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A Strategic Plan for the Elimination of Tuberculosis in the United States

A Strategic Plan for the Elimination of Tuberculosis in the United States Message to the Readers of Morbidity and Mortality Weekly Report I am pleased to provide you with "A Strategic Plan for the Elimination of Tuberculosis in the United States" describing actions necessary to achieve the goal by the year 2010, with an interim target of a case rate of 3.5 per 100,000 population by the year 2000. At a national conference in 1984, Dr. James O. Mason, then Director of the Centers for Disease Control, challenged the public health community to develop a strategy to eliminate tuberculosis from the United States. This plan was developed by the Centers for Disease Control/Department of Health and Human Services' Advisory Committee for Elimination of Tuberculosis. Many experts from both within and outside the Department played a significant role in its development. We are grateful to all those who participated in the process. I am pleased to report that the House of Delegates of the American Medical Association and the Governing Council of the American Public Health Association have passed resolutions in support of the plan, and the American Lung Association and the American College of Preventive Medicine have also endorsed the goal. We thank these organizations for their support and anticipate that other organizations will take similar actions in the near future. We must commit ourselves to the objective of eliminating tuberculosis and making that objective widely known so others can join in this effort. The Centers for Disease Control is identifying activities for short- and long-term implementation. The plan is being distributed to a wide variety of public and private organizations with the recommendation that they take similar action. The goal of eliminating this disease and its tragic consequences from the United States is achievable, and we believe it will be broadly supported by all sectors of our society. Walter R. Dowdle, Ph.D. Acting Director Centers for Disease Control

INTRODUCTION In 1987, the Secretary of the U.S. Department of Health and Human Services established an Advisory Committee for Elimination of Tuberculosis* to provide recommendations for developing new technology, applying prevention and control methods, and managing state and local tuberculosis programs targeted at eliminating tuberculosis as a public health problem. After review and feedback from numerous interested people and organizations, this plan was completed. The committee urges the nation to establish the goal of tuberculosis elimination (a case rate of less than one per million population) by the year 2010, with an interim target of a case rate of 3.5 per 100,000 population by the year 2000. The U.S. case rate for 1987 was 9.3 per 100,000 (1). Three factors make this a realistic goal: 1) tuberculosis is retreating into geographically and demographically defined pockets; 2) biotechnology now has the potential for generating better diagnostic, treatment, and prevention modalities; and 3) computer, telecommunications, and other technologies can enhance technology transfer. Therefore, a three-step plan of action was developed:

1. more effective use of existing prevention and control methods, especially in high-risk populations
 - 2.the development and evaluation of new technologies for treatment, diagnosis, and prevention
 - 3.the rapid assessment and transfer of newly developed technologies into clinical and public health practice
- The committee brings this plan to the attention of the medical community and the public to stimulate positive, constructive discussion and action, to increase the public's level of awareness of tuberculosis, and to encourage a commitment to the elimination of tuberculosis. In the past, the

United States has spent hundreds of millions of dollars annually on tuberculosis treatment and control activities. Unless alternative action is taken, large and unnecessary expenditures will continue indefinitely. Expenditures on tuberculosis treatment may increase over the next few years because of high morbidity rates among people infected with the human immunodeficiency virus (HIV), the homeless, the foreign-born, the elderly, and various minority groups. Furthermore, tuberculosis has the potential for spreading more widely in the community. The mission of all tuberculosis control programs should now be to eliminate this disease by the year 2010. Strategies for eliminating tuberculosis are set out in this document. These strategies are based on the needs and responsibilities of the various groups of people involved in this effort (Appendix). The committee realizes the task will not be an easy one; it will require considerable commitment at all levels. The challenge to carry out this plan is a test of our willingness and ability as a society to respond to a very serious health problem that disproportionately affects its disenfranchised members. A great nation such as ours can carry out this plan. It is time to commit to a tuberculosis-free society!

BACKGROUND INFORMATION Tuberculosis is a communicable disease caused by bacteria (*Mycobacterium tuberculosis* complex) that are usually spread from person to person through the air. When people with tuberculosis of the respiratory tract cough, airborne infectious particles are produced. If these bacteria are inhaled by other people, they cause an infection that spreads throughout the body. Most individuals who become infected do not develop a clinical illness because the body's immune system brings the infection under control; however, infected people do develop a positive reaction to a tuberculin skin test. The infection can persist for years, perhaps for life, and infected persons remain at risk of developing disease at any time, especially if the immune system becomes impaired. Although the disease usually affects the lung, it can occur at virtually any site in the body. Despite the great strides that have been made in the control of tuberculosis, the disease continues to be a public health problem in the United States. There remain isolated and potentially dangerous enclaves of this preventable, but frequently severe and occasionally fatal, disease. If more aggressive action is not taken, thousands of preventable cases and deaths will continue to occur in the United States each year until well into the next century. This document has been prepared to identify the steps necessary to eliminate tuberculosis. Ongoing analyses of tuberculosis morbidity data continue to identify the magnitude and extent of the problem. These data have important implications for the control and elimination of tuberculosis in the United States. From 1953 through 1984, the number of tuberculosis cases reported decreased an average of 5% annually (1). However, in 1985, the number of tuberculosis cases remained stable and, in 1986, cases increased by 2.6% (2,3). This increase was, at least in part, caused by the occurrence of tuberculosis among persons infected with HIV (2-4). HIV infection appears to have increased the incidence of tuberculosis by causing immunosuppression, which allows latent tuberculous infection to progress to clinically apparent disease. Therefore, tuberculosis screening and prevention efforts will need to be targeted to persons with, or at risk for, HIV infection. Although tuberculosis case rates have progressively declined for all races over the past two decades, the decrease has been much less among nonwhites than among whites. Nearly two-thirds of cases now occur among blacks, Hispanics, Asians, and Native Americans (5-10). Although specific data are not available, the higher risk in these minority populations may be related primarily to socioeconomic conditions, such as poor housing and nutrition. Thus, prevention and control strategies should be formulated in consultation with, and targeted toward, these high-risk minority populations. Tuberculosis is also common among immigrants, refugees, and migrant workers from countries where the disease is prevalent (10). In these patients, organisms responsible for disease are frequently resistant to commonly used antituberculosis drugs, especially isoniazid (INH). If not recognized and managed appropriately, drug-resistant disease and infection may lead to failure of treatment or preventive measures. Almost half the cases among immigrant Asians occur within the first 2 years of arrival in the United States. Specific control efforts should thus be directed at recent immigrants before or shortly after their arrival. Over two-thirds of cases in foreign-born persons

occur in those who are less than 35 years old at the time of arrival in the United States (10). These cases are potentially preventable. More than 80% of childhood cases occur in minority groups. Childhood cases are geographically focal. Less than 12% (363) of U.S. counties reported one or more tuberculosis cases among children in 1986 (CDC unpublished data). Using childhood cases as sentinel health events, health departments can target certain populations for preventive intervention. Among all racial and ethnic groups and both sexes, tuberculosis case rates are highest among the elderly. Although case rates are higher among the 5% of the elderly living in nursing homes, the majority of cases occur among 95% of the elderly who live in the community. Good epidemiologic surveillance data are essential for an effective tuberculosis- elimination effort. These data target the populations and geographic areas experiencing the problem and provide clues as to how to deal with it. Additional data are needed to define the extent to which correctional institution populations, homeless people, lower socioeconomic groups, and others are at increased risk. While analyses of national data are useful, analyses of state and local data will be even more important for targeting elimination efforts.

STEP 1 -- MORE EFFECTIVE USE OF EXISTING PREVENTION AND CONTROL METHODS

The emphasis in this section is on currently available prevention and control strategies not being fully utilized and on new strategies using existing technology. Although new technologies will be needed to eliminate tuberculosis (see Step 2), much can be achieved through efforts to improve existing tuberculosis control programs. Detailed recommendations for diagnosis, prevention, treatment, and program management are included in various American Thoracic Society and CDC statements and in CDC's Tuberculosis Policy Manual. Our recommendations are quite general and will need to be adapted at the state, community, and individual level. They are meant to serve as guidelines and not to establish rigid standards of practice or to discourage creativity and innovation. Priorities for Step 1 include adequate and appropriate treatment for all persons with tuberculosis, identification of high-risk population groups within each geographic area, and the use of preventive treatment in the appropriate members of these groups. Strategies are organized in terms of surveillance, prevention of disease and infection, containment of disease, and program evaluation and assessment.

Improving Surveillance

The identification and reporting of tuberculosis cases, suspected cases, and contacts is often slow or incomplete, thus delaying treatment and preventive intervention. Some cases are not diagnosed or reported, and contact investigation is not done. This is more likely to occur among the poor, the elderly, the homeless, drug users, and prisoners. By January 1, 1991, systems should be in place to assure that: 1) all persons with signs and symptoms suggestive of tuberculosis receive an appropriate diagnostic evaluation within 2 weeks of initial contact with a health-care provider; 2) suspected or diagnosed cases are reported to health departments within 3 days of the time the diagnosis is made or suspected, or a positive laboratory result is obtained, so that contacts can be identified and examined; 3) active population-specific casefinding, screening, and preventive intervention programs are established and maintained by health departments; and 4) achievement of the above objectives is measured and assessed.

Methods

2. Health departments, medical and nursing schools, schools of public health, volunteer agencies, professional societies, and minority advocacy groups should educate health-care providers and high-risk groups in the community about the signs and symptoms of tuberculosis and the methods of diagnosis, treatment, and prevention.
 2. To speed up case reporting and make it easier for health-care providers to report, health departments should initiate telephone reporting systems for reportable infectious diseases, including tuberculosis, as a replacement or supplement to written notification. This system should include a telephone answering machine to record off-hour reports. Computer-to-computer reporting using telecommunications systems should be developed to further improve surveillance.
 3. Physician, laboratory, and hospital reporting of cases to health departments should continue. Pharmacy reporting of persons who receive a supply of antituberculosis drugs should be undertaken on a pilot basis to determine whether additional cases are found.
 4. Health

department staffs should routinely monitor the time between the diagnosis of tuberculosis and the date the case is reported to the health department. Delays of more than 3 days should be investigated and action taken to prevent similar delays in the future. 5. Health department staff should conduct periodic reviews of selected records systems (e.g., laboratory reports, pharmacy reports, AIDS registries, and death certificates) to validate the surveillance system and to detect any failures to report cases. 6. Clinicians and public health officials should identify groups of people in the community among whom tuberculosis and transmission of infection are occurring. This may require collection and analysis of data (e.g., residence, occupation, socioeconomic-status indicators, and HIV-antibody status) not now included on the individual case-report form. These data are necessary to identify high-risk populations and areas in which active casefinding and preventive intervention programs should be conducted. Members of high-risk groups and their health-care providers should be apprised of the problem and involved in the design, implementation, and evaluation of casefinding and prevention programs. Improving Case Prevention Preventable tuberculosis cases continue to occur in the United States. By definition, preventable cases include all those for whom one or more of the currently recommended interventions should have been utilized but were not. These interventions include contact identification and examination, preventive therapy for infection, prompt diagnosis of disease, prompt reporting, isolation of persons with suspected and diagnosed tuberculosis, adequate ventilation of buildings, the use of ultraviolet lights in high-risk areas of buildings, chemotherapy for disease, and directly observed therapy. Some of these interventions (e.g., isolation) are designed to prevent transmission of infection among residents and staff of high-risk institutions such as hospitals, nursing homes, correctional institutions, and shelters for the homeless. Other interventions (e.g., preventive therapy) are designed to prevent disease among those already infected. INH preventive therapy reduces the risk of tuberculosis by more than 90% among persons who complete a full course of treatment. To prevent infection among persons potentially exposed to an infectious case of tuberculosis and to prevent tuberculosis among contacts and other infected persons for whom preventive therapy is recommended, the following methods should be implemented by January 1, 1991. Methods

3. All U.S. residents should have the results of at least one tuberculin skin test in their medical records, and those whose test result is positive should be evaluated and counseled regarding their risk of developing tuberculosis. 2. Each health department should assess the prevalence, incidence, and sociodemographic characteristics of cases and infected persons in the community. On the basis of these data, health departments should initiate tuberculin screening programs specifically targeted to each community's high-risk groups. Screening may be done to identify suspects, undiagnosed cases, diagnosed cases lost to follow-up, and infected persons in need of preventive therapy. At a minimum, health departments should ensure that such programs are extended to persons with symptoms compatible with tuberculosis, all foreign-born persons (and their families) from high-prevalence areas, high-risk minority groups, the homeless, migrant workers, persons being admitted to nursing homes, people entering correctional institutions, and people known to be infected with HIV. In addition to their prevention value, screening programs have the potential for providing publicity and generating goodwill for the tuberculosis program. 3. Tuberculin skin-testing programs should be conducted annually among the staffs of tuberculosis clinics, mycobacteriology laboratories, shelters for the homeless, nursing homes, substance-abuse treatment centers, dialysis units, and correctional institutions. The staffs of hospitals, mental institutions, and home health-care agencies should be tested annually if the prevalence of infection exceeds 5%. 4. Consideration should be given to installing and properly maintaining ultraviolet lights in high-risk facilities such as jails, prisons, and shelters for the homeless (10-13). 5. Hospitals that admit untreated tuberculosis patients or persons suspected of having tuberculosis should have proper facilities and procedures for instituting respiratory isolation. 6. Consideration should be given to routinely obtaining sputum for mycobacterial smear and culture from symptomatic nursing home residents thought to have a

lower respiratory infection. 7. Tuberculosis patients and persons suspected of having tuberculosis should be interviewed within 3 days after the health department receives the case report by a person who has had specific training in contact interviewing. 8. Close contacts should be examined within 7 days after the index case is diagnosed. 9. Infected contacts should be placed on preventive therapy if there is no evidence of clinical disease. 10. A child whose skin test shows no evidence of infection and who is a close contact of someone with infectious tuberculosis should be placed on preventive therapy until repeat skin testing (3 months after contact is broken) confirms the absence of infection. 11. All persons identified with HIV infection should be tuberculin tested. Those with positive tuberculin reactions or a history of a positive tuberculin reaction (without active disease) should be considered for preventive therapy, regardless of age. 12. All other recognized high-risk, infected persons should be considered for preventive therapy regardless of age. This includes recently infected persons (i.e., persons who had negative skin-test results who have converted to positive test results), persons with chest radiographic findings consistent with past tuberculosis, and those with medical risk factors known to substantially increase the risk of tuberculosis (e.g., silicosis, below ideal body weight, gastrectomy, immunosuppressive therapy). 13. Screening of refugees, immigrants, and entrants from high-incidence countries should be continued and infectious persons with tuberculosis excluded until they become noninfectious. These groups should also be screened for tuberculous infection (without disease). Unless contraindicated, those with infection (without disease) should be started on preventive therapy either before, or within 2 months after, their entry into the United States. 14. Infected persons placed on preventive therapy should complete a full course of treatment. 15. Twice-weekly, directly observed preventive therapy should be used whenever necessary to ensure compliance, especially if the number of persons on daily supervised preventive therapy would overextend the personnel resources assigned to the program. 16. Patients on INH preventive therapy must be carefully monitored on a monthly basis for compliance and signs and symptoms of toxicity. Spot testing of urine for INH metabolites is highly recommended when therapy cannot be observed directly. If signs or symptoms of toxicity appear, therapy should be stopped immediately and the patient reevaluated. No more than a 1-month supply of medicine should be dispensed at any visit. 17. BCG vaccine should be considered in those rare situations in which other control measures cannot be applied and uninfected children are exposed to infectious persons who remain untreated. Improving Disease Containment Many tuberculosis patients do not complete a recommended course of therapy. More than 25% of sputum-positive patients are not known to have converted from positive to negative sputum culture within 6 months. In addition, almost 12% of patients are not known to be currently receiving therapy, and more than 17% of tuberculosis patients do not take their medication continuously (14). Beginning immediately, all patients with tuberculosis should complete treatment with an appropriate regimen.

Methods

4. For each new case of tuberculosis in the United States, a specific health department employee should be assigned the responsibility and held accountable for ensuring the education of the patient about tuberculosis and its treatment, ensuring continuity of therapy, and ensuring that contacts are examined. The health-care worker should visit the patient within 3 days of diagnosis to identify contacts and possible problems related to compliance with therapy. 2. For each new infectious case, a specific treatment and monitoring plan should be developed within 4 days of diagnosis. This plan should include drugs to be used (doses, duration, and frequency of administration), assessment of toxicity, and methods to be used to assess and ensure compliance. 3. Appropriate antituberculosis drugs, laboratory services, contact investigations, contact examinations, and other necessary services should be provided to patients by health departments without regard to the patients' ability to pay. 4. Incentives may be necessary to enhance compliance. To be most effective, incentives should be tailored to the individual needs and desires of the patients. An incentive may be as simple as offering a cup of coffee and talking with a patient while he or she is waiting in the clinic, or as

complex as providing food and housing for a homeless patient. Particular attention must be given to ensuring that patients have transportation to the clinic. 5. Twice-weekly, directly observed therapy should be used whenever needed. Specific funding for outreach staff should be encouraged at the federal, state, and local level. Alternatives to federally funded outreach staff might include, for example, appropriately instructed home health-care workers or maternal and child health staff to supervise therapy. 6. Quarantine measures, including temporary institutionalization, should be used in those instances when an infectious patient refuses to comply with self-administered or directly observed therapy. State and local laws and regulations should be modernized to facilitate the cure of persons with infectious tuberculosis. For example, court-ordered compliance with directly observed therapy should be available. Program Assessment and Evaluation In many areas, there is incomplete assessment of community tuberculosis control problems and inadequate evaluation of community prevention and control efforts. As a result, programs do not function as effectively and efficiently as they should. By January 1, 1991, a system should be in place to achieve an ongoing, effective assessment of the tuberculosis problem and evaluation of the activities being performed at all levels for the control and elimination of tuberculosis. Methods

5. The Federal Government and state and large metropolitan health departments should annually evaluate their progress toward the elimination of tuberculosis. This evaluation should include an analysis of morbidity and mortality data, case reporting, case finding, treatment, and prevention activities. Annual evaluations could be done in collaboration with interested constituencies such as lung associations, minority organizations, and professional societies. Regional meetings to share information among states are encouraged. 2. Expert assessment should be conducted annually for local health departments by the state, CDC, or the American Lung Association/American Thoracic Society and for state health departments by CDC or the American Lung Association/American Thoracic Society. A similar assessment of federal tuberculosis prevention and control activities should be conducted by the CDC Advisory Committee for Elimination of Tuberculosis or other outside consultants. 3. Priority for continued federal funding of state and local programs should be, at least in part, contingent upon improved program performance and productive activities in high-risk populations. 4. A prototype computerized record system should be developed by CDC for use by local programs for case reporting, patient management, and program assessment. CDC should provide microcomputers, with appropriate software and training, to state and major city health department tuberculosis control programs in high-incidence areas. 5. Each state and major metropolitan area should develop and publish an annual community tuberculosis summary and program plan (including objectives, methods, a discussion of program progress or failure, and corrective action needed). 6. Health departments should review each new tuberculosis case and each death from tuberculosis to determine if the case or death could have been prevented had the American Thoracic Society/CDC recommendations been followed. Based on these reviews, new policies should be developed and implemented to reduce the number of preventable cases.

Conclusion Implementation of Step 1 of this plan will require strong commitment at the national, state, and community levels. State and local tuberculosis advisory groups, with broad representation from public, private, and voluntary medical groups, should develop and help implement Step 1 strategies appropriate for the state or community. STEP 2 -- DEVELOPMENT AND EVALUATION OF NEW PREVENTION, DIAGNOSTIC, AND TREATMENT TECHNOLOGIES In June 1985, CDC, the National Institutes of Health, the American Thoracic Society, and the Pittsfield Antituberculosis Association cosponsored a conference in Pittsfield, Massachusetts. The objective of this conference was to identify areas for research that would lead to improved technologies for eliminating tuberculosis from the United States. The complete report of this conference was published in the August 1986 issue of the American Review of Respiratory Disease (15). Consequently, only selected priority projects are mentioned here. The five headings under which research projects and activities are listed represent critical objectives for eliminating

tuberculosis. They are presented in priority order. These projects should also be regarded in terms of type of research, i.e., basic, applied, and epidemiologic/operational (Table 1). Basic research is intended to obtain a better understanding of structure, processes, and mechanisms of tuberculosis. While the findings from this research can often be applied for some clinical or public health purpose, basic research does not proceed with a specific application in mind. As already implied, applied research has as its goal the application of knowledge to the solution of a particular clinical or public health problem. Epidemiologic studies are designed to assess the magnitude, distribution, and determinants of disease in a population. Operational research studies assess the actual impact of interventions on health outcomes in the population. Improving Methods for Preventing Disease in Infected Persons The vast majority of new cases of tuberculosis arise in persons who have had a latent period of infection. The most critical element in tuberculosis elimination is the detection and treatment of infected persons before disease emerges. At present, INH is usually administered for 6-12 months for preventive therapy. However, this approach has major deficiencies. These include the expense of treating and monitoring patients for such a long time, noncompliance with preventive therapy of long duration, and the occurrence of drug toxicity, especially hepatotoxicity. The first-priority objective of Step 2 is to develop shorter, safer, more effective and more economical means of preventing the emergence of clinical disease from the infected state. Methods Areas of research to be pursued are as follows:

6. A drug that is more effective and less toxic than INH should be identified. This will require research at several levels.
 - a. The mechanisms by which current antituberculosis drugs act are poorly understood. Consequently, studies of microbial metabolism, with identification of target sites for drug activity, should be conducted to develop new approaches to preventive therapy.
 - b. In vitro models of drug efficacy, especially those allowing assessment of the interactions of drug, phagocyte, and organism, should be developed to help select drugs for in vivo studies.
 - c. Animal models for studying preventive therapy of latent infection should be developed.
 - d. Based on present and developing knowledge, candidate drugs should be evaluated in high-risk groups both in the United States and in other countries.
 2. Alternatives to daily INH preventive therapy regimens (e.g., multi-drug regimens, rifampin alone, twice-weekly INH) should be evaluated.
 3. Because hepatotoxicity is a major limitation to the use of INH preventive therapy, research efforts should be encouraged that
 - a) contribute to the understanding of the mechanisms of INH-hepatitis,
 - b) contribute to the understanding of the mechanism by which INH acts, which will in turn facilitate the development of congeners that retain antimicrobial potency while eliminating sites of hepatotoxic potential,
 - c) investigate the cytoprotective effects of agents that may block or interfere with the toxic effects of INH, and
 - d) identify more specific risk factors, other than age, for the development of INH-hepatitis.
 4. High priority should be given to the development of a postinfection vaccine to boost the specific immune response.
 5. Modification of the host immune response to *M. tuberculosis* infection should be evaluated as a supplement to chemoprophylaxis to boost the immune response and increase destruction of intracellular parasites.

Improving Methods for Identifying Infected Persons at Risk of Disease The use of the Mantoux test with tuberculin, purified protein derivative (PPD), to identify persons infected with *M. tuberculosis* is well established. However, the test suffers from a lack of sensitivity and specificity. In addition, the test is difficult to interpret in serial testing programs because of the "booster effect." In conjunction with the skin test, epidemiologic factors and patient characteristics have been used to identify persons at high risk of developing disease. The risk of developing clinically apparent tuberculosis is increased by recently acquired infection, young adulthood, leanness, and disease states in which T-lymphocyte function is disturbed (16). Despite this knowledge, we currently have a very limited ability to predict which infected persons are most likely to develop disease. Preventive therapy would be a much more efficient intervention for reducing tuberculosis morbidity if there were better methods for identifying persons infected with *M. tuberculosis* (i.e., those who are at risk of

developing disease). Ideally, a test is needed that is capable of specifically differentiating those who harbor living tubercle bacilli from those who do not. Methods

7. Genes that code for species-specific epitopes of mycobacteria should be identified and characterized. This should permit amino acid analysis and synthesis of epitopes which may be useful for serologic or skin-test diagnosis. 2. T-lymphocytes are the key responding cellular elements of the immune response to *M. tuberculosis*. These cells should be studied to identify subpopulations of T-lymphocytes that influence progression or containment of infection.

3. Genetic differences, such as those related to histocompatibility complex antigens, between infected persons who develop disease and those who do not should be sought. 4. The absolute and relative risk of disease among persons infected with both the tubercle bacillus and HIV should be determined. 5. Socioeconomic status, immunodeficiency status, stress (both physical and psychological), body weight, nutrition, and environmental factors (e.g., incarceration, sunlight, ventilation) should be investigated as risk factors in prospective or case-control studies. Improving Methods for Preventing Infection or the Establishment of Infection in Various Body Sites Transmission of *M. tuberculosis* infection usually occurs via the airborne route. Current methods for preventing the transmission of infection to uninfected persons include early identification, isolation, and treatment of infectious source cases; environmental control to reduce the number of airborne infectious particles through the use of nonrecirculated ventilation to the outdoors and ultraviolet light; and drug therapy of uninfected persons who are exposed to infection sources. Vaccination with BCG does not prevent infection but may limit the spread and complications of the disease (17). Each of these measures has certain drawbacks, and transmission of infection is still occurring at unacceptable levels. Therefore, more reliable methods are needed for preventing infection and for limiting its spread within the body. Methods

1. Source case factors a. Patient characteristics that influence infectiousness should be thoroughly examined. 2. Environment- or bacteria-oriented factors a. Research on systems for better air disinfection should be conducted. b. Studies that would increase our understanding of the pathogenicity of *M. tuberculosis* and how this may affect infectivity and virulence should be pursued. 3. Studies on the host's native resistance a. Host factors (e.g., nutritional state, genetic makeup, level of stress) that affect susceptibility and resistance to tuberculous infection should be identified. b. More refined epidemiologic methods for identifying groups and persons at risk of becoming infected should be investigated. c. In vitro studies of the immune and nonimmune macrophage's ability to handle virulent and avirulent strains of *M. tuberculosis* should be undertaken to identify factors that affect the macrophage's ability to destroy these organisms. 4. Vaccination a. Studies to identify protective immunogenic component antigens of *M. tuberculosis* should be undertaken and procedures for large-scale production, purification, and synthesis of these antigens should be developed. b. Different immunization techniques, with and without biological response modifiers, should be evaluated. 5. Populations in which a vaccine trial could be carried out should be identified. 6. Studies should be done to determine if persons or groups differ with regard to infectibility and whether this could be altered in some way. Improving Methods for Treating Disease Current drug regimens are effective, well tolerated, and can be given with minimal effects on the patient's mode of living. Nevertheless, major problems remain. With current drugs, a minimum of 6 months of multi-drug therapy is necessary to achieve a high probability of cure (18). There are at least four obstacles to achieving a cure: 1) the failure of patients to comply with regimens of long duration, 2) drug-resistant organisms, 3) adverse reactions that require interruption and modification of the original, and usually optimal, drug regimen, and 4) the cost of the most effective regimens. The following steps should be taken to develop more effective approaches to therapy for tuberculosis. Methods

2. All new antimicrobial agents should be routinely evaluated in vitro for antimycobacterial activity. In addition, drug combinations should be examined for synergy. 2. Classes of compounds that should receive high priority in the search for better treatment regimens are beta-lactam compounds, long-acting sulfones and sulfonamides, rifamycins, and 4-quinolones. 3. Improved delivery systems--including longer acting drug-release systems, such as injectable suspensions, implantable rods, and membrane-enclosed drugs-- should be sought. 4. Research to define enzyme targets for antituberculosis drugs should be carried out. This information will facilitate the design of new drugs with higher affinity for these target enzymes, or indicate rational modifications of existing drugs for the same purpose. High priority should be placed on finding rapidly effective, bactericidal agents that affect mycobacteria in all metabolic states. 5. Because mycobacteria within macrophages are not readily accessible to many drugs, a knowledge of drug transport mechanisms should be acquired to allow modification of drugs to facilitate uptake. 6. Pharmacologic agents that activate T-lymphocytes and macrophages should be identified and evaluated in patients with mycobacterial diseases. 7. Manipulation of the microenvironment in the phagosome should be attempted to improve the efficiency of the microbicidal activity of phagocytic cells. 8. Effective compliance enhancers or incentives should be identified and psychometric and other tests should be developed to identify persons for whom various enhancers are likely to be most effective. Improving Methods for Diagnosing Disease Current techniques for diagnosing tuberculosis are beset by a number of serious limitations and problems. Available techniques are slow, resource intensive, and not ideally sensitive and specific. One objective of this program is to develop better diagnostic techniques that will rapidly identify persons with current disease and distinguish them from persons with past disease or infection without disease. Methods
3. High priority should be placed on the search for genus- and species-specific epitopes. 2. DNA probes specific for *M. tuberculosis* should be produced and evaluated. 3. Similarly, genus- and species-specific monoclonal antibodies should be produced and evaluated for their ability to rapidly detect and identify *M. tuberculosis* and other medically significant mycobacteria. 4. Studies to detect free mycobacterial antigens with appropriate antibodies or probes in clinical specimens should be undertaken. 5. Systems that would assay material produced by the diseased host's lymphocytes or macrophages might be useful for diagnosis. A related area to be explored is the study of the T-lymphocyte antigen receptor. Conclusion There is an urgent need for competent investigators to submit well-designed proposals for all of the above studies. CDC should continue to work with the National Institutes of Health, the Food and Drug Administration, state and local health departments, private industry, academia, volunteer agencies, foundations, and other groups to encourage the funding and conducting of this research. A report from federal and private research funding agencies should be submitted annually to the Secretary's Advisory Committee for Elimination of Tuberculosis detailing progress made in achieving these research objectives. STEP 3 -- TECHNOLOGY ASSESSMENT AND TRANSFER This step of the elimination plan focuses on the actions necessary to facilitate the adoption of new tools, procedures, and ideas into clinical and public health practice. (This has been called technology transfer or translation.) Because we are generally discussing the assessment and transfer of technologies not yet developed, it is not possible to be as specific in this section as in the preceding two sections. Technology Assessment and Transfer in General Impediments to the technology and assessment transfer process must be identified and strategies devised to resolve them. Problems arise if the new technology requires retraining, additional resources, or a change in habits. Problems also arise if cost-effectiveness data on a new technology are not available or if cost savings from a new procedure do not accrue to those who spend the resources to adopt the new technology. It is important to ensure the widespread, rapid, and efficient use of new technologies for tuberculosis control in field operations. Methods Technologies for transfer should be chosen on the basis of their potential impact on the tuberculosis-elimination effort. Before a program is initiated to "sell" a new technology, it is crucial

to develop a consensus on its appropriateness, identify persons who will be using the new technology, enlist their aid, identify potential resistance points to the introduction of new technologies and innovations, and develop strategies for overcoming the resistance. Methods to be used in specific sectors are as follows:

4. The Federal Sector a. Lead responsibility for setting standards for technology transfer should rest with CDC through its ongoing work with the American Thoracic Society's Scientific Assembly on Microbiology, Tuberculosis, and Pulmonary Infection; the American Academy of Pediatrics LP*RedbookLP' Committee; and other expert groups. These groups should critically assess information about new technologies and make recommendations about further evaluation and implementation. b. The involvement of other federal agencies (including the National Institutes of Health, the Food and Drug Administration, the Health Care Financing Administration, the Health Resources and Services Administration, the Veterans Administration, and the Immigration and Naturalization Service) on an Interagency Task Force will be important in the technology assessment and transfer process. c. CDC Public Health Advisors and their state and local counterparts should continue to translate national recommendations into local practice. Public Health Advisors should be assigned the tuberculosis control program of each state and big city requesting such assistance. These programs should be encouraged to develop their own program-management capacity to transfer new technology. d. When available, federal grant funds should continue to be used as seed money for implementing new tuberculosis technology, demonstration projects, and technology assessments. States and localities should continue to fund ongoing community tuberculosis control efforts and eventually assume the cost of each new technology as its advantages become apparent. e. CDC should explore with the Health Care Financing Administration the possibility of Medicare and Medicaid reimbursement for tuberculosis control services such as directly observed therapy, nursing services, translation services, transportation services, and halfway housing for tuberculosis patients. Resources to provide these services to persons not covered by Medicare or Medicaid must also be sought. f. CDC should continue to disseminate information about new technologies to as wide an audience as possible. Current vehicles for this information exchange include the Morbidity and Mortality Weekly Report, articles and editorials in peer-reviewed medical and nursing journals, training courses (such as "TB Today!"), and national tuberculosis conferences. These should be supplemented with new educational tools such as videotapes, satellite teleconferencing, computerized bulletin boards, and programmed instruction packages. g. The Division of Tuberculosis Control, Center for Prevention Services, CDC, should continue to work with national organizations (e.g., the American Hospital Association, major health maintenance organizations, and nursing home organizations) to assist in establishing policies for tuberculosis control. h. The mycobacteriology laboratory at CDC should continue to play an important role in the assessment and transfer of technology in the diagnostic and laboratory areas through premarketing and postmarketing evaluation of new technologies and scientific publications. i. The Division of Quarantine, Center for Prevention Services, CDC, should apply new technology for controlling tuberculosis among immigrants, refugees, and other entrants.
5. The State and Local Public Sector a. Technology-assessment and -transfer activities of state and local tuberculosis control programs should complement those of the federal sector. Strengthening state and local health department infrastructure (noted in Step 1) will enhance the implementation of new technologies. b. The American Public Health Association, Association of State and Territorial Health Officials, the Council of State and Territorial Epidemiologists, the National Association of County Health Officers, the U.S. Conference of Local Health Officers, the Association of State and Territorial Public Health Nursing Directors, the Association of State and Territorial Laboratory Directors, state and local advisory committees, and other similar organizations can play a vital role by recommending the adoption of the elimination plan and new

prevention and control technologies. c.State and locally funded evaluations of new technologies through demonstration programs will be important to their adoption locally. d.Promulgation of information on new technologies through state and local public health newsletters can help to spread new technologies through the public sector and into the private sector as well. e.This sector should link with the academic institutions to educate the private medical sector about new technologies in tuberculosis. This might involve making telephone calls or personal visits to physicians who report and/or manage cases and providing them with current literature.

6. The Volunteer Sector a.Since the turn of the century, the American Lung Association has led our nation's efforts to establish effective public health programs to deal with the problem of tuberculosis. Continuation of these educational and advocacy activities, including support of local American Lung Association/American Thoracic Society educational activities, will be essential to the technology- transfer effort. To enhance its effectiveness, the American Lung Association should continue to form national, state, and local coalitions with other groups, such as the American Public Health Association and the American Academy of Pediatrics, to urge that resources be made available for eliminating tuberculosis. b.Advocacy groups representing populations with high rates of tuberculosis can play an important role in technology transfer when they are involved in decision-making and in the education of their constituents and health care providers who serve them. cFOUNDATIONS can serve in technology assessment and transfer by providing funding for demonstration projects and educational programs.
7. Professional Medical Societies and the Private Medical Sector a.Some medical specialty groups, such as the American Thoracic Society and the American College of Chest Physicians, have assisted in the transfer of new technology through the preparation and dissemination of authoritative statements on tuberculosis, educational programs, and consensus conferences. In the future, these and other professional groups (including the American Academy of Pediatrics, the American Medical Association, the National Medical Association, the American College of Physicians, the Infectious Diseases Society of America, the American Academy of Family Physicians, the American Osteopathic Association, the Society of Hospital Epidemiologists, the Association of Practitioners of Infection Control, and the American Nurses Association) should increase their educational efforts in tuberculosis and produce and distribute written, audio, and video programs on various new tuberculosis control techniques. b.Selected physicians who are respected in their communities will serve as opinion leaders in technology transfer. Such persons must be sought out and their assistance requested for educational programs. c.Health-maintenance organizations, occupational health clinics, hospitals, and other health-care groups can assist in technology transfer by holding seminars and conferences on new technologies in tuberculosis, incorporating new technology into routine patient-management protocols, and by distributing educational materials on tuberculosis to employees in their institutions. d.Important audiences to reach with education messages are infection-control nurses, medical and nursing educators, medical and nursing students, and house staff. These groups must be mobilized for informed action in any elimination campaign.
8. The Business Sector a.Health-insurance providers can assist in technology transfer by paying for treatment and prevention modalities shown to be cost effective. Otherwise, the higher costs of less effective treatments will be borne by the carrier. An example would be the provision of twice-weekly, directly observed therapy that prevents unnecessary hospitalization, drug resistance, and treatment failure. b.Industry can serve a role in transferring new technology, especially when it anticipates a profit in the adoption of the technology. Industry might also fund demonstration projects, especially if a successful outcome would lead to increased use of the technology being investigated. Pharmaceutical companies have assumed the important role of sponsoring conferences and seminars.

9. The Media a. Articles on advances in the diagnosis, treatment, and prevention of tuberculosis should be published in newspapers and magazines to educate the general public, thereby increasing support for tuberculosis programs and increasing the demand for adoption of the new technology. Television news stories or public service announcements, billboards, and posters will serve the same function. Special Technology Transfer Issues This section concerns specific recommendations about methods and strategy for the transfer and implementation of specific new technologies that have been developed, but not adopted, or that are likely to be developed in the near future. The examples are divided into the same categories under which research efforts were outlined in Step 2 of this plan. Transferring Technologies for Preventing Disease in Infected Persons
10. Because the largest number of cases arise from the pool of persons infected in the past, highest priority must be given to the rapid evaluation and implementation of new technology in this area. It is likely that shorter (e.g., 2- or 3-month) preventive treatment regimens can be developed using currently available drugs. 2. To have a major impact on tuberculosis morbidity, newly developed short-course preventive therapy must be widely implemented by the private medical sector. This will require comprehensive education programs aimed at all physicians likely to see patients with tuberculosis. Professional organizations should assist in this effort. Increased emphasis on the prevention of tuberculosis in the curricula of medical schools and schools of public health should be undertaken. Cooperative agreement, grant, or contract funds might be used to stimulate these educational efforts. 3. Health departments should begin now to develop registers containing the names and addresses of untreated infected persons so that they can be readily identified, contacted, and treated when improved prevention methods are available. 4. Public education is important for creating a demand for this service. Consumer groups and organizations representing populations experiencing high rates of tuberculosis should be involved. Transferring Technologies for Defining Infected Persons at Risk of Disease New diagnostic tests will probably be developed in the near future. Before widespread adoption of the new tests, evaluation studies will be needed to determine whether they have significant advantages over the PPD-tuberculin skin test. Transferring Technologies for Preventing Infection A reduction in the number of tubercle bacilli in the environment may be achieved by the proper use of ultraviolet lights. Field studies of this technology in selected high-risk settings (e.g., hospital emergency rooms, correctional institutions, nursing homes, and shelters) should be undertaken as soon as possible. Transferring New Technologies for Treating Disease
11. Recent experiences with the slow diffusion of short-course, directly observed, and intermittent therapy into clinical and public health practice suggest that new approaches will be required in the future to promote more rapid and widespread adoption of new treatments. 2. A strong recommendation for a new therapy from the American Thoracic Society and the Advisory Committee for Elimination of Tuberculosis will be essential. Demonstration projects in selected states and communities showing feasibility, patient acceptability, and improvement in program performance will speed acceptance of new approaches to treatment. 3. Federal support will be necessary for the wider application of new therapy regimens in the public sector. For the private sector, incorporation of instruction on new tuberculosis therapies into continuing medical education programs will be helpful. Such programs could be funded by pharmaceutical companies that market the drugs used in the recommended treatment regimens. Transferring and Assessing New Technologies for Diagnosis of Tuberculosis

With the use of new DNA probes, it may soon be possible to make a specific diagnosis of tuberculosis in several hours. Before the use of these new diagnostic tests is recommended, they should be carefully assessed. Support for technology assessments might come from the commercial firm developing the

product, other private groups, or the public sector. Transfer of Communication Technologies

1. Improved communication is essential for transfer of state-of-the-art technology. The principal means by which this will be accomplished is frequent and timely telephone communication and on-line electronic transfer of information. It will be essential to develop and maintain an electronic network in which the public and private sector can submit and rapidly obtain current information about tuberculosis. CDC should standardize hardware and software requirements for this communication network and, to the extent possible, assist state and local health departments in obtaining hardware and software. The American Medical Association, the National Medical Association, and other professional groups should be approached regarding communication with the private sector. 2. Computerization of health department data bases will enhance the actions advocated in Step 1 of this plan. Conclusion Technology assessment and transfer in our society is a complex process involving many participants. Successful achievement will require federal coordination and some federal funding but will depend heavily on the active participation of state and local officials, private practitioners, private industry, and volunteer groups. The Advisory Committee can function as a focal point for these interactions.

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- A. The public needs: 1. current and accurate information about tuberculosis and progress toward its

elimination; 2.to be protected from infection with *M. tuberculosis*; and 3.if already infected, to be protected from disability and death from tuberculosis. The public has a responsibility to: 1.insist that adequate resources be made available for tuberculosis control and that those resources be used efficiently and effectively. B.Tuberculosis patients need: 1.quality diagnostic, preventive, and curative medical care that is available, accessible, and acceptable; 2.accurate and current information about the nature and risks of the disease and about the risks and benefits associated with treatment; and 3.confidentiality to the extent possible. Tuberculosis patients have a responsibility to: 1.prevent transmission of their infection to others; 2.assist in the identification of contacts; 3.take medicine as prescribed and to cooperate with necessary clinical, radiographic, and sputum examinations; and 4.report problems with taking prescribed treatment, improvement or deterioration of symptoms, and symptoms suggestive of adverse drug effects. C.Health-care providers need the following services from local health departments: 1.contact identification and evaluations; 2.regular follow-up of patients on treatment; 3.up-to-date patient-management guidelines and expert medical consultation; and 4.antituberculosis drugs, laboratory services, and directly observed therapy for their patients when needed. Health-care providers have a responsibility to: 1.maintain a high index of suspicion for tuberculosis, especially for persons from high-risk populations; 2.report cases, suspected cases, and laboratory results to the health department within 72 hours; 3.treat patients and monitor their compliance and response to therapy, and monitor for adverse drug reactions within accepted medical guidelines; 4.promptly notify health departments when patients under their care do not take treatment as prescribed or do not return for necessary follow-up examinations; 5.update health departments at specified intervals about current treatment (including degree of compliance), laboratory results, and disease status of each patient; and 6.cooperate with the health department in: a.contact identification and examination; b.the screening of other high-risk groups for infection and disease; and c.the application of preventive therapy in those groups. D.State and local health departments need: 1.information from health-care providers to ensure that persons with diagnosed tuberculosis do not continue to spread the disease within the community and that persons with tuberculosis, suspected tuberculosis, or tuberculous infection are receiving appropriate examinations and treatment; and 2.the resources and authority to carry out their responsibilities. State and local health departments have a responsibility to: 1.establish guidelines for the identification, reporting, treatment, and prevention of tuberculosis in the community; 2.ensure that patients with tuberculosis do not continue to transmit infection in the community; 3.provide rapid follow-up for persons diagnosed or suspected of having tuberculosis; 4.ensure that laboratory services, drugs, and the staff needed to provide follow-up, contact examination, and directly observed therapy are available; 5.ensure that high-risk groups, including those under the supervision of other state agencies (e.g., prisoners), are identified and screened for tuberculous infection and tuberculosis; 6.provide health education to the public; 7.appropriately use preventive therapy; 8.provide quality tuberculosis medical consultation for medical-care providers; 9.provide outpatient and inpatient medical care for tuberculosis at no cost to the patient when such care is not available from other sources; 10.rapidly transfer patient information from one jurisdiction to another when a patient moves; 11.establish and maintain a records system (register) that is effective for monitoring and evaluating the tuberculosis problem in the community; and 12.coordinate all state and local tuberculosis control activities. E.The Federal Government needs: 1.the resources required to carry out its responsibilities; and 2.accurate and timely reports from state and local programs (e.g., case reports, reports of outbreaks). The Federal Government has a responsibility to: 1.establish goals and priorities and publicize guidelines and standards; 2.provide expert medical and program consultation, program evaluation, public health education and training, and national morbidity and mortality surveillance; 3.conduct or support the basic and applied research studies, developmental work, demonstration projects, and technology assessments necessary for the development of new technologies for prevention and control; 4.ensure that aliens entering the United States are free of infectious or potentially infectious tuberculosis; 5.supplement,

as necessary, local and state resources to carry out the elimination plan set forth in this document; 6. publicize progress made toward the elimination of tuberculosis in the United States; 7. assure that federal programs that provide direct or indirect clinical services to high-risk populations (e.g., Bureau of Prisons, Indian Health Service) appropriately screen for and treat tuberculosis infections and tuberculosis; and 8. direct health-care providers to coordinate patient care with state and local public health authorities. F. Academic centers need to: 1. compete fairly for federal, state, and foundation funds for tuberculosis education and research projects. Academic centers have a responsibility to: 1. provide high-quality educational and tuberculosis control programs for their students, staff, and affiliated hospitals; 2. provide high-quality care to tuberculosis patients; and 3. use grant and contract funds to carry out well-designed and well-executed research studies and disseminate the results. G. Private enterprise needs:

1. adequate return for its investments in tuberculosis prevention and control. Private enterprise has a responsibility to: 1. use its resources to develop more effective methods for prevention and control of tuberculosis. H. The American Lung Association and other voluntary/professional agencies should continue to: 1. be advocates for the appropriation of resources and the enactment of legislation to achieve elimination of tuberculosis; 2. support, and encourage the support of, medical research and pilot demonstration projects; 3. provide public, medical, and professional health-worker education; 4. participate in developing standards for prevention, diagnosis, and treatment; and 5. form coalitions with other organizations to achieve the above aims. Finally, it is assumed that our society will continue to make progress in ensuring that all citizens have access to adequate nutrition, housing, and medical care.

- The Advisory Committee membership is as follows: Dr. William C. Banton II, Dr. George W. Comstock, Chairman, Dr. James L. Hadler, Mr. Anthony P. Najera, Ms. Carol J. Pozsik, Dr. Robert J. Reza, Dr. John A. Sbarbaro, Dr. Margaret H.D. Smith, Dr. William W. Stead, Dr. Patricia N. Whitley; Ex officio members: Dr. William A. Robinson (HRSA), Dr. Darrel D. Gwinn (NIH), Dr. Sotiros D. Chaparas (FDA), Dr. Bruce Tempest (IHS); Liaison members: Mr. Shane McDermott (ALA), Dr. Shirley Kellie (AMA), Dr. Dixie E. Snider, Jr., Executive Secretary.

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