



Global Medium-Term Programme

Programme 13.8

TUBERCULOSIS

The risk of tuberculosis infection in developing countries has shown a gradual decrease over the last 10 years. The rate of decrease correlates with the extent of the implementation of control activities. In many countries expansion of tuberculosis control, especially to rural areas, remains a formidable problem. Advocacy and training as well as health systems research are required to further application within the primary health care programme. Basic research must be carried out to find more effective and simpler techniques that may generate new ways of addressing the problem.

The objectives of the programme are to reduce suffering, disability and death from tuberculosis and to eliminate the disease as a public health problem by strengthening diagnostic, treatment and vaccination services.

The approach will be through (a) support to Member States in the formulation and implementation of control programmes through their present comprehensive health systems; (b) epidemiological surveillance of the risk of infection and of the mycobacterial sensitivity to antituberculosis drugs on a regional scale; (c) cooperation with national programmes in the training of health personnel; (d) health systems research on the application of tuberculosis control within primary health care programmes; (e) promotion of basic research directed to increasing the scientific knowledge on which the tuberculosis programmes are based and to strengthening the control technology.

CONTENTS

	<u>Page</u>
1. INTRODUCTION AND POLICY BASIS	2
2. SITUATION ANALYSIS	2
3. OBJECTIVE	4
4. TARGETS	5
5. APPROACHES	5
6. ACTIVITIES	7
7. PROGRAMME MANAGEMENT AND RESOURCES	9
8. MONITORING, EVALUATION AND INDICATORS	9
9. LINKAGES	10

1. INTRODUCTION AND POLICY BASIS

Three decades after the formulation of a comprehensive policy for tuberculosis control programmes, the epidemiological situation in many developing countries has been improving very gradually, this in sharp contrast with that in developed countries where a steep decline has been observed for many years. Concern about this state of affairs was expressed by the Thirty-third World Health Assembly (Resolution WHA.33.26, 1980).

A joint IUAT/WHO Study Group (Techn. Rep. Ser. 671, 1982) found the basic concepts of tuberculosis control as described in the 9th Report of the Expert Committee on Tuberculosis (Techn. Rep. Ser. 552, 1974), sound and valid and stressed its implementation through the existing health systems, notably primary health care. A WHO Study Group on BCG vaccination policies (Techn. Rep. Ser. 652, 1980) recommended vaccination of the newborn and young infants within the Expanded Programme of Immunization and called for its prompt evaluation. The recommendations of the Study Groups were endorsed by the WHO Executive Board (EB69/1982/Rec/1, p.22 and EB67/1981/Rec/1, p.26). In accordance with these recommendations as well as with the results of extensive enquiries and consultations with Member States carried out by the Regional Offices, a programme has been formulated which was reviewed by the WHO Executive Board (EB71.R11, 1983) and discussed by the 36th World Health Assembly in 1983 (Resolution WHA 36/30). The control strategy was reviewed with experts in primary health care in 1986 (Document TRI/TR/87/151).

2. SITUATION ANALYSIS

2.1 The problem

Epidemiological resurveys in recent years have clearly demonstrated - for the first time - that the risk of tuberculosis infection in developing countries is assuming a declining trend. In many Latin American, Arabic speaking and Western Pacific countries the annual decline is from 5% to over 10%, in Asian countries it is up to 7%, and in some African countries 2% to 4%. The decline in the risk of infection is not immediately paralleled by a decline in incidence, but in the lower age groups a similar decline will occur soon. In Botswana, where the tuberculosis problem used to be among the highest in the world, the annual incidence of new cases diminished by about 50% over the last decade. However, over the same period of time the population increased by 50% so that the annual number of cases still remains high. It is estimated that there are each year 4-5 million new smear-positive cases and another 4-5 million smear-negative and extrapulmonary cases. The prevalence of cases is two to three times the incidence. Since the number of both defaulting and untreated patients is very large, there are still 2-3 million tuberculosis deaths annually in the world.

In the developed countries tuberculosis continued to decline at an average rate of 12% per year, but a disturbing exception has been observed in the USA, where the incidence, in 1986, actually showed a slight increase. This has been explained, at least partially, from the current HIV infection epidemic. It is most likely that a similar or even amplified development will occur in other countries, notably in central Africa.

The interaction of mycobacterial and HIV infections was first observed from the high incidence of disease caused by mycobacteria of the *Mycobacterium avium-intracellulare* (MAI) complex in AIDS patients. It soon appeared, however, that in populations with a high prevalence of *M.tuberculosis* infection tuberculosis is predominant in HIV-infected persons, and often occurs as an early manifestation of AIDS. Thus, in Florida the incidence of tuberculosis among AIDS patients was about 10%

among non-Haitians, and over 60% among Haitians. These percentages are very much of the same order of magnitude as the estimated tuberculosis infection prevalence in these populations, which means that persons infected with both M.tuberculosis and HIV have a very high risk indeed of developing tuberculosis. One implication is that in populations where the risks of M.tuberculosis and HIV infection are high the incidence of tuberculosis must be expected to increase considerably. In actual fact a recent study in Zaire showed that one third of new tuberculosis patients were HIV seropositive. Unfortunately this may only be a very preliminary indication of the increase in case-load to be expected. Epidemiological research and surveillance is required to appraise and monitor the situation in more quantitative terms.

Mycobacterial disease in HIV-infected persons poses several problems for tuberculosis programmes. The clinical picture is different from that usually seen in adult-type tuberculosis, cavitory pulmonary disease being relatively rare and bacteraemia common and resulting in many peculiar extra-pulmonary manifestations, from lymphatic involvement to intracranial tuberculomas. Case-finding and diagnosis, therefore, will be difficult if it is based on sputum-smear examination of persons presenting with cough. When diagnosis of tuberculosis is early in the HIV infection stage, the response to intensive treatment usually is fairly good, but the optimal duration of treatment is unknown. Clearly, case-finding, diagnosis and appropriate treatment will be problems for routine tuberculosis programmes in developing countries and further research in this field is urgently needed.

2.2 The programme

The strategy for tuberculosis control programmes has hardly changed over the last 25 years, the main components of the programme being case-finding with diagnosis by microscopy examination of the sputum among persons with respiratory symptoms, domiciliary chemotherapy and BCG vaccination. The current emphasis is to apply these strategies through the newly developed primary health care system, which has provided now impetus to tuberculosis control programmes; most developing countries have formulated integrated programmes. The step from theory to practice, however, has often proved a difficult one. The need for training and motivating the peripheral staff presents a main obstacle. WHO's support to national programmes has focused on developing managerial expertise and the provision of training materials. A manual on methods and procedures for integrated programmes has been made available in 1986. Training courses, seminars and workshops have been organized for key staff at various levels.

Regular budgetary expenditure in the WHO regions on cooperation with countries in the development of integrated tuberculosis programmes has been some \$3,000,000 per biennial period; extrabudgetary resources mustered for support amount to some \$1,700,000 per biennium.

Research has been carried out on the effectiveness of BCG vaccination of the newborn in a global programme of contact and case-control studies. Protection against childhood tuberculosis was found to be substantial, especially against the most severe forms, such as meningitis. A new problem is the safety of BCG vaccination for children at risk of HIV infection. This will have to be approached through similar studies in selected countries. Also the long-term effectiveness of BCG vaccination and the value of revaccination need to be assessed.

A number of new quinolones and derivatives of the rifamycins with anti-tuberculosis activity have become available. To allow these drugs to be adequately tested and efficient regimens to be formulated expediently a comprehensive chemotherapy research programme has been set up.

The immunological research programme has progressed substantially; it is being conducted under the guidance of MLM.

Tuberculosis programmes had been formulated to deal primarily with the social objective of tuberculosis control. The epidemiological objective, however, will be addressed very gradually. To obtain an objective assessment of the current technology in developing countries intervention studies have been designed to measure the epidemiological impact of alternative strategies.

Case-holding always has been a problem in integrated programmes. The introduction of short-course regimens, if correctly applied, may bring substantial improvement in the cure rate. Such regimens, however, require, at least during the first phase, the same intensive patient supervision as the classical one-year regimens. Rather than being a short-cut measure for weak programmes, they may lessen the workload for programmes that perform adequate supervision and then actually may be more efficient in spite of the higher drug costs. Health systems research is required to arrive at the optimal application of chemotherapy in different settings.

Tuberculin resurveys have been undertaken in selected countries to estimate the trend of the risk of infection. Such surveys had been carried out in many countries in the 1950s. A programme of surveillance of resistance to the major tuberculosis drugs has been organized through WHO Collaborating Centres. The work has started in Latin America, Africa and the Eastern Mediterranean region.

The research programme has been funded largely from extra-budgetary sources. For the BCG studies some \$200,000 were made available to WHO by UNICEF and several Member States and for several projects bilateral arrangements have been ensured. The chemotherapy research programme has received support from a donor agency, and epidemiological research is being arranged through bilateral cooperation. The surveys have been supported from the regular budget.

Support to country programmes, to research and to epidemiological surveillance is provided in close technical cooperation with the International Union against Tuberculosis and Lung Disease. Evaluation of programme activities is carried out by a joint body, the Tuberculosis Surveillance Research Unit, the Hague, Netherlands, which reviews the situation every two years.

3. OBJECTIVES

3.1 General objective

To prevent and control major communicable and non-communicable diseases

3.2 Specific objectives

The social objective is to reduce suffering, disability and death from tuberculosis by strengthening diagnostic, treatment and vaccination services.

The epidemiological objective is to eliminate tuberculosis as a public health problem by effectuating, through these control measures, a perpetual decrease in the transmission of the disease.

4. TARGETS

4.1 Targets of the 8th General Programme of Work

By 1992, 80% of the developing countries will have incorporated case-finding and treatment activities in control programmes integrated into primary health care.

By 1995 the epidemiological effectiveness of these programmes will be increased through earlier detection and closer supervision of treatment.

4.2 Specific targets

(a) Programme planning and implementation

- By 1992 all countries will have formulated national tuberculosis control programmes as an integrated component of their primary health care system; tuberculosis will be included within the training programme of regular health staff and of community health workers in every country.
- By 1995 diagnostic and curative tuberculosis services will be available to 80% of rural populations.

(b) Research

- By 1992 strategies for increasing the epidemiological impact of tuberculosis control in primary health care will have been identified; the interaction of tuberculosis and HIV infection will have been elucidated and diagnostic procedures will have been developed; the long-term effectiveness of BCG vaccination will have been assessed in developing countries and short-course chemoprophylaxis regimens will have been evaluated.
- Chemotherapy studies will be continued throughout the programme period.

5. APPROACHES

At the country level WHO will cooperate in strengthening programme management, including supervision, monitoring and evaluation capacities. Countries will be encouraged to establish progressive targets with the aim of achieving earlier case detection and better case-holding. WHO will support the planning and expansion of diagnostic and control measures to the periphery and will promote intersectoral research and development with a view to ensuring optimal use of available technology by the health infrastructure. National training programmes will be supported. WHO will provide guidelines on methods and procedures for the prevention and control of tuberculosis and will support the development of health education materials for community workers aimed at increasing awareness and motivation in the population. Support will be given for strengthening the management and technical aspects of diagnostic services, and for the procurement and distribution of drugs for ambulatory chemotherapy. Support to BCG vaccination of children will be provided through programmes of immunization.

At the regional level WHO will monitor the planning and implementation of country programmes. Seminars and workshops will be organized for national programme managers and technical cooperation between countries will be promoted. Approaches for health systems research on the application of tuberculosis control within primary health care will be developed in close cooperation with other specific programmes. Studies will be undertaken, both in the population and among health workers, on the influence of

cultural, behavioural and social factors on control policies. The network of collaborating centres for epidemiology and bacteriology will be strengthened in support of the national tuberculosis control programmes and with a view to applying new technologies.

At the global level WHO will maintain global surveillance and coordinate research aimed at improving tuberculosis control methods and techniques. Resources will be mobilized and international cooperation will be promoted to support regional and national efforts. Surveillance will include periodic measurement of the risk of infection as well as of the levels of primary and acquired drug resistance in random samples of patients in countries throughout the world. Intervention studies will be undertaken to provide a solid epidemiological basis for tuberculosis control policies and to evaluate the efficiency of alternative approaches not only to individual care but also to reduction of transmission. Studies will be made of the interaction of HIV and mycobacterial infections and of the epidemiological and operational implications. The technical guidelines for the control of tuberculosis through primary health care that were made available during the Seventh General Programme of Work will be reviewed periodically. Immunological research will focus on new preparations for detecting infection and disease, new vaccines and immunotherapeutic substances. Chemotherapy research will be maintained for the expeditious testing of new drugs and new regimens.

6. ACTIVITIES

6.1 Programme planning and implementation

Targets

- By 1992 all countries will have formulated national tuberculosis control programmes as an integrated component of their primary health care system; tuberculosis will be included within the training programme of regular health staff and of community health workers in every country.
- By 1995 diagnostic and curative tuberculosis services will be available to 80% of rural populations.

Activities	1990 - 1991	1992 - 1993	1994 - 1995	Linkages ⁽¹⁾
1. Support to Development of National Programmes				
(a) Programme advocacy and collaboration in the formulation of plans of operation and dissemination of technical guidelines for the integration of tuberculosis control in the primary health care system.		All Regions, HQ		PHC IUAT* CLR HST
(b) Support to analysis of availability and use of resources, identification of needs, and mobilization of supplementary resources.		All Regions, HQ		COE
(c) Support to the establishment of appropriate diagnostic and treatment services as an integral part of the primary health care system network.		All Regions		CLR EDV
2. Evaluation and Surveillance				
(a) Evaluation of national programmes as regards the status of integration of tuberculosis control into the primary health care system.		All Regions		PHC HST
(b) Support to operational evaluation of accessibility and acceptability (KAP studies) of the programme.		All Regions		HST HSR
(c) Support to surveillance of the epidemiological situation, including determination of the risk of infection, of the risk of breakdown to disease, of mycobacterial sensitivity to the essential antituberculosis drugs and of the quality of BCG vaccination.		All Regions, HQ		HST DSE CLR IUAT CCs
(d) Support to laboratory services for the identification and classification of mycobacteria through WHO collaborating centres.		All Regions, HQ		CCs CLR
3. Training				
(a) Regional and national seminars and workshops on tuberculosis control for programme managers and for supervisors on training community health workers.		All Regions		PHC HMD IUAT
(b) Production and testing of training materials on tuberculosis and learning modules for different levels of courses: managers and supervisors, laboratory microscopists and community health workers.		HQ		HST
(c) Inter-regional and regional training courses on epidemiology and control of tuberculosis				
- in English		WPRO		Japan
- in French		AFRO, EURO		France
- in Spanish		AMRO		Algeria, IUAT Argentina Chile, Cuba Mexico
(d) Inter-regional and regional courses and workshops in bacteriology of tuberculosis				
- in English		AMRO		Canada, IUAT
- in Spanish		AMRO		Argentina

(1) Linkages resulting in activities undertaken jointly by two or more programmes are identified by *; those activities budgeted jointly by two or more programmes are underlined.

6.2 Research

Targets

- By 1992 strategies for increasing the epidemiological impact of tuberculosis control in primary health care will have been identified; the interaction of tuberculosis and HIV-infection will have been elucidated and diagnostic procedures will have been developed; the long-term effectiveness of BCG vaccination will have been assessed in developing countries and short-course chemoprophylaxis regimens will have been evaluated.
- Chemotherapy studies will be continued throughout the programme period.

Activities	1990 - 1991	1992 - 1993	1994 - 1995	Linkages
<u>1. Health Systems Research</u>				
(a) Support to health systems research on the optimal application of the available tuberculosis control methods in primary health care programmes.		All Regions		IUAT PHC HSR
(b) Support to studies of technical, operational and sociological factors influencing the application of tuberculosis control within the primary health care system.		All Regions		PHC HSR
<u>2. Epidemiological Research</u>				
(a) Studies on the transmission and pathogenesis of tuberculosis in developing countries and on the epidemiological impact of alternative control programmes.		HQ		IUAT
(b) Evaluation of the long-term effectiveness of BCG vaccination through case-control studies in developing countries and of the value of revaccination.	HQ			UNICEF EPI
(c) Studies of the interaction of BCG vaccination and HIV-infection.	HQ			SPA
(d) Studies on the risk of tuberculosis in HIV-infected persons and AIDS patients and on appropriate diagnostic methods.		All Regions, HQ		CLR, SPA
(e) Studies on the feasibility and effectiveness of short-course chemoprophylaxis in children.	HQ			
<u>3. Research on chemotherapy</u>				
(a) Evaluation of new anti-tuberculosis drugs and treatment regimens in laboratory studies and field trials in developing countries.		HQ		EDV DSE
(b) Studies on regimens suitable for MAl patients, and for HIV-infected patients and on treatment to reduce sequels from meningitis.		HQ		SPA
<u>4. Dissemination of information</u>				
Analysis and distribution of information on advances in control methods and their applicability to the programme, on epidemiology and on immunology.		HQ, all Regions		THAT* IHH

7. PROGRAMME MANAGEMENT AND RESOURCES

WHO's technical policy for tuberculosis control has been guided by expert committees, study groups and scientific groups. The policies formulated have been advocated jointly by WHO and IUATLD. In view of the intimate linkage of the tuberculosis programme with other health sectors and the multidisciplinary approach required for the formulation of programme strategies, consultations with primary health care organizers have been held to assist in the evaluation of the programme activities, including research.

The network of Collaborating Centres, presently includes regional centres for training in bacteriology, surveillance of drug resistance and typing of strains (Algeria, Canada, Czechoslovakia, Japan and Mauritania); epidemiological surveillance and research (Argentina, India and Japan); and chemotherapy research (United Kingdom).

Specific budgetary resources for WHO Regions to cooperate with countries in the organization of tuberculosis control problems are in the range of 3 to 4 million dollars per biennial period. Efforts are being made to attract extrabudgetary funds, especially for the less developed countries, in the similar range.

For the global research programme some priority subjects are being covered from the regular budget allocation. Health systems research, epidemiological investigations and chemotherapy research need to be implemented on a large scale and require funding from other sources.

8. MONITORING, EVALUATION AND INDICATORS

Whereas most individual components of WHO's programme will be evaluated by means of output indicators, e.g. numbers of collaborating centres, of staff trained, or of cooperative programmes and research projects, an overall evaluation will be made in the same terms as the stated targets. This evaluation will focus on the general progress in the development of tuberculosis programmes integrated in the primary health care system. In this respect, evaluation will be both quantitative and qualitative.

Simple quantitative indicators are the numbers and percentages of patients detected at the primary health care level (as against the estimated number of new patients in the community). The diagnostic procedures used (proportions) are a further indicator of the degree of implementation of the programme strategy. A highly relevant qualitative performance indicator of chemotherapy is the degree of treatment default; in national programmes this is generally more easily determined than the actual cure and relapse rates. The proportions of previously treated and currently treated patients among the patients detected in limited prevalence surveys provide objective quantitative information on the performance of the chemotherapy programme. Similarly, monitoring the bacteriological status of "old" patients provides a useful operational indicator.

The BCG vaccination programme is usually evaluated in terms of coverage, but qualitative assessment (by means of determining vaccine-induced tuberculin sensitivity, lesion size and complications) as well as determination of effectiveness (through contact and case-control studies) should be carried out at the national level.

A specific indicator of the effectiveness of the case-finding and treatment programme in terms of problem reduction is the prevalence of infection among young contacts of newly discovered cases. More generally, the risk of infection and its trend are suitable indicators of the tuberculosis problem in the community. They reflect, however, the overall trend of the problem on which many factors other than the activities may exert considerable influence.

9. LINKAGES

WHO's support to national efforts in tuberculosis control will have to take place through a number of its specific programmes. Programmes concerned with the organization of health systems based on primary health care (PHC), health systems research (HSR), epidemiological surveillance and health situation and trend analysis (HST) and health manpower development (HMD), will work closely with the tuberculosis programme, both to supply useful information on the ways of organizing tuberculosis control as part of the general health system and to ensure adequate training of the staff involved. BCG vaccination forms part of the Expanded Programme on Immunization (EPI). The programme of Health Laboratory Technology (LAB) will include training of field laboratory workers in sputum smear microscopy. The Programme of Essential Drugs (DAP) will ensure that antituberculosis drugs become more widely available to developing countries, at the lowest possible cost; the quality of BCG vaccines and tuberculin will be monitored in cooperation with Drug and Vaccine Quality, Safety and Efficacy (BLC). The programmes in Public Information and Health Education (IEH) will promote people's understanding and involvement. Assistance from UNICEF provided to Member States in accordance with WHO's technical policies. Contributions from bilateral donors will be coordinated as far as possible. Cooperation will be maintained with the International Union against Tuberculosis and Lung Disease (IUATLD) as regards the development of technical policy, the direct support to national programmes and global surveillance (through the Tuberculosis Surveillance Research Unit). Immunological research will be organized by the programme on immunology (MIM). Epidemiological research will be carried out in cooperation with EAM and research related to HIV infection will be coordinated with SPA. WHO collaborates with many national institutions on the global survey of mycobacterial drug resistance.

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