberculosis. Bull World Health Organ 1964;31:247-71.
4. Banerji D, Andersen S. A sociological study of awareness of symptoms among persons with pulmonary tuberculosis. Bull World Health Organ 1963;29:665-83.
5. Dye C, Scheele S, Dolin P, Pathania V, Raviglione MC. Global burden of tuberculosis: estimated incidence, prevalence, and mortality by country. JAMA 1999;282:677-86.
6. Grzybowski S. Natural history of tuberculosis: epidemiology. Bull Int Union Tuberc Lung Dis 1991;66:193-4.
7. World Health Organization, International Union Against Tuberculosis and Lung Disease, Royal Netherlands Tuberculosis Association. Revised international definitions in tuberculosis control. Int J Tuberc Lung Dis 2001;5:213-5.
8. Treatment of tuberculosis: guidelines for national programmes. 2nd ed. Geneva: World Health Organization, 1997. (WHO/TB/97.220.)
9. Uplekar MW, Rangan S. Private doctors and tuberculosis control in India. Tuber Lung Dis 1993;74:332-7.
10. World Bank. World development report 1997: the state in a changing world. Oxford, England: Oxford University Press, 1997.
11. Tuberculosis control — India. New Delhi, India: Directorate General of Health Services, 2002. (Accessed October 7, 2002, at http://www.tbcindia.org.)
12. Joint tuberculosis programme review: India. New Delhi, India: WHO Regional Office for South-East Asia, 2000. (WHO/SEA/TB/224.)
13. Paramasivan CN, Bhaskaran K, Venkataraman P, et al. Surveillance of drug resistance in tuberculosis in the state of Tamil Nadu. Indian J Tuberc 2000;47:27-33.
14. Frieden TR, Sterling T, Pablos-Mendez A, Kilburn JO, Cauthen GM, Dooley SW. The emergence of drug-resistant tuberculosis in New York City. N Engl J Med 1993;328:521-6.
15. The WHO/IUATLD Global Project on Anti-tuberculosis Drug Resistance Surveillance. Anti-tuberculosis drug resistance in the world. Report no. 2: prevalence and trends. Geneva: World Health Organization, 2000. (WHO/CDS/TB/2000.278.)
16. De Cock KM, Weiss HA. The global epidemiology of HIV/AIDS. Trop Med Int Health 2000;5:A3-A9.
17. Swaminathan S, Ramachandran R, Baskaran G, et al. Risk of development of tuberculosis in HIV-infected patients. Int J Tuberc Lung Dis 2000;4:839-44.
18. Gilks CF, Godfrey-Faussett P, Batchelor BIF, et al. Recent transmission of tuberculosis in a cohort of HIV-1-infected female sex workers in Nairobi, Kenya. AIDS 1997;11:911-8.
19. Wilkinson D, Pillay M, Crump J, Lombard C, Davies GR, Sturm AW. Molecular epidemiology and transmission dynamics of Mycobacterium tuberculosis in rural Africa. Trop Med Int Health 1997;2:747-53.
20. Palittapongarnpim P, Luangsook P, Tansuphaswadikul S, Chuchottaworn C, Prachaktam R, Sathapatayavongs B. Restriction fragment length polymorphism study of Mycobacterium tuberculosis in Thailand using IS6110 as probe. Int J Tuberc Lung Dis 1997;1:370-6.
21. Suarez P, Watt CJ, Alarcon E, et al. The dynamics of tuberculosis in response to 10 years of intensive control effort in Peru. J Infect Dis 2001;184:473-8.