· Review ·

Worldwide trends in epidemiology and control of tuberculosis

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[**ABSTRACT**] Tuberculosis (TB) is a global burden disease and is being resurrected as a major worldwide public health problem after two decades of neglect. In 1993, the World Health Organization (WHO) declared that TB had been a global emergency because of the scale of the epidemic and the urgent need to improve global tuberculosis control. China is one of the countries with the largest population, and also the top of the 22 TB high-burden countries in the world. In the United States, the longstanding downward trend in TB incidence was interrupted in the mid-to-late 1980s, where the national TB incidence peaked in 1992. Sub-Saharan Africa is one of the three regions to dominate the worldwide distribution of notified TB cases. Of the 15 countries with the highest estimated tuberculosis incidence rates in the world, 13 are in sub-Saharan Africa, where HIV is the most important single predictor of tuberculosis incidence. The largest share of the global burden of HIV-related tuberculosis falls on this region. The reasons for the persisting global tuberculosis burden include increased poverty in some regions, immigration from countries with high tuberculosis prevalence, the impact of HIV, and most importantly, the failure to maintain the necessary public health infrastructure under the mistaken belief that tuberculosis was a problem of the past. Relying on currently available methods of diagnosis and treatment, the DOT strategy promoted by the WHO for global tuberculosis control is effective, affordable, and adaptable in different settings.

[**KEY WORDS**] epidemiology; China; United States; sub-Saharan Africa; tuberculosis

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Tuberculosis (TB) is an infectious disease that can affect many organs. The causative organisms of TB include *Mycobacterium tuberculosis*, *Mycobacterium bovis*, and *Mycobacterium africanum*.

TB is a global burden disease, most possibly ranking high among diseases over the coming several decades with 2 million deaths and over 8 million new cases annually[1]. Anyone can get TB, people of all races, all nationalities, the rich and the poor and at any age, though there is much difference about control and prevention of the disease in different areas of the world. The infectious rate is higher in developing countries than in developed countries. The aim of this paper is to review the TB epidemiology and control in countries of different economic states.

1 EPEDEMIOLOGY OF TUBERCULOSIS

1.1 TB in China TB is a disease of overcrowding and poverty. China and India are 2 top countries with the largest populations in the world, and also the first 2 of the 22 TB high-burden countries. TB seriously affects the health of people and remains to be a major public health problem in China. During 1950-1980, TB control activities were carried out in cities only. In Beijing and Shanghai, the active pulmonary TB prevalence was 4 000-5 000/100 000, and the TB mortality was more than 200/100 000 in the early 1950s. No data of nationwide epidemiology was obtainable due to the lack of proper information systems. In 1979, the results of the first nationwide random sampling survey for the epidemiology of TB showed that the active pulmonary TB prevalence and the smear-positive TB prevalence were 796/100 000 and 218/100 000, respectively. The incidence of pulmonary TB in the rural areas was higher than that in the urban areas (2.8 : 1)[2].

The National TB Program (1981-1990) was designed and the program activities were carried out. The National Tuberculosis Control Center was established within the Beijing Tuberculosis Research Institute in 1982, which provides guidance to each province in implementing a national TB control plan. A reporting and recording system was established in 1982. TB service facilities had been established in most provinces (85%) and counties

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(70%) by 1990. Not until the early 1980s was short-course chemotherapy introduced in China. By 1986 it had expanded to most areas of China. Directly observed treatment was implemented in some cities. However, TB institutions in poorer provinces with a weaker primary health care infrastructure were unable to provide sufficient financial support and adequate supervision due to resource constraints. In 1990, the results of the third nationwide epidemiological survey showed that the TB prevalence had not been reduced significantly. The active pulmonary TB prevalence was 523/100 000 and the smear-positive pulmonary TB prevalence was 134/100 000. Compared with the results of the first survey in 1979, the former reduced by 34.3%, and the latter, by 38.5%, with an annual reduction rate 3.7% and 4.3%, respectively [3].

The second National TB Program (1991-2000) was formally established in 1991. The Government introduced a TB control project using the WHO-recommended 5 points strategy called DOTS, which was a cost-effective mechanism to detect and treat TB cases. The project, entitled the Infectious and Endemic Disease Control (IEDC), was assisted by a World Bank Loan and was implemented in 12 provinces and 1 municipality (Chongqing) with a population of 573 million, roughly a half population of China in 1991. In 1993, the WHO declared that TB had been a global emergency. The Ministry of Finance gave the national budget to promote DOTS expansion in 15 additional provinces, autonomous regions and municipalities covering a 140 million population. The project, entitled the Strengthening and Promoting Tuberculosis Control, was different from the IEDC project including partly free-of-charge treatment for smear-positive cases.

In 2000, the data of the fourth TB epidemiology survey by the Ministry of Health (MOH) showed that the active pulmonary TB prevalence was 367/100 000 and the smear-positive pulmonary TB prevalence was 122/100 000. From 1991-2000, standardized prevalence of active pulmonary TB and smear-positive pulmonary TB decreased by 42.6% and 27.6%, respectively, with an annual reduction rate 5.4% and 3.2%, respectively. In China, drug resistant rates were still high. The incidence rates of primary drug resistance and acquired drug resistance were 7.6% and 17.1%, respectively. The incidence rate of MDR was 10.7%[4], the main cause of which was inadequate application of anti-TB drugs including insufficient use of active drugs, irregular drug administration, non-compliance, irregular drug supply, and unsupervised treatment.

The decline of nationwide TB prevalence was sluggish especially in the non-project areas. There was an unbalance between the project areas and the non-project areas. From 1990 to 2000, according to the standardized data, the national extent of decline in the smear-positive prevalence of pulmonary TB in project areas was 44.4% and 12.3% in the non-project areas, averaging 27.6% nationally. The annual reduction rates were 5.7%, 1.3% and 3.2%, respectively. However, in western China, the extent of decline in the smear-positive prevalence of pulmonary TB was 33.4% in the project areas and was 11.7% in the non-project areas.

Chen *et al*[5] reported that DOTS expanded rapidly from 1991-1995 in China, covering more than 90% of the target population and counties. By 2000, 8 million TB suspects had received free diagnostic evaluation: 1.8 million of TB cases were diagnosed, free treatment was provided to 1.3 million smear-positive cases, and more than 90% were cured. The global target of an 85% cure rate was quickly achieved. Nevertheless, the majority of TB cases were diagnosed in the hospital system. Some received treatment in hospitals but then failed to complete a full course of treatment. In the non-project areas, the completed cure rate was only 27.3%. The detection rate for new smear-positive cases in the project areas was estimated to be only 54% in 1998, and 41.2% in the counties which had a below average or low level of case-finding, far below the global target of a 70% case-detection rate. This may be due to poor program management, inadequate human resources, poor staff motivation, financial constraints, poor primary health care infrastructure, and a lack of community involvement.

1.2　TB in the United States　The epidemiology of

TB in the United States has changed remarkably over the last 2 centuries. In the 19th century, TB was the leading cause of death in the United States. After the *Tubercle bacillus* was identified as the causative agent of TB by Robert Koch in 1882, the approach to TB control changed greatly, and the concepts of public health, prevention, and segregation of TB patients gained more acceptance[6,7]. In 1904, the first voluntary health agency, the National Tuberculosis Association (now the American Lung Association), was organized and dedicated to TB[8]. In 1920 it published the first Diagnostic Standards and Classifications of TB to assist health care providers and standardize diagnostic criteria[9]. National TB mortality and morbidity data, coordinated by the National Tuberculosis Association, became available in 1933. In 1944, the United States Public Health Service Act mandated the creation of a national TB control program[5]. With the introduction of the therapeutic agents streptomycin, p-aminosalicylic acid, isoniazid and pyzazinamide, TB mortality rates decreased dramatically. Between 1930 and 1960, the mortality rate decreased by 92%, from 71 to 6 deaths per 100 000 population. In 1952, the United States Pubic Health Service (USPHS) Tuberculosis Control Program instituted procedures to report new cases of TB. Not until 1953, through the cooperation of the States, did the USPHS receive reports from the entire United States, heralding the birth of the national TB surveillance system [10,11]. TB incidence continued to decrease. From 1953 to 1985, the number of TB cases decreased by 74%, from 84 304 to 22 201 cases, and the case rate decreased by 82%, from 53.0 to 9.3 cases per 100 000 population. As a result, many people no longer considered TB to be a major problem and federal fundings allocated for TB control services was dismantled[12,13].

In the mid-to-late 1980s, the longstanding downward trend in TB incidence was interrupted. In 1986, a 216% annual increase in the case number was documented, signaling the beginning of the TB resurgence. Between 1985 and 1992, the change in the TB incidence trend resulted in an estimated excess of 52 100 TB cases[14]. During the resurgence, the national TB incidence peaked in 1992 at 26 673 cases (10.5 cases per 100 000 population). The distribution of TB cases and case rates among age groups remained relatively stable. In 2003, 34.2% of TB patients were 25 to 44 years old, 28.9% were 45 to 64, and 20.2% were 65 years and older. In contrast, among persons who were 65 years and older, TB case rates (cases per 100 000 population) were the highest (8.4) followed by a rate of 6.3 for those aged from 45 to 64.

In the United States, TB resurgence was related to deterioration of the TB control program infrastructure. Immigration from other countries with high rates of TB also contributed to the resurgence and continues to be a major contributing factor. The proportion of reported TB cases among foreign-born persons had increased from 22% in 1986 to 30% in 1993, and the proportion was steadily increasing from 49% to 53.4% of total cases from 2001 to 2003. In 2003, the TB rate among all foreign-born persons was 8.8 times that among US-born persons, and 12 states and the District of Columbia reported case rates above the national average, and 20 states reported increases in case number compared with that in 2002. The majority of foreign-born persons with TB have consistently come from Mexico, the Philippines, Vietnam, India, China, Haiti and South Korea where TB is endemic[15]. TB among foreign born persons is a major component of TB morbidity in the United States and reflects the global TB situation. The HIV/AIDS epidemic also strongly influenced the resurgence of TB disease in the United States. Today, any discussion about TB is incomplete without a discussion about HIV/AIDS. HIV infection is considered to be the greatest risk factor known today for TB. MDRTB is a serious challenge for TB control programs. National drug susceptibility surveys on TB cases conducted by CDC in 1991 revealed that 14.2% of all cases were resistant to at least one drug and 3.5% were resistant to at least isoniazid and rifampin (MDRTB). However, of 2883 isolates obtained from TB patients reported between 1993 and 2002, 287 (10%) were resistant to INH, 11 (< 1%) were resistant to RMP, and 40 (1%) were

MDRTB. 81% of patients with INH resistance and 85% of patients with MDR were born outside the United States [16]. The highest MDRTB rate in the United States was seen in New York city (13%), accounting for more than 60% of the total MDRTB cases reported in the US[17]. Almost all (90%) of the MDRTB cases had pulmonary involvement, making transmission of these drug-resistant M. tuberculosis strains likely, especially in congregate and institutional settings.

In 1993, the WHO declared tuberculosis a global emergency because of the scale of the epidemic and the urgent need to improve global tuberculosis control [18,19]. In the United States, a monumental public health effort to control TB was initiated[20,21]. Federal funding was increased and used to rebuild the TB infrastructure, strengthen surveillance, augment case finding and contact investigations, advance laboratory capacity (e. g. drug-susceptibility testing and new diagnostic tools), and ensure each patient to complete therapy through the use of DOT. From 1992 to 2001, the TB incidence decreased by 40% and the annual decline averaged 5%-6%; however, from 2000 to 2003, the annual TB incidence decreased by only 2%. In 2003, 14 874 TB cases were reported in the United States, with a rate of 5. 1 per 100 000 population that remains higher than the national interim goal of 3. 5 cases per 100 000 population set for 2000[22]. The smallest decline since the resurgence was seen in 2003, raising the concern about a possible slowing of the progress against TB or even a reversal of the decline. Despite increasing health care costs and demands for increased programmatic and operational efforts, funding for TB control has not increased[23]. The elimination of TB in the United States will require sustained efforts such as identifying and targeting populations at high risk for TB, remaining actively involved in the global effort against TB, and maintaining adequate resources.

1. 3　TB in sub-Saharan Africa　Not until the 19th century was TB disease known in sub-Sahara Africa. Rapid spread of infections due to *Mycobacterium tuberculosis* occurred during the 20th century and was in up to 50% of the adult population by the 1950s[24]. It is one of the 3 regions that dominate the worldwide distribution of notified TB cases. Of the 15 countries with the highest estimated tuberculosis incidence rates, 13 are in sub-Sahara Africa; in most of these countries the prevalence of HIV infection among tuberculosis patients is high [25]. HIV is now the most important single predictor of tuberculosis incidence. Sub-Saharan Africa is the region most severely affected by this disease. HIV fuels the TB epidemic: nearly three-quarters of people infected with both HIV and *Mycobacterium tuberculosis* live in sub-Saharan Africa [26]. By the end of 2003, an estimated 38 million adults and children worldwide had contracted HIV infection or AIDS, of whom 25 million(66%) was in sub-Saharan Africa. This region is bearing the burnt of the HIV pandemic, and HIV-associated tuberculosis has become a major clinical and public health problem. Of the 11. 4 million adults co-infected with *Mycobacterium tuberculosis* and HIV worldwide by the end of 2000, 70% were in sub-Sahara Africa[27]. In several African countries, including those with well-organized control programs, annual tuberculosis case notification rates have risen more than five folds since the mid 1980s, reaching more than 400 cases per 100 000 population[25]. The largest share of the global burden of HIV-related tuberculosis falls on sub-Sahara Africa, where 31% of new cases of tuberculosis (all forms) and 34% of tuberculosis deaths are attributable to HIV. Because HIV infection rates are higher in women than in men, more tuberculosis cases are also being reported among women, especially those aged from 25 to 34 years (45%) and residents in urban areas (37%). Although tuberculosis case notifications typically show a male gender predominance, in several African countries with high rates of HIV infection, the majority of notified tuberculosis cases are now women. Data on tuberculosis case fatality in the pre-chemotherapy era in sub-Sahara Africa are lacking, but data from clinical trials of combination chemotherapy in Eastern Africa in the 1970s showed a low case fatality[28]. HIV has dramatically increased tuberculosis case fatality because of their greater degree of immunosuppression. The increase of TB deaths in populations with high HIV prevalence in sub-Sahara Africa may change the popular perception of tuberculosis as a curable disease. In early 1994, the WHO's Global Tuberculosis Programme joined forces with the International Union Against Tuberculosis and Lung Disease (IUATLD) and started the Global Project on Anti-tuberculosis Drug Resistance Surveillance. The Global Project did not specifically test the association between individuals with HIV and MDR-TB, but no correlation was found at the ecological level. In fact, the countries with the highest HIV seroprevalence among tuberculosis patients living in sub-Saharan generally had a low prevalence of MDR-TB; the opposite occurred in Eastern Europe. HIV is not an independent risk factor for MDR-TB[29].

Despite the poor health infrastructure in Africa, standardized combination chemotherapy is provided at least to all patients with smear-positive pulmonary TB. 55% of the population is covered by DOTS, 60% of TB cases notified are treated under a DOTS programme, and 63% of such cases successfully complete treatment. This treatment cures the disease and aims to prevent further transmission of infection. The targets for control include curing 85% of detected new smear-positive cases of pulmonary TB and detecting 70% of existing cases[30]. However, the implementation of a good DOTS programme is not easy and requires adequate funding and human resources [31]. 20%-30% of HIV-positive with smear-positive pulmonary TB patients die before the end of treatment[30]. African countries with good DOTS programmes continue to have escalating notifications of TB cases in the face of high HIV infection rates[32]. DOTS alone may not be sufficient to control TB in areas of epidemic HIV infection. In Africa, preventive therapy for HIV-related infections in general and for HIV-related TB is currently based on cotrimoxazole and isoniazid, respectively. Cotrimoxazole significantly reduced the case-fatality rate in HIV-positive TB patients[33] and reduced morbidity in HIV- infected patients without TB [34]. The Joint United Nations Programme on HIV/AIDS has therefore provisionally recommended that cotrimoxazole be given to all patients in Africa living with AIDS, which, by definition, includes HIV-positive patients with TB[35]. Although there are doubts about the value of isoniazid preventive therapy as a TB control strategy, it deserves to be included as part of the package of care offered to HIV-positive individuals[36]. As HIV is the main factor responsible for the current epidemic of TB in Africa, an integrated programme has a greater chance of affecting the TB burden here than any course of action undertaken by TB control programmes alone. TB is the main opportunistic infection resulting from HIV. Even with treatment regiments that are highly effective in HIV-negative pulmonary tuberculosis patients, cohort deaths for HIV-positive pulmonary tuberculosis patients in some sub-Saharan African countries are now as high as 20% for sputum smear-negative cases and 50% for sputum smear-positive cases[12].

2 TARGET OF CONTROL

About 8-10 million new cases and 3 million deaths are being reported each year. About 95% of these occur in developing countries and only about 5% in the developed world. But frequent travel and migration between countries has brought TB back to almost all countries. Worldwide, TB causes more deaths than any other infectious disease. A global strategy is required.

2.1 Implementation of DOTS The most important reasons for the persisting global tuberculosis burden is the failure to maintain the necessary public health infrastructure and an unwillingness to provide necessary financial and manpower resources under the mistaken belief that tuberculosis was a problem in the past. In 1993, the WHO declared tuberculosis a global emergency. Since then, WHO has promoted the strategy for global tuberculosis control known as DOTS. It includes 5 elements: (1) Sustained government commitment to tuberculosis control. (2) Diagnosis based on quality-assured sputum-smear microscopy mainly among symptomatic patients presenting to health services. (3) Standardized short-course chemotherapy for all cases of TB, under proper case-management conditions including direct observation of treatment. (4)

Uninterrupted supply of quality-assured drugs. (5) A standard recording and reporting system enabling program monitoring by systematic assessment of treatment outcomes of all patients registered[39]. Relying on the methods of diagnosis and treatment currently available, the DOTS strategy is effective, affordable, and adaptable in different settings. There is now general agreement that DOT with a short-course anti-TB regiment (DOTS) is the only effective way to reverse the TB epidemic. The use of DOTS has 3 very important results: it cures patients, renders them noninfectious, and prevents the development of drug-resistant organisms. DOTS can literally stop the TB epidemic at its source, the sick and infectious TB patient. It is clear that DOTS is the most effective weapon we have in the fight against TB. Rather than going on the defensive and trying to protect uninfected groups, DOTS takes the offensive and can stop the disease at its source. Investment in TB control programmes involving DOTS is essential, particularly in the worst-affected parts of the world. The global aims of DOTS programmes are to detect at least 70% of all new infectious cases and to cure at least 85% of those detected by 2005[40]. Global efforts to implement the DOTS strategy widely and effectively resulted in a global case detection rate of 37% in 2002, more than half of the target of 70%, and treatment success for the 2001 cohort of 82%, on average, close to the target. As the number of patients receiving DOTS increased, the number of new TB cases decreased.

2.2 Development of new tools An important component of disease control is the development of new diagnostic tests, pharmacologic agents, and vaccines. The resurgence of TB in the mid-to-late 1980s to 1992 was associated with delays in the diagnosis and identification of drug resistance.

During the past few years, TB diagnostic capabilities have improved through new techniques that include more rapid detection of growth and tests to identify RNA or DNA of *Mycobacterium tuberculosis* complex directly in clinical samples[41]. The emergence of multidrug-resistant strains of *Mycobacterium tuberculosis* is an increasing problem which adversely affects patient care and public health. In contrast to other bacteria, resistance of *Mycobacterium tuberculosis* is exclusively associated with chromosomal mutations. Recently developed molecular biological techniques have significantly helped in understanding the basis of drug action and resistance mechanisms in this organism. Our understanding of TB transmission dynamics has been refined by genotyping of *Mycobacterium tuberculosis* strains. The National Tuberculosis Genotyping and Surveillance Network in the United States was established in 1996 and implemented to systematically evaluate the role of genotyping technology in improving TB prevention and control activities. Genotyping proved to be a useful adjunct to investigations of outbreaks, unusual clusters, and laboratory cross-contamination[42].

Identifying persons with latent tuberculosis infection (LTBI) is crucial to the goal of TB elimination. There is no reliable means of detecting latent *Mycobacterium tuberculosis* infection, and even in patients with active TB, infection is often unconfirmed. However, in 2001, a new test (QuantiFERON-TB or QFT; manufactured by Cellestis Limited, Carnegie, Victoria, Australia) that measures the release of interferon-gamma in whole blood in response to stimulation by purified protein derivative was developed. The QuantiFERON-TB test is a promising *in vitro* diagnostic test for LTBI that has potential advantages over the tuberculin skin test (TST) [43].

A new vaccine against TB more potent than the current inadequate vaccine, *Mycobacterium bovis* BCG, is urgently needed. Recombinant bacillus Calmette-Guerin strains, DNA-based vaccines, live attenuated *Mycobacterium tuberculosis* vaccines and subunit vaccines formulated with novel adjuvants have shown promise in preclinical animal challenge models. Three of these vaccines are being evaluated in human clinical studies, and several other vaccine preparations are being targeted for clinical trials in the near future. We describe a recombinant BCG vaccine (rBCG30) expressing and secreting the 30 000 major secretory protein of *Mycobacterium tuberculosis*, the primary causative agent of TB, that affords greater survival after challenge than parental BCG in the highly demanding guinea pig model of pulmonary TB. Animals immunized with rBCG30 and then challenged by aerosol with a highly virulent strain of *Mycobacterium tuberculosis* survived significantly longer than animals immunized with conventional BCG. rBCG30, the first vaccine against TB more potent than nearly century-old BCG, is under way for human clinical trials[44].

Because of the global health problems of TB, the increasing rate of MDR-TB and the high rate of a co-infection with HIV, the development of potent new antituberculous drugs without cross-resistance with known antimycobacterial agents is also urgently needed. Rifamycin derivatives (rifabutin, rifapentine, and rifalazil), fluoroquinolones (ciprofloxacin, ofloxacin, sparfloxacin, levofloxacin, gatifloxacin, sitafloxacin, moxifloxacin, and others), and new macrolides (clarithromycin, azithromycin, and roxithromycin) are considered effective for the disease. New antimycobacterial, especially antituberculous agents including oxazolidinone (PNU-100480), 5'-nitroimidazole (CGI 17341), 2-pyridone (ABT-255), new riminophenazines, nitroimidazopyran (PA-824), new ketolides (ABT-773, telithromycin) and defensins (human neutrophil peptide-Ⅰ) are already under preliminary clinical investigation or appear to be promising candidates for future development. New critical information on the whole genome of *Mycobacterium tuberculosis* recently elucidated and increasing knowledge on various mycobacterial virulence genes will promote the progression in the identification of genes that code for new drug targets. Using such findings on mycobacterial genomes, drug development using quantitative structure-activity relationship may be possible in the near future[45,46].

Faster progress toward global targets depends on future development of new drugs, diagnositics, and vaccines. Meanwhile, overcoming health system constrains to intensified implementation of the DOTS strategy and to its adaptations in areas with high prevalence of MDR tuberculosis is very important.

[**REFERENCES**]

[1] Ishikawa N. How to cope with the global tuberculosis burden-experiences and perspectives for Japan's international cooperation[J]. Kekkaku, 2005, 80: 359-364.

[2] Zhao FZ, Zhao Y, Liu XQ. Tuberculosis control in China[J]. Tuberculosis, 2003, 83: 15-20.

[3] 全国结核病流行病学抽样调查技术指导组. 第四次全国结核病流行病学抽样调查报告[J]. 中华结核和呼吸杂志, 2002, 25: 3-7.

[4] 刘宇红, 姜广路, 赵立平, 等. 第四次全国结核病流行病学抽样调查-结核分支杆菌耐药性分析与评价[J]. 中华结核和呼吸杂志, 2002, 25: 224-227.

[5] Chen XY, Zhao FZ, Duanmu HJ, et al. The DOTS strategy in China: results and lessons after 10 years[J]. Bull World Health Organ, 2002, 80: 430-436.

[6] Lowell AM. Tuberculosis morbidity and mortality and its control[M]//Lowell AM, Edwards LB, Palmer CE. Tuberculosis. Cambridge (MA): Harvard University Press, 1969: 1-65.

[7] Jacobs PP. The control of tuberculosis in the United States [R]. New York: National Tuberculosis Association, 1940: 1-387.

[8] Shryock RH. National Tuberculosis Association, 1904-1954 [R]. New York: National Tuberculosis Association, 1957: 1-342.

[9] Long ER, Hopkins FD. History of diagnostic standards and classification of tuberculosis of the National Tuberculosis Association[J]. Am Rev Tuberc, 1952, 65: 494-504.

[10] Reichman LB. The U-shaped curve of concern[J]. Am Rev Respir Dis, 1991, 144: 741-742.

[11] Brown RE, Miller B, Taylor WR, et al. Health-care expenditures for tuberculosis in the United States[J]. Arch Intern Med, 1995, 155: 1595-1600.

[12] Dermot M, Mario R. Global epidemiology of tuberculosis[J]. Clin Chest Med, 2005, 26: 167-182.

[13] Schneider E, Castro KG. Tuberculosis trends in the United States, 1992-2001[J]. Tuberculosis, 2003, 83: 21-29.

[14] Cantwell MF, Snider DE, Cauthen GM, et al. Epidemiology of tuberculosis in the United States, 1985 through 1992[J]. JAMA, 1994, 272: 535-539.

[15] Centers for Disease Control and Prevention. Reported tuberculosis in the United States, 2003[C]. Atlanta (GA): US Department of Health and Human Services, 2004.

[16] LoBue PA, Moser KS. Isoniazid- and rifampin-resistant tuberculosis in San Diego County, California, United States, 1993-2002[J]. Int J Tuberc Lung Dis, 2005, 9: 501-506.

[17] Bloch AB, Cauthen GM, Onorato IM, et al. Nation-wide survey of drug-resistant tuberculosis in the United States[J]. JAMA, 1994, 271: 665-671.

[18] World Health Organization. 47th World Health assembly: provisional agenda item 19. Tuberculosis programme-Progress report by the Director-General [R]. Geneva (Switzerland): WHO, 1994.

[19] World Health Organization. WHO declares tuberculosis a global emergency [R]. Geneva (Switzerland): WHO, 1993.

[20] Frieden TR, Fujiwara PI, Washko RM, et al. Tuberculosis in New York City-turning the tide[J]. N Engl J Med, 1995, 333: 229-233.

[21] McKenna MT, McCray E, Jones JL, et al. The fall after the rise: tuberculosis in the United States, 1991 through 1994[J]. Am J Pub Health, 1998, 88: 1059-1063.

[22] Eileen S, Marisa M, Kenneth G. Epidemiology of tuberculosis in

the United States[J]. Clin Chest Med,2005,26:183-195.

[23] National Coalition for Elimination of Tuberculosis. Tuberculosis elimination: the federal funding gap[R]. National Coalition for Elimination of Tuberculosis,2004.

[24] Pallangyo KJ. Clinical features of tuberculosis among adults in sub-Saharan Africa in the 21st century[J]. Scand J Infect Dis, 2001,33:488-493.

[25] World Health Organization. Global tuberculosis control: surveillance, planning, financing [R]. Geneva (Switzerland): World Health Organization,2004.

[26] Dye C, Scheele S, Dolin P, et al. Consensus statement. Global burden of tuberculosis: estimated incidence, prevalence, and mortality by country. WHO Global Surveillance and Monitoring Project[J]. JAMA,1999,282:677-686.

[27] Corbett EL, Watt CJ, Walker N, et al. The growing burden of tuberculosis: global trends and interactions with the HIV epidemic[J]. Arch Intern Med,2003,163:1009-1021.

[28] Second East African/British Medical Research Council Kenya Tuberculosis Survey follow-up 1979. Tuberculosis in Kenya: follow-up of the second (1974) national sampling survey and a comparison with the follow-up data from the first (1964) national sampling survey. An East and British Medical Research Council co-operative investigation[J]. Tubercle,1979,60:125-149.

[29] Espinal MA, Laserson K, Camacho M . Determinants of drug-resistant tuberculosis: analysis of 11 countries[J]. Int J Tuberc Lung Dis,2001,5:887-893.

[30] Maher D, Chaulet P, Spinaci S. Harries AD for the Global Tuberculosis Programme. Treatment of tuberculosis: guidelines for national programmes[R]. 2nd ed. Geneva: WHO,1997.

[31] Volmink J, Matchaba P, Garner P. Directly observed therapy and treatment adherence[J]. Lancet,2000,355:1345-1350.

[32] Raviglione MC, Harries AD, Msiska R, et al. Tuberculosis and HIV: current status in Africa[J]. AIDS, 1997, 11 Suppl B: S115-S123.

[33] Kenyon TA, Mwasekaga MJ, Huebner R, et al. Low levels of drug resistance amidst rapidly increasing tuberculosis and human immunodeficiency virus co-epidemics in Botswana[J]. Int J Tuberc Lung Dis,1999,3:4-11.

[34] Wiktor SZ, Sassan-Morroko M, Grant AD, et al. Efficacy of trimethoprim-sulphamethoxazole prophylaxis to decrease morbidity and mortality in HIV-1 infected patients with tuberculosis in Abidjan, C te d'Ivoire: a randomised controlled trial[J]. Lancet,1999,353:1469-1475.

[35] Anglaret X, Chene G, Attia A, et al. Early chemoprophylaxis with trimethoprim-sulphamethoxazole for HIV-1-infected adults in Abidjan, C te d'Ivoire: a randomised trial[J]. Lancet, 1999,353:1463-1468.

[36] Provisional WHO/UNAIDS secretariat recommendations on the use of cotrimoxazole prophylaxis in adults and children living with HIV/AIDS in Africa[R]. Geneva: Joint United Nations Programme on HIV/AIDS,2000.

[37] Harries AD, Nyangulu DS, Hargreaves NJ, et al. Preventing antiretroviral anarchy in sub-Saharan Africa[J]. Lancet, 2001, 358:410-414.

[38] Quinn TC, Wawer MJ, Sewankambo N, et al. Viral load and heterosexual transmission of human immunodeficiency virus type 1[J]. New Engl J Med,2000,342:921-929.

[39] World Health Organization. Stop TB. An expanded DOTS framework for effective tuberculosis control [R]. Geneva (Switzerland): WHO,2002.

[40] World Health Organization. Fifty-third World Health Assembly. Resolutions and decisions. Resolution WHA 53. 1[R]. Geneva (Switzerland): WHO,2002.

[41] Woods GL. The mycobacteriology laboratory and new diagnostic techniques[J]. Infect Dis Clin North Am,2002,16:127-145.

[42] Castro KG, Jaffe HW. Rationale and methods for the national tuberculosis genotyping and surveillance network[J]. Emerg Infect Dis,2002,8:1188-1191.

[43] Centers for Disease Control and Prevention. Guidelines for using Quanti FERON-TB Test for diagnosing latent *Mycobacterium tuberculosis* infection [J]. MMWR Morb Mortal Wkly Rep,2003,52:15-18.

[44] Marcus AH, Gunter H. A new vaccine against tuberculosis affords greater survival after challenge than the current vaccine in the Guinea pig model of pulmonary tuberculosis[J]. Infect Immun,2003,71:1672-1679.

[45] Tomioka H. Prospects for development of new antituberculous drugs[J]. Kekkaku,2002,77:573-584.

[46] Mitchison DA. The search for new sterilizing anti-tuberculosis drug[J]. Front Biosci,2004,1:1059-1072.

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全球结核病的流行与控制

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[摘要] 结核病是一个全球性的疾病,在被忽略近 20 年后又死灰复燃,成为当今世界一个主要的公共卫生问题。1993 年,世界卫生组织因结核病的流行规模及控制全球结核病的迫切需要,宣布全球进入结核病紧急状态。中国是世界上人口最多的国家,位居全球结核病感染最严重的 22 个国家之首位。在 20 世纪 80 年代中晚期,美国也终止了其长期以来结核病的下降趋势,1992 年美国结核病的发病率达到一个高峰。撒哈拉以南非洲地区是世界结核病例分布最多的三个区域之一,世界结核病发病率最高的 15 个国家有 13 个在这个地区内,并且 HIV 是这一区域结核病发病率最主要的单一预计因子。世界最严重的 HIV 相关结核病发病也是在这个区域。全球持续的严重结核感染状态,是由于贫困人口的增加和来自于结核高发病率国家的人口流动和 HIV 的影响,最主要的是没有维持必需的公共卫生组织及设施,以及错误的认为结核病已成为一个过去的问题。依靠现有的诊断和治疗方法,WHO 推荐的 DOT 方案有效而经济,适用于全球在不同条件下的结核控制。

[关键词] 流行病学;中国;美国;撒哈拉以南非洲;结核病
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