

This report contains the collective views of an international group of experts and does not necessarily represent the decisions or the stated policy of the World Health Organization.

Tuberculosis control

Report of a Joint
IUAT/WHO Study Group

World Health Organization
Technical Report Series
671



World Health Organization, Geneva. 1982

ISBN 92 4 120671 3

© World Health Organization 1982

Publications of the World Health Organization enjoy copyright protection in accordance with the provisions of Protocol 2 of the Universal Copyright Convention. For rights of reproduction or translation of WHO publications, in part or *in toto*, application should be made to the Office of Publications, World Health Organization, Geneva, Switzerland. The World Health Organization welcomes such applications.

The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of the Secretariat of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries.

The mention of specific companies or of certain manufacturers' products does not imply that they are endorsed or recommended by the World Health Organization in preference to others of a similar nature that are not mentioned. Errors and omissions excepted, the names of proprietary products are distinguished by initial capital letters.

PRINTED IN SWITZERLAND

81/5167 - Schüler SA - 10 000

CONTENTS

| | Page |
|--|------|
| 1. Introduction | 7 |
| 2. Current epidemiological situation in developing countries | 10 |
| 3. Impact of current control measures | 10 |
| 4. Planning and organization of national tuberculosis programmes | 11 |
| 5. Case-finding | 14 |
| 6. Tuberculosis laboratory services | 14 |
| 7. Chemotherapy | 17 |
| 8. BCG vaccination and preventive treatment | 19 |
| 9. Socioeconomics of tuberculosis control | 20 |
| 10. Research | 21 |
| 11. Conclusions and recommendations | 24 |
| Acknowledgements | 26 |

JOINT IUAT/WHO STUDY GROUP ON TUBERCULOSIS CONTROL

Geneva, 14-18 September 1981

Members*

- Dr V. K. Agadzi, Epidemiology Division, Ministry of Health, Accra, Ghana
Professor P. Chaulet, Pneumophthisiology Clinic, Beni-Messous Hospital and University Centre, Algiers, Algeria (*Vice-Chairman*)
Dr A. R. Farah, Director, Preventive and Social Medicine, Ministry of Public Health, Tunis, Tunisia
Dr L. Farer, Director, Tuberculosis Control Division, Centers for Disease Control, Atlanta, GA, USA
Professor Wallace Fox, Director, Tuberculosis and Chest Diseases Unit, Medical Research Council, London, England (*Chairman*)
Dr S. Nkinda, Senior Medical Officer, Ministry of Health, Dar-es-Salaam, United Republic of Tanzania
Dr W. P. Ott, Chief, Tuberculosis Control Programme, State of Rio Grande do Sul, Porto Alegre, Brazil
Dr T. Shima, Director, Tuberculosis Research Institute, Japan Antituberculosis Association, Tokyo, Japan
Professor H. A. Sillastu, Chair of Tuberculosis, Tartu University, Medical Faculty, Tartu, Estonia, USSR
Dr S. P. Tripathy, Director, Tuberculosis Research Centre, Madras, India (*Rapporteur*)

Observer

- Dr V. Srdanovic, Procurement Officer, UNICEF Office for Europe, Geneva

IUAT Secretariat

- Professor G. Dahlström, Director, Department of Pulmonary Diseases, Uppsala, Sweden
Dr S. Grzybowski, Department of Medicine, University of British Columbia, Vancouver, Canada
Dr P. Mercenier, Head, Unit of Research and Education in Public Health, Institute of Tropical Medicine, Antwerp, Belgium
Professor D. A. Mitchison, Director, Unit for Laboratory Studies of Tuberculosis, Medical Research Council, London, England
Dr A. Rouillon, Executive Director, International Union against Tuberculosis, Paris, France (*Joint Secretary*)
Dr K. Stýblo, Director of Scientific Activities, International Union against Tuberculosis, Paris, France
Dr H. T. Waaler, Unit for Health Services Research, Norwegian Research Council for Science and the Humanities, Oslo, Norway

* Unable to attend: Professor J. Grosset, Director, Department of Bacteriology, Pitié-Salpêtrière Faculty of Medicine, Paris, France.

WHO Secretariat

- Dr A. Pio, Tuberculosis and Respiratory Infections, WHO, Geneva, Switzerland
(Joint Secretary)
- Dr H. Stott, Tuberculosis and Chest Diseases Unit, Medical Research Council,
London, England *(Temporary Adviser)*
- Dr E. Tarimo, Director, Division of Strengthening of Health Services, WHO,
Geneva, Switzerland
- Dr A. Zahra, Director, Division of Communicable Diseases, WHO, Geneva,
Switzerland
-



TUBERCULOSIS CONTROL

Report of a Joint IUAT/WHO Study Group

1. INTRODUCTION

A Study Group on Tuberculosis Control, jointly sponsored by the International Union against Tuberculosis and by the World Health Organization, met in Geneva from 14 to 18 September 1981 with the following objectives:

(a) to consider the effectiveness, in terms of the reduction of the problem, of various tuberculosis control strategies at different levels of applications;

(b) to review the obstacles encountered in the implementation of recommended strategies and to consider ways of overcoming these; and

(c) to propose research relevant to the feasibility and efficiency of alternative strategies aimed at defining optimal programmes.

Dr I. D. Ladnyi, Assistant Director-General, WHO, and Dr A. Rouillon, Executive Director, International Union against Tuberculosis, opened the meeting. Dr Ladnyi pointed out that the meeting was being held to join forces and to mobilize the required collaborative planning, research, and resources that would be needed to align the tuberculosis operations with the front-line programmes oriented towards the target of "Health for all by the year 2000". Dr Rouillon observed that the present situation of tuberculosis in the world constitutes a paradox: tuberculosis represents the prototype of a disease for which the natural history is known and substantially quantified and against which an effective, simplified, standardized technology has been developed and organized into national tuberculosis programmes, and yet there is a continuing gap between expectations and achievements which is creating concern.

The Group decided to concentrate on objectives (b) and (c), with particular reference to the developing countries, but making comments relevant to technically advanced countries, wherever specially appropriate.

1.1 General considerations

Technically advanced countries have achieved spectacular results in the control of tuberculosis over the last three decades. This has been possible because of chemotherapy and an abundance of manpower and technical and financial resources, and in spite of certain mistakes—for example: overdiagnosis, unduly prolonged institutional treatment, and lack of mass BCG vaccination of children at a time when the risk of infection was high. It must, however, be stressed that, although there has been a considerable reduction in the tuberculosis problem in the countries concerned, the disease will occur—although at a decreasing rate—for many years to come in subjects already infected. Specific problems, such as indigenous high-risk groups, refugees, and immigrants from high-prevalence countries, will continue to require special attention even though they are unlikely to have a significant long-term effect on the overall tuberculosis situation in the technically advanced countries.

Unfortunately, in the majority of *developing countries* there has been little, if any, improvement in the epidemiological situation. In fact, there has been an overall increase in the *absolute* number of tuberculosis cases in these countries during the last three decades, because the population has doubled during this period.

1.2 The WHO policy on tuberculosis control

The current WHO policy on tuberculosis control, based on the concept of a comprehensive programme implemented on a country-wide scale through the network of existing health service institutions, was formulated nearly two decades ago, in the eighth report of the WHO Expert Committee on Tuberculosis¹ and reaffirmed and enlarged in the ninth report in 1974.² The Group re-examined the tuberculosis control strategy outlined in the ninth report and concluded that the main concepts were sound and valid. The case-finding/treatment complex has been further strengthened by the recently acquired knowledge of the high efficacy of short-course chemotherapeutic regimens. Further, the newly developed strategy of primary health care also offers major new operational opportunities. The present report is therefore meant to supplement, and not to replace, the ninth report.

¹ WHO Technical Report Series, No. 290, 1964.

² WHO Technical Report Series, No. 552, 1974.

Primary health care envisages the provision of health care facilities to all parts of a country, offering equity in health care for every member of the community, as well as active involvement and participation of the community in health care programmes through the activities of individuals, of families, and of the community collectively.¹ The community health worker, whose importance in the health care system is increasingly recognized, provides a link between the health services and the community and could be expected to play a significant role in tuberculosis control.

The Study Group was aware of the major technical and administrative difficulties and resource constraints which, in the field of tuberculosis, stand in the way of achieving "Health for all by the year 2000".² Although the global target envisages that some communicable diseases in the developing countries will be of no greater public health significance in the year 2000 than they were in technically advanced countries in the year 1980, the current high incidence and the natural history of tuberculosis in man suggest that such a level of control would be extremely difficult to achieve during so short a span. Nevertheless, with adequate and sustained resources and inputs, a substantial reduction in the problem could be achieved. Even this, however, would be possible only if appropriate lessons were drawn from past experience.

The Group was convinced of the necessity of attempting to implement tuberculosis control measures through the primary health care system. Integration of case-finding and treatment within this system is likely to benefit the control programme. The effect, however, will depend on the quality and rate of development of primary health care and the degree of integration. The Group considered it important to study the programme modifications which integration of tuberculosis control with primary health care implies, while retaining or even enhancing the expertise necessary for tuberculosis control.

¹ *Alma-Ata 1978. Primary Health Care.* Geneva, World Health Organization, 1978 ("Health for All" Series, No. 1).

² *Global Strategy for health for all by the year 2000.* Geneva, World Health Organization, 1981 ("Health for All" Series, No. 3).

2. CURRENT EPIDEMIOLOGICAL SITUATION IN DEVELOPING COUNTRIES

2.1 Estimated incidence of tuberculosis

It has been estimated that, in developing countries, 4–5 million highly infectious cases of smear-positive tuberculosis occur each year, with an equal number of less infectious cases, including those positive by culture only and culture-negative cases, the latter being the most frequent form of pulmonary disease in children. Thus, each year about 10 million persons still develop tuberculosis and at least 3 million die from this disease.

2.2 Epidemiological trend

Because of the absence of reliable data on smear-positive tuberculosis in most developing countries, the epidemiological trend of tuberculosis is measured by estimating the annual risk of infection derived from the results of tuberculin-testing a representative sample of unvaccinated children. In most developing countries the risk is of the order of 2–5%, about 20–50 times greater than in technically advanced countries. The gap has been constantly increasing, because in technically advanced countries the annual risk of infection continues to decrease rapidly, whereas in many developing countries the risk has remained unchanged for many years or has only been declining very slowly.

3. IMPACT OF CURRENT CONTROL MEASURES

After careful consideration of the evidence, the Group emphatically stated that the most powerful weapon in tuberculosis control is the combination of case-finding and chemotherapy. These are considered as an entity, as case-finding is a preliminary to treatment and cure.

In addition to their direct effect of reducing suffering and death, case-finding and treatment eliminate sources of infection. In technically advanced countries it appears that intensive case-finding and adequate treatment measures have resulted in a parallel decline in the incidence of disease and of infection. However, because of different socioeconomic, nutritional, and other conditions, the impact of case-

finding and treatment on the rate of decline in developing countries may not necessarily be the same as in technically advanced countries, even if these control measures are applied with the same intensity and quality.

Although BCG vaccination of uninfected individuals (usually children) can prevent tuberculosis in them, it can have only a relatively small epidemiological effect in that it will not contribute significantly to the reduction in the overall risk of infection in the community as a whole.

Preventive treatment (chemoprophylaxis) with isoniazid can prevent the development of tuberculosis in infected individuals but its impact on the community will be minimal because it cannot be applied on a mass scale, even in technically advanced countries.

4. PLANNING AND ORGANIZATION OF NATIONAL TUBERCULOSIS PROGRAMMES

The Group reaffirms the statement made in the ninth report of the WHO Expert Committee on Tuberculosis that the control of tuberculosis deserves a high priority on the list of rewarding health activities.¹ This is because an effective tuberculosis control programme can be delivered under any situation if case-finding and treatment facilities are provided and planning and application are guided by a clear understanding of the epidemiological, technical, operational, economic, and social aspects.

In planning for the future, the reasons for the past failure of programmes to achieve a decrease in the incidence of tuberculous infection and disease must be carefully considered. These reasons also apply in general to many other health problems, particularly those that require a number of activities efficiently sustained over a long period of time. Key areas for improvement include the following (they are not set out in order of priority):

(a) It is obvious that the programme needs strong technical support and supervision. At the central level, it should be actively initiated and promoted by the Ministry of Health. Specialized managerial teams might also have to be organized at intermediate levels. How-

¹ WHO Technical Report Series, No. 552, 1974, p. 22.

ever, these teams should harmonize with the normal line of command of the general health structure. They should be regarded as a means of specialized technical support for the general health administration. Their scope should not necessarily be limited to tuberculosis. In consequence, their impact should be evaluated in terms not only of their specific programme achievements, but also of their influence on the functioning of the whole health system.

(b) The process of integration has not received adequate attention, and has usually, and erroneously, been considered to be a straightforward administrative problem. The complexity of the process, involving the interaction between two systems—namely, one specialized and the other multipurpose—has been much underestimated. General health workers assign low priority to tuberculosis activities or do not accept them as a part of their routine duties. They regard these activities as additional duties imposed on them without compensation or relief from other duties.

(c) It is essential that split responsibility should be avoided. There are a number of groups involved in diagnosing and treating cases of tuberculosis, for example government and quasi-government agencies, municipal corporations, university institutions, private practitioners, and others. Every effort must be made to bring all these groups together to work in a concerted and integrated manner towards the common goal of tuberculosis control, avoiding rivalries and different general policies.

(d) In many countries the peripheral health services are too sparse to be readily accessible to all the population and an ample coverage cannot be achieved until primary health care is fully developed. It must be stressed, however, that much improvement could currently result from an adequate implementation of the programme by the existing health infrastructure.

(e) Among the main reasons for lack of progress are insufficient financial resources and, to a lesser extent, the uneven allocation of the available resources. Governments must recognize their financial obligations and commit sufficient funds, in the context of the country's resources, to the programme and ensure that these funds are distributed on an equitable basis throughout the country.

(f) Essential for the proper functioning of the programme is the maintenance of a sufficient and constant supply of drugs, vaccines, chemicals, and equipment at every level of the programme. Also essential is an efficient microscopy network for the whole country (see sections 5 and 6).

(g) The training of staff is vital. It is important that key medical staff should have expertise in tuberculosis and a commitment to the tuberculosis programme. All cadres of staff should be provided with special training in managerial tasks.

The inadequate training of technical, laboratory, and general health service staff at the intermediate and peripheral levels, particularly in case-finding and case-holding, has been a great weakness. Apart from formal training, which needs to be strengthened, the Group laid special emphasis on the importance of on-the-spot training in both technical and managerial functions.

(h) The managerial teams should have a stable, appropriately salaried career appointment, with prospects of promotion equal to those of equivalent workers in other health activities.

(i) Frequent transfers of all grades of staff, particularly in peripheral health units, are a major reason for the disorganization and deficiencies of all health programmes.

(j) Evaluation is a continuous process. Whenever deficiencies in tuberculosis control operations are found, they should be corrected by the workers with specialized knowledge and responsibility for tuberculosis in close collaboration with those from the general health services.

The programme must be evaluated at all levels. At the simplest level this can be achieved through routine statistical returns and data compiled from tuberculosis registers (often maintained at a district level), which can provide information on numbers and types of cases treated, methods of diagnosis, and treatment results. Among the more sophisticated assessments, periodic countrywide surveys of cohorts of patients coming under treatment are valuable in providing information on epidemiological trends, and the overall efficiency of the service, including diagnosis, methods of treatment, and the results achieved. They identify operational deficiencies, some of which are usually readily rectifiable within the available resources and facilities.

(k) Involvement of the community itself is a key factor in the successful implementation of the programme, but has received inadequate attention in the past. Health education of the community so that it both understands and plays its due role in tuberculosis control is important.

(l) The Group considers that in addition to basic research, which is essential, applied research directed particularly to the problems of programme delivery is urgently needed. The problems of programme delivery should be studied in the conditions prevailing in different developing countries.

(m) While recognizing that individual countries might wish to maintain their own national modifications to some aspects of their programmes relevant to their own special local circumstances, the Group expressed the view that due consideration should always be given to the necessity and justification for such modifications. The continuing need for them should be reviewed regularly and at frequent intervals.

5. CASE-FINDING

The Group reviewed the case-finding methods recommended in the ninth report of the Expert Committee and confirmed that they were still valid.¹ Since case-finding activities in many developing countries depend principally on the examination of patients presenting themselves with relevant symptoms to a health facility, the Group emphasized that this activity, at both the intermediate and peripheral levels, should be given the utmost priority. All staff that have direct contact with persons attending health centres should be encouraged and appropriately trained to identify tuberculosis suspects and arrange for the bacteriological examination of their sputum. Microscopy services should be strengthened to deal with the workload rapidly. In areas where chest radiography is also used in case-finding, every effort should be made to have the diagnosis of tuberculosis confirmed bacteriologically so that overdiagnosis is avoided.

The Group reviewed studies on the possibility of expanding case-finding by active measures at the peripheral levels of health care, involving, for example, the interrogation of household heads and community leaders to identify suspects. These methods might lead to the diagnosis of a high proportion of the smear-positive cases in the community. Such activities could become routine for primary health care workers.

6. TUBERCULOSIS LABORATORY SERVICES

The tuberculosis laboratory service of a developing country consists, under favourable circumstances, of central specialized laborato-

¹ WHO Technical Report Series, 1974, No. 552, pp. 14-17.

ries in large cities and a network of multipurpose laboratories throughout the country which carry out direct smear examinations by the Ziehl-Neelsen method as part of their work.^{1, 2} In the less developed of these countries, this basic organization may be incomplete. In richer developing countries some of the laboratories in the network perform cultures, and even sensitivity tests, in addition to direct smears.

The laboratory service is often ineffective in its two functions of support for case-finding and control of chemotherapy. Some of the deficiencies that may exist will now be considered, together with the measures (which may require an experimental approach) that might bring about improvements.

6.1 The central laboratory

The central laboratory, often housed within a national microbiology or pathology institute, should be capable of providing a culture and sensitivity test service in addition to direct smear examination, all at a high technical level. It should advise the management teams on all laboratory aspects of the national programme and should play an important part in staff training, equipment specification, supervision, and quality control. Not all countries have central laboratories fulfilling these requirements. The Group emphasized that the development of a strong central laboratory which accepts its nationwide responsibilities is an essential objective.

6.2 Extension to the periphery

Efficient peripheral laboratories could play a crucial role in the success of case-finding programmes based on the detection of smear-positive cases. However, the extent to which direct smear examination should be extended to the periphery is a question of local policies and resources. Often it will depend on the level at which intensive case-finding starts, as well as the extent to which microscopes are provided for other purposes, such as parasitology. There are, however, special difficulties in making examinations for tubercle bacilli as this task

¹ WHO Technical Report Series, 1972, No. 491.

² Laboratory services at primary health care level (unpublished WHO document WHO/LAB/79.1). A limited number of copies of this document is available, on request, from Health Laboratory Technology, World Health Organization, 1211 Geneva 27, Switzerland.

requires high-power microscopes working at the limits of optical resolution and used for long periods while examining smears. The microscopes must be efficient and well maintained, and there must also be regular provision of stains and other supplies. All this may be difficult to achieve; if the difficulties cannot be overcome, it may be advisable to carry out tuberculosis bacteriology at a more centralized level of the laboratory network. Evaluation of the extent to which microscopy should be extended to the periphery, the yield of cases, and methods for transporting sputum are important operational research activities.

6.3 Isolation of the intermediate and peripheral laboratory network

Laboratories in many countries fail to work efficiently because they are out of contact with their clinical colleagues and do not appreciate how the results of their tests are used. Tuberculosis bacteriology carried out in all laboratories will be strengthened if there is regular contact with clinical colleagues and with members of the appropriate management team.

6.4 Culture

Culture of tubercle bacilli is necessary for carrying out sensitivity tests, which are of value for epidemiological purposes and for guiding re-treatment if first-line chemotherapy has failed. It might also be of value as a check on the effectiveness of diagnosis through direct microscopy. While direct smear examination has the highest priority, the extension of culture examination to symptomatic suspects may result in more frequent and earlier diagnosis, and its introduction might thus be a means of obtaining a significant improvement in bacteriological case-finding. This question is, however, controversial and it would be of value to explore in a few selected laboratories the feasibility of introducing culture examination for symptomatic subjects and its impact on the effectiveness of case-finding. The question of whether symptomatics should be selected for sputum culture by prior radiographic examination is complex and requires operational research.

6.5 Quality control

Quality control of every form of tuberculosis bacteriology, including direct smears, cultures, and sensitivity tests, is essential. It is probable that quality control of smears is best carried out by sending cen-

trally prepared specimens with known results to peripheral laboratories for examination. This can easily be done on a national scale with direct smears. Control of culture and sensitivity tests, however, will involve new approaches and international cooperation. Experience in technically advanced countries suggests that communication of the results to the peripheral laboratories acts as a potent stimulus for improving the reliability of results. Research on quality control methods would be useful.

6.6 Other laboratory methods

The development of good immunological methods for diagnosing tuberculosis, particularly effective and simple serological techniques, would be of great value. These are likely to be particularly useful in diagnosing types of tuberculosis usually inaccessible to bacteriological examination, such as nonpulmonary and most childhood disease, as well as for smear-negative but presumed active pulmonary tuberculosis.

7. CHEMOTHERAPY

The Group reviewed the major advances that have recently been made in short-duration chemotherapy.¹ There are now a number of short-course regimens of 6–9 months' duration that are very highly effective, of low toxicity, and well tolerated. Some are daily regimens, others intermittent after an initial intensive daily phase, and some intermittent throughout. They are nearly as effective in patients whose strains are initially resistant to isoniazid, to streptomycin, or even to both drugs, as in patients with fully sensitive strains. Moreover a high proportion of patients are cured even within the first 3 months of treatment, so that these regimens offer an important degree of protection against failure due to premature default from treatment. These potent regimens are based on an initial intensive phase of isoniazid, rifampicin, and pyrazinamide supplemented by a fourth drug (streptomycin or ethambutol), and isoniazid plus rifam-

¹ FOX, WALLACE. Whither short-course chemotherapy? *British journal of diseases of the chest*, **75**: 331–357 (1981); reprinted in *Bulletin of the International Union against Tuberculosis* **56**, No. 3–4 (1981).

picin in the continuation phase. There is a choice between 6-month regimens with rifampicin throughout, which are expensive, or cheaper regimens of 8–9 months' duration with the expensive drugs given in an initial intensive phase that is followed by a much less costly continuation phase.

The Group noted that a number of technically advanced countries have recommended the use of short-course chemotherapy and that some developing countries are already basing their national programmes on short-course regimens.

In the ninth report of the WHO Expert Committee on Tuberculosis, two regimens are recommended for use in programme conditions in developing countries: (a) isoniazid plus thioacetazone, a combination often supplemented by streptomycin in the initial intensive phase; (b) a twice-weekly, fully supervised regimen of streptomycin plus isoniazid, preceded, whenever possible, by an initial intensive daily phase. The recommended duration of both is 12 months. The Group affirmed that these still remain basic regimens for use under programme conditions in many developing countries. Nevertheless, the aim should be to make available effective short-course regimens for all countries, whether technically advanced or developing.

The efficiency of both standard and short-duration regimens in programme conditions will depend on the quality of the organizational framework of the programme. The primary health care system, with its multitude of community health workers, offers the best scope for organizing a network of treatment facilities and making it more accessible to a greater number of patients, with supervision and checks on drug regularity by the community health workers. An efficient primary health care system implies the active participation of the patient and his family in treatment.

7.1 Essential antituberculosis drugs

In the light of the above, the Group recommended that the next revision of the WHO model list of essential drugs^{1, 2} must include the following in the "Main list" for tuberculosis: isoniazid, rifampicin, pyrazinamide, streptomycin, thioacetazone, and ethambutol.

¹ WHO Technical Report Series, No. 615, 1977.

² WHO Technical Report Series, No. 641, 1979.

7.2 Procurement of drugs

With the aim of improving the supply of antituberculosis drugs (as well as drugs for other diseases), the Group recommended that the IUAT support UNICEF and WHO in their effort to establish a joint pool procurement scheme for essential drugs so that lower drug prices may be obtained. The Group also recommended that the national authorities be informed of the possibility of obtaining loans on favourable terms from multilateral financial institutions, such as the World Bank and the regional development banks, for the procurement of antituberculosis drugs in adequate quantities, uninterruptedly, and on a long-term basis. Many developing countries, however, would not be able to avail themselves of such loans and would need to be provided with special grants to cover the cost of drug procurement and supply.

The Thirty-third World Health Assembly (in resolution WHA 33.26) had requested the Director-General of WHO to take appropriate measures to increase extrabudgetary support for health research on integrated tuberculosis control programmes and to secure adequate allocations from the Organization's regular budget for promoting national programmes in developing countries. The Group suggested that, in keeping with this recommendation of the World Health Assembly, due consideration be given to the foundation of an international fund for the supply of essential antituberculosis drugs free of charge, uninterruptedly, and on a long-term basis to those developing countries that organize an efficient delivery network including suitable storage facilities and logistic support, the latter being a most important managerial function. The Group stressed the importance of the assistance of the WHO Action Programme on Essential Drugs in strengthening the distribution network in Member States.

8. BCG VACCINATION AND PREVENTIVE TREATMENT

The Group reaffirmed the conclusions and recommendations of the WHO Study Group on BCG Vaccination Policies.¹ When given early in life, BCG can play a major role in developing countries, where the risk of infection is high, in preventing morbidity and mortality from

¹ WHO Technical Report Series, No. 652, 1980.

tuberculosis in children. This is particularly important because, in many developing countries, diagnosis rests largely on examination by direct microscopy of sputum of persons presenting themselves with appropriate respiratory symptoms. Although children may have serious forms of tuberculosis, they seldom produce smear-positive specimens; consequently they are less likely to be correctly diagnosed and so treated appropriately for tuberculosis. The Group endorsed the inclusion of BCG vaccination in the WHO Expanded Programme on Immunization as an appropriate component of primary health care for children during the first year of life in developing countries.

Research on BCG remains of primary importance. WHO's current research programme gives priority to studies that contribute directly to elucidating the problems raised by the Indian trial.¹

Although the most logical use for preventive treatment (chemoprophylaxis) would be in easily identified, young, infected contacts of newly diagnosed infectious cases, in practice it has virtually no role in developing countries. This is because preventive treatment cannot be an appropriate component of a tuberculosis control programme unless resources can be allocated to it without compromising the ability of the programme to provide curative treatment to virtually all tuberculosis cases. There is a need for research in preventive treatment to determine if potent new drug combinations given to selected tuberculin-positive individuals for very short periods of time is effective and can help to improve the epidemiological situation.

9. SOCIOECONOMICS OF TUBERCULOSIS CONTROL

The Study Group emphasized that a close relationship exists between the socioeconomic situation and the incidence of tuberculosis. In addition, a relationship exists between the level of socioeconomic development and the efficiency of the operational performance of the programme activities. For both these reasons all efforts directed at the rapid improvement of the general socioeconomic situation will be fundamental to the achievement of targets in the field of tuberculosis, as in so many other health fields.

In countries where the primary health care system already exists and is working well, the tuberculosis programme can be integrated

¹ WHO Technical Report Series, No. 651, 1980.

into the primary health care system at very small cost (indeed, this might actually save funds). However, in most developing countries, the primary health care system is still not working well, or is organized only in a part of the country. The tuberculosis programme in such countries will not succeed unless adequate funds (not necessarily large) are provided to organize and operate the primary health care system over the whole country and to integrate the tuberculosis programme into it.

The Group emphasized the major role played by underprivileged countries in the development of modern chemotherapy, from which the affluent countries have been the major beneficiaries because they have all the necessary facilities and resources and can afford expensive drugs. Great benefits are being realized throughout the developed world because of the shift from hospital to ambulatory care, and from prolonged to short-course treatment, the value of both having been demonstrated first in developing countries. Unsatisfactory tuberculosis programmes in less developed countries may affect developed countries directly because of the migratory phenomena of our times (immigrants, refugees, guest workers, and the rapid expansion of tourism to the countries of the third world). The technically advanced countries thus not only have an obligation to support a continuing programme of research on tuberculosis as part of the fight against the disease on a global scale, but have a direct interest in doing so.

The Group fully agreed with the view that fundamental changes in the world economic structure are called for and are basic for the long-term solution of health problems, emphasizing that mechanisms for increased bilateral and multilateral transfers of resources should be promoted.

10. RESEARCH

Research in the field of tuberculosis is necessary not only to solve specific problems but to stimulate the interest of staff and improve the precision of their work. In recent years, the false assumption, particularly in technically advanced countries, that the tuberculosis problem has been solved has led to a reduction of funding for research and of the recruitment of young research workers. The Group emphasized that the trend must be reversed and that this would benefit technically advanced as well as developing countries. The following areas of

research merit particular support, in addition to those already referred to in earlier sections.

10.1 Immunization

1. Research on the factors that influence the effectiveness of BCG programmes is essential (see section 8).

2. There is an urgent need to assess the effectiveness of BCG vaccination in the prevention of tuberculosis in infants and children.

10.2 Immunology

Recent developments in immunology will result in a very rapid improvement of our knowledge of the pathogenesis of tuberculosis. Areas of promise are the unravelling of the details of the immune system by such *in vitro* studies as the lymphokine-activation of macrophages, isolation of pure antigens with monoclonal antibodies, and the detailed study of how macrophages kill mycobacteria. Once mechanisms are understood, immunotherapeutic agents can be developed to control the operation of the immune system.

(a) By the use of immunotherapeutic agents it might be possible to stimulate the immune system to kill dormant bacilli and thus reduce the risk of endogenous reactivation or improve the efficacy of chemotherapy.

(b) The development of good serological tests would lead to improved diagnosis of childhood tuberculosis, and of nonpulmonary and smear-negative active pulmonary disease.

(c) Pure antigens, or more specific tuberculins, would be of value for skin testing and for other immunological tests including techniques designed to indicate infection with specific atypical mycobacteria.

10.3 Bacteriology

1. Further laboratory work should be done on the genetics of mycobacteria.

2. Continuation of studies on geographical variation in the characteristics of tubercle bacilli and on bacteriophage typing are of value for epidemiological purposes.

10.4 Case-finding and treatment

1. Research on aspects of case-finding, including symptoms which best identify suspects and certain facets of the laboratory programmes (see section 6), is of great importance.
2. Research on the development of regimens of short-course chemotherapy is still highly important. The objectives should include reduction of drug costs, better acceptability to patients, and ease of delivery by the health services.
3. Investigation of the advantages to be gained by the use of short-course chemotherapy under field conditions is urgently needed.
4. Since smear-negative pulmonary tuberculosis comprises a large proportion of all cases in a community, it is desirable to explore the minimum amount of chemotherapy necessary for its cure.
5. Further work is desirable on the diagnosis and treatment of childhood tuberculosis.

10.5 Epidemiology

1. Surveillance of diagnostic and treatment measures under various programme conditions and their impact on the epidemiological situation merits high priority.
2. The epidemiological significance of chronic cases of tuberculosis in developing countries should be thoroughly studied.
3. Quantitative relationships between various indices—risk of tuberculous infection, incidence, prevalence, and mortality rate—need to be evaluated in various socioeconomic conditions and epidemiological situations.
4. Prevalence and incidence surveys combined with tuberculin surveys should be organized, at least in some countries, and repeated at intervals of about 5 years.

10.6 Sociology

1. Sociological studies on the integration of the tuberculosis and primary health care programmes should be carried out with the participation of the workers concerned at all levels to measure its impact on both programmes and to identify factors influencing integration.
2. The influence of different incentives on the motivation of health workers should be studied in order to learn how to overcome the problems of programme integration.

3. Investigations of the nature of symptoms, including their symbolic value in the social system, should be studied because of their importance in case-finding and treatment.

4. Research on the relationship between social attitudes, including those to alternative systems of medicine and the health system, should be encouraged.

10.7 Health education

There is a need for research to determine the value of using the mass media of communication to educate the public about the symptoms of tuberculosis, in order to encourage individuals with symptoms to seek health care earlier, and to stimulate the community to participate actively in tuberculosis control measures. Such studies, however, should be carried out only in those areas where adequate facilities for diagnosis and treatment have been provided.

10.8 Economics

Research into the economics of tuberculosis control programmes and their integration into primary health care is necessary.

11. CONCLUSIONS AND RECOMMENDATIONS

1. In the hundredth year after Robert Koch's discovery of the tubercle bacillus, tuberculosis is still a major unsolved health problem of worldwide dimensions, even though it is a disease that can be controlled and eventually eradicated. The established tuberculosis technology, strengthened by recent developments and particularly by short-course chemotherapy, greatly enhances the prospects of success. While realizing that tuberculosis control activities in developing countries compete with alternative demands on scarce resources, the Group emphatically states that tuberculosis control deserves a high priority from decision-makers responsible for the allocation of even limited health resources. However, tuberculosis control is inevitably a long-term activity, and so it requires a sustained and long-term national commitment. The Group strongly urges that there should be a concerted collaborative effort by the developing countries themselves along the lines of the WHO special action programmes such as the

Expanded Programme on Immunization and the programme on diarrhoeal disease control.

2. The principles laid down in the ninth report of the WHO Expert Committee on Tuberculosis are still basically valid, but the difficulties involved in transforming them into operational programmes have been greatly underestimated. Primary health care offers new opportunities to improve tuberculosis control because, if well organized, it should fully involve both the health infrastructure and the community. Tuberculosis programmes should be integrated into primary health care in such a way that the benefits of case-finding and the supervision of medication at the periphery are realized. At the same time, skilled programme management and supervision of personnel must be provided at all levels.

3. The Group lays great emphasis on the role of experts, knowledgeable in all aspects of tuberculosis control, including clinical skills. Such experts will remain essential, even within the context of primary health care, and they can ensure that integration results in the strengthening, not weakening, of the tuberculosis control effort. A review of the existing training courses, both international and national, should be made to assess whether they are of a sufficiently high calibre and sufficiently comprehensive in scope to train the necessary number of experts whose career will be devoted primarily to tuberculosis control. Adequate training of all cadres of staff is of particular importance.

4. Every patient suffering from tuberculosis, irrespective of where he lives or his socioeconomic status, is entitled to accessible diagnostic services and effective treatment, both free of charge, within the context of the best possible use of the available resources.

5. The development of efficient facilities for bacteriological diagnosis is the key to countrywide case-finding programmes. These include a widespread but judiciously disposed microscopy network backed by a high quality central laboratory and, where possible, the opportunity for culture examination.

6. Every effort should be made by the individual countries and, the Group urges, also by the foundation of an international fund to ensure that an uninterrupted supply of essential antituberculosis drugs is made available, free of charge and on a long-term basis, to the developing countries. The aim is to make potent short-course regimens widely available to them.

7. Six drugs—isoniazid, rifampicin, pyrazinamide, streptomycin, thioacetazone, and ethambutol—should all be on the WHO model list of essential drugs.

8. There is still much to be learned about many aspects of tuberculosis and its control. A large-scale programme of basic, applied, and operational research undertaken by both developed and developing countries in cooperation could make a vital contribution to the successful control of the disease. (A number of projects are referred to in section 10.) It should be borne in mind that the developed countries, in particular, are benefiting from the results of research in the developing countries—a full justification for their active participation in joint research projects.

9. It is a common misapprehension in technically advanced countries that tuberculosis is no longer a problem in them. In spite of low incidence and prevalence rates, tuberculosis will continue to require special efforts for many years to come in their indigenous high-risk groups and in immigrants from high-prevalence countries, and also as a consequence of the rapid expansion of tourism, particularly to countries of the third world.

10. Economic development based upon basic egalitarian principles is paramount for the final control of tuberculosis.

11. The Group affirms the continuing importance of the close association of IUAT and WHO in facilitating the promotion of tuberculosis control programmes in developing countries, especially within the context of primary health care. The IUAT plays an important complementary role to WHO. Being a nongovernmental agency, it has the particular advantage of flexibility of approach and action. The relationship between the two organizations should be maintained and intensified.

ACKNOWLEDGEMENTS

The Study Group acknowledges the special contributions of the following staff members to its deliberations: Mr H. G. ten Dam, Tuberculosis and Respiratory Infections, WHO, Geneva; Dr S. Endo, Regional Adviser on Chronic Diseases, WHO Regional Office for the Western Pacific, Manila, Philippines; Dr L. Houang, Health Laboratory Technology, WHO, Geneva, Switzerland; Dr J. Leowski, Tuberculosis and Respiratory Infections, WHO, Geneva, Switzerland; Dr W. B. Wanandi, Action Programme on Essential Drugs, WHO, Geneva, Switzerland.

**WORLD HEALTH ORGANIZATION
TECHNICAL REPORT SERIES**

| <i>Recent reports:</i> | <i>Sw. fr.</i> |
|--|----------------|
| No. | |
| 628 (1978) Arterial hypertension | |
| Report of a WHO Expert Committee (58 pages) | 5.— |
| 629 (1978) The application of advances in neurosciences for the control of neurological disorders | |
| Report of a WHO Study Group (83 pages) | 9.— |
| 630 (1978) Immunodeficiency | |
| Report of a WHO Scientific Group (80 pages) | 7.— |
| 631 (1978) Evaluation of certain food additives and contaminants | |
| Twenty-second report of the Joint FAO/WHO Expert Committee on Food Additives (39 pages) | 5.— |
| 632 (1979) Cancer statistics | |
| Report of a WHO/IARC Expert Committee (47 pages) | 5.— |
| 633 (1979) Training and utilization of auxiliary personnel for rural health teams in developing countries | |
| Report of a WHO Expert Committee (35 pages) | 5.— |
| 634 (1979) Safe use of pesticides | |
| Third report of the WHO Expert Committee on Vector Biology and Control (44 pages) | 5.— |
| 635 (1979) The African trypanosomiasis | |
| Report of a Joint WHO Expert Committee and FAO Expert Consultation (96 pages) | 7.— |
| 636 (1979) Controlling the smoking epidemic | |
| Report of the WHO Expert Committee on Smoking Control (87 pages) | 9.— |
| 637 (1979) Parasitic zoonoses | |
| Report of a WHO Expert Committee with the participation of FAO (107 pages) | 10.— |
| 638 (1979) WHO Expert Committee on Biological Standardization | |
| Thirtieth report (199 pages) | 20.— |
| 639 (1979) Human viruses in water, wastewater and soil | |
| Report of a WHO Scientific Group (50 pages) | 4.— |
| 640 (1979) WHO Expert Committee on Malaria | |
| Seventeenth report (71 pages) | 5.— |
| 641 (1979) The selection of essential drugs | |
| Second report of the WHO Expert Committee (44 pages) | 3.— |
| 642 (1980) Viral respiratory diseases | |
| Report of a WHO Scientific Group (63 pages) | 4.— |
| 643 (1980) Epidemiology and control of schistosomiasis | |
| Report of a WHO Expert Committee (63 pages) | 4.— |
| 644 (1980) Optimization of radiotherapy | |
| Report of a WHO Meeting of Investigators (89 pages) | 6.— |
| 645 (1980) WHO Expert Committee on Specifications for Pharmaceutical Preparations | |
| Twenty-seventh report (54 pages) | 4.— |

| | | |
|-----|---|------|
| 646 | (1980) WHO Expert Committee on diabetes mellitus Second report (80 pages) | 5.— |
| 647 | (1980) Recommended health-based limits in occupational exposure to heavy metals Report of a WHO Study Group (116 pages) | 8.— |
| 648 | (1980) Evaluation of certain food additives Twenty-third report of the Joint FAO/WHO Expert Committee on Food Additives (45 pages) | 3.— |
| 649 | (1980) Environmental management for vector control Fourth report of the WHO Expert Committee on Vector Biology and Control (75 pages) | 5.— |
| 650 | (1980) Problems related to alcohol consumption Report of a WHO Expert Committee (72 pages) | 5.— |
| 651 | (1980) Vaccination against tuberculosis Report of an ICMR/WHO Scientific Group (21 pages) | 2.— |
| 652 | (1980) BCG vaccination policies Report of a WHO Study Group (17 pages) | 2.— |
| 653 | (1980) Evaluation of certain food additives Twenty-fourth report of the Joint FAO/WHO Expert Committee on Food Additives (38 pages) | 3.— |
| 654 | (1980) Peripheral neuropathies Report of a WHO Study Group (138 pages) | 9.— |
| 655 | (1980) Resistance of vectors of disease to pesticides Fifth report of the WHO Expert Committee on Vector Biology and Control (82 pages) | 6.— |
| 656 | (1981) Assessment of public health and social problems associated with the use of psychotropic drugs Report of the WHO Expert Committee on Implementation of the Convention on Psychotropic Substances, 1971 (54 pages) | 4.— |
| 657 | (1981) The effect of female sex hormones on fetal development and infant health Report of a WHO Scientific Group (76 pages) | 5.— |
| 658 | (1981) WHO Expert Committee on Biological Standardization Thirty-first report (324 pages) | 21.— |
| 659 | (1981) Wholesomeness of irradiated food Report of a Joint FAO/IAEA/WHO Expert Committee (34 pages) | 3.— |
| 660 | (1981) Nongonococcal urethritis and other selected sexually transmitted diseases of public health importance Report of a WHO Scientific Group (142 pages) | 9.— |
| 661 | (1981) Rapid laboratory techniques for the diagnosis of viral infections Report of a WHO Scientific Group (60 pages) | 4.— |
| 662 | (1981) Health effects of combined exposures in the work environment Report of a WHO Expert Committee (76 pages) | 4.— |
| 663 | (1981) Education and training in occupational health, safety and ergonomics Eighth report of the Joint ILO/WHO Committee on Occupational Health (48 pages) | 3.— |
| 664 | (1981) Recommended health-based limits in occupational exposure to selected organic solvents Report of a WHO Study Group (84 pages) | 6.— |