Page 11, line 20 delete reasonably efficient, simplified, but insert simplified, but reasonably efficient,
At the thirty-first session of the Executive Board a suggestion was made by several members that it would be of value for a regular and comprehensive review of one of the Organization's programme activities to be undertaken at each future session of the Executive Board.

The Director-General has considered it appropriate for the programme review at the thirty-second session of the Executive Board to be on the subject of "Tuberculosis", which was amongst the subjects suggested during the discussion. Accordingly, there is attached an outline document, which will be amplified when it is introduced to the Executive Board.
OUTLINE OF WHO'S TUBERCULOSIS PROGRAMME

1. INTRODUCTION

A conservative estimate of today's global tuberculosis problem would be: a pool of 10-15 million infectious cases, which is augmented each year by 2-3 million new cases and depleted by 1-2 million deaths together with an unknown number of spontaneous and induced cures. The overwhelming part of this problem is faced in the developing countries, as illustrated by the fact that, in some of these countries more than 70 per cent. of children are infected at the age of 14 years, as against less than two per cent. in certain economically more favoured countries. These figures express the problem of tuberculosis symbolically but the social aim of any tuberculosis control programme is obviously to lessen the real problem of human suffering and economic losses caused by the disease. It is often maintained that such economic losses are negligible in countries where there is unemployment. This argument stems from a static concept of the economies of disease. In a dynamic concept of cumulative economic growth, the main purpose of neutralizing and preventing infectious sources of tuberculosis today is to contribute towards making the new generations fit to meet the demand for efficient manpower when the economic take-off accelerates. For this purpose, as well as for that of creating confidence in developing health services through the alleviation of present suffering, the diminution of tuberculosis as a public health problem has been allotted a high priority by public health administrators in most of the developing countries.

2. WHO'S RESEARCH PROGRAMME IN TUBERCULOSIS

The apparent excess of knowledge over its application has sometimes encouraged the view that there is no need for WHO to spend time and money on research in tuberculosis. However, an analysis of the logistics of tuberculosis programmes in the developing countries over the last decade demonstrates the difficulties inherent in applying a knowledge originally developed for affluent socio-economic conditions, e.g., the fragility of liquid BCG vaccine and the cost of individualized chemotherapy.

WHO's assistance in the field of research takes various forms. A number of high-quality research programmes have arisen out of WHO-assisted service projects. In other instances, WHO's assistance has been directly aimed at setting up permanent
national research centres. Finally, much of WHO's research is carried out on a contractual basis by a large number of existing research institutes and laboratories; here, WHO's role is mainly confined to suggesting technical problems for investigation, and co-ordinating and analysing results, in addition to making modest financial grants to the institutes concerned. A few examples of this research - arising out of which more than 125 papers have been published during the last five years - are mentioned below.

Standardization and simplification of products and techniques

WHO-directed research has proved that the diversity of testing/reading techniques and tuberculin products used has been impeding inter- and intra-country epidemiological comparisons of infection levels. It has also proved that, if a standard tuberculin is given in a standard dose and if the reaction is read according to a standardized technique, such a test is probably the most significant instrument available in tuberculosis epidemiology. This finding made WHO stimulate the production and standardization of a batch of PPD tuberculin large enough to satisfy world needs for several decades. By this means it is possible not only to avoid repetition of extensive costly assays in animals and human beings, but to facilitate comparison of data from different areas and for different periods. This research also demonstrated large variations in potency between PPD dilutions due to variable adsorption of tuberculin to the inner surface of the container. A stabilizing diluent was therefore introduced together with the above mentioned international PPD batch, leading to tuberculin dilutions of accurate potency and high stability.

The major difficulty in culturing Myco. tuberculosis in simple laboratories such as are found in most developing countries is the complicated technique of preparing the culture media. Preliminary results from a co-operative study of a liquid medium prepared, transported, and stored in freeze-dried form show that this medium is as sensitive as the routinely employed solid medium and does not have a higher contamination rate.

In order to identify the underlying etiological causes for the so-called non-specific allergy commonly encountered in tropical countries, a co-operative project has worked on the development of standard methods for the classification of myco-
bacteria and, at the same time, on providing information concerning the geographical distribution of different types of mycobacteria causing infection and disease in man. From the available data it appears that the occurrence of atypical strains is concentrated in certain geographical regions.

In view of the alarmingly high prevalences of acquired and primary drug resistance of Myco. tuberculosis that are being reported, there is an urgent need to introduce international standards in this field. Three fully quantitative methods developed by different experienced laboratories are now being studied by WHO in consultation with a number of national research institutions.

Many different BCG strains are used for the mass production of BCG vaccines by various methods. Internationally recognized requirements for BCG vaccines would therefore seem most desirable. Three series of co-operative studies completed so far have provided the foundation for the elaboration of minimum requirements for BCG vaccine.

**Epidemiology**

A great amount of epidemiological material collected with uniform methods and techniques in about 30 sample surveys in developing countries has yielded important information on the scope and limitations of current survey methodology. For instance, the striking lack of correlation between a substantial proportion of X-ray shadows, on the one hand, and positive bacteriological findings and tuberculin reactions, on the other, has made it clear that many such shadows are probably of a non-tuberculous nature.

In several longitudinal studies large populations under the influence of various types and intensities of antituberculosis measures are followed-up at short intervals to measure the parameters necessary for perfecting epidemetric models that can be used for calculating realistic forecasts of long-term control and eradication interventions. Important findings are: the long interval between primary infection and the appearance of the disease; that the great majority of new cases arise in previously infected adults; and that it is possible among the latter to pick out small high-risk groups on which preventive efforts can be concentrated.
Public health

Studies on simultaneous BCG and smallpox vaccination have been undertaken to examine the possible interaction in terms of immunity and frequency of local complications. Preliminary data indicate that this is a safe public health procedure which may reduce cost and increase coverage.

Considerable gains in terms of cost, training, integration, and coverage, could be achieved in many developing countries through indiscriminate BCG vaccination, that is, dispensing with the tuberculin test prior to BCG vaccination. The first results from pilot studies indicate that this vaccination procedure will not give rise to an intolerable frequency or gravity of local complications.

As there are indications that persons with non-specific sensitivity have some degree of acquired immunity to tuberculosis, a trial has been designed to assess the protective effect of BCG vaccination in one of the many tropical and sub-tropical countries in which low-grade sensitivity has been found to be highly prevalent.

Several research centres are investigating the clinical efficiency and applicability of domiciliary/ambulatory chemotherapy of tuberculosis in populations living in adverse socio-economic conditions. The first basic finding was that one year's well supervised domiciliary chemotherapy is as effective as one year's hospital treatment with the same combination of drugs, and that it does not expose the patient's contacts to any special risk. Further trials are under way to find the cheapest possible - yet efficient and non-toxic - regimens. A most delicate problem for controlling tuberculosis is the indispensable long-term co-operation of patients. The alarming increase in cases with bacilli that have acquired resistance to the standard drugs is the consequence of inadequate co-operation. Directly supervised, intermittent chemotherapy could go a long way towards improving this situation; the first results were promising enough to prompt a complete series of investigations to determine patients' response to various frequencies of administration of both first- and second-line drugs.

In sociological investigations, attempts have been made to disclose the main reasons for treatment default. This problem is being approached through the analysis of inter- and intra-individual differences in the regularity of self-
medication with varying intensities and systems of motivation. No clear-cut correlation has been found between regularity and such apparently important factors as education, living standards, personality, etc. But in a controlled study of awareness of symptoms in villagers, it was found, contrary to expectations, that more than three-quarters of all persons with highly infectious tuberculosis not only are aware of symptoms indicative of tuberculosis, but have already taken some action to seek help - a finding of great potential importance for treatment motivation.

Another project has studied, in a community, the usefulness of isoniazid chemoprophylaxis in preventing infection from developing into disease. Whereas patients with infectious tuberculosis living in the same area took the prescribed drugs with reasonable regularity, less than one-fifth of the group receiving chemoprophylaxis did so. This finding may explain why the distribution of isoniazid did not significantly prevent infection from developing into disease in this study population.

The utility of operations research methodology in tuberculosis control is being tested in several field projects. Because this "science of common sense" deals with the total - ecological and sociological - system in a country, it promises better results in developing public health strategies in tuberculosis control than the conventional pragmatic, and, by necessity, often biased, approach.

3. WHO'S CONTROL PROGRAMME IN TUBERCULOSIS

WHO-assisted activities in the past

BCG vaccination was the obvious first choice when the need for some international measure to reduce the tuberculosis problem was realized more than a decade ago. To date, approximately 400 million people have been tuberculin-tested and of these approximately 150 million have been BCG-vaccinated, in internationally-assisted programmes covering 61 countries and territories. Twelve WHO/UNICEF-assisted programmes are still in progress with a monthly output of about 2.5 million tests and one million vaccinations. However impressive these figures may be, certain technical and operational observations must be considered in assessing the influence of these campaigns on the tuberculosis problem in the countries concerned. Special
assessment surveys have shown that less than satisfactory levels of allergy have been found in several tropical countries owing to difficulties in ensuring adequate protection of the fragile vaccine against heat and light. There are also indications that in some programmes the vaccination coverage of the susceptible population has been insufficient. Increasing emphasis has therefore been placed on the integration of BCG vaccination into a more comprehensive control programme and on the use of heat-stable, freeze-dried, BCG vaccine.

Demonstration and training centres were designed to demonstrate and teach modern diagnostic and curative methods. Initially these highly specialized centres could not serve the needs of a gradually expanding control service as the methods demonstrated - copied from clinical tuberculosis services in the economically advanced countries: surgery, collapse therapy, isolation - were out of tune with local needs and resources. The advent of inexpensive oral chemotherapy has now made possible a gradual evolution of the purpose of these centres towards referral and evaluation functions within the framework of the national tuberculosis programme.

Prevalence surveys have been an invaluable aid in overcoming a difficulty encountered in many of the countries that request international assistance for their tuberculosis programmes: the lack of precise information on the extent and nature of the tuberculosis problem. Specially trained WHO teams were therefore set up to assist countries in carrying out sample surveys of the prevalence of tuberculosis and simultaneously to study and develop practical and reliable survey methods and techniques. A vast amount of epidemiological data has been accumulated from more than 30 such surveys, and relatively precise estimates of the prevalence of tuberculosis in many countries, particularly on the African continent, have been obtained.

Summing up past WHO assistance in the field of tuberculosis control, two features stand out: the feasibility of applying control measures on a country-wide scale, and the limitations in transposing specialized services from economically advanced countries to those with limited financial and medical resources.
WHO-assisted control activities today: national tuberculosis programmes

The objective of a national tuberculosis programme is the control of tuberculosis, that is, the gradual reduction of the number of infectious and infected persons - in the context of, and in consonance with, the developmental process in the country as a whole. Inexpensive means exist for putting such a control programme into effect partly through a direct attack with drugs upon the tubercle bacilli in the reservoir of human infectors and partly through increasing the specific resistance of the susceptible population with BCG vaccination against the consequences of unavoidable exposure to tubercle bacilli.

But the character of tuberculosis epidemiology is such that there is little prospect of lessening the problem rapidly. To control tuberculosis, therefore, services must have the character of permanent programmes and not of emergency campaigns: even if, for instance, a very substantial diminution in the present infectious pool were to be brought about by a single case-finding and treatment campaign, there is every likelihood that almost the same size of infectious pool would build up again in a few years' time because most new infectious cases seem to result from the breakdown of an infection that took place several years ago.

Furthermore, owing to the ubiquity of tuberculosis, only such control measures as lend themselves to application throughout the national territory can make an epidemiological impact. In this connexion, it is worth noting that mass BCG vaccination of "susceptibles" has proved to be a comparatively cheap and operationally simple measure, and that a considerable part of the infectious case-load can be dealt with by a basic health unit - after very little specialized training - through simple microscopy diagnosis and ambulatory treatment. At this juncture, and taking all other priorities into consideration, a minimum national programme relying on these two elements would seem to be within the reach of all countries.

If control measures are to be applicable nationally, they must be socially acceptable. For instance, the long-term success of the essential preventive services in tuberculosis depends on the amount of curative activities that are linked with them. In turn, the felt need for curative services depends on the general public's awareness of the disease. It has been shown that this awareness is much greater
than previously suspected, and curative services must therefore be made available to all persons whose symptoms prompt them to report for assistance and in whom tuberculosis is diagnosed. This can be achieved if all non-specialized health agencies are guided and assisted in diagnosing and curing the disease in the course of their routine functions.

In short, the national tuberculosis programme, if it is to exert an impact on the problem of tuberculosis, must take into account the epidemiological efficiency of the tools, and their applicability and acceptability. The methods recommended by WHO for developing national tuberculosis programmes are derived from the analysis of key variables in this system of epidemiological, medical, operational, and sociological factors. The functional relationships of these methods may be illustrated as follows:

WHO's assistance to national tuberculosis programmes is most often given through a team comprising a medical officer, a statistician, an X-ray technician, a laboratory technician, and a public health nurse. This team normally stays in the country for two to four years until a nationally applicable programme has been defined and tested, training of all types of personnel consolidated, and national
expansion begun. In some of the Regions, inter-country teams assist governments in assessing the epidemiological magnitude of the tuberculosis problem, the potentiality of developing tuberculosis control, and the operational performance of the national tuberculosis programme. Several of the Regions have found it useful to co-ordinate all WHO assistance in tuberculosis through a Regional Epidemiological and Training Centre - which permits the immediate pooling of experience; inservice training of national and international personnel; and centralization of complex statistical work.

To meet the shortage of key planners and organizers for national tuberculosis programmes, inter-regional training courses in the epidemiology and control of tuberculosis have been organized: 35 WHO fellows from 29 countries attended these courses in 1963. A substantial number of fellowships are also awarded for individually arranged training.

A very important function of WHO is to propound uniform methods and techniques through technical guides, manuals, forms, etc., developed on the basis of all the field experience acquired. Reports of expert committees play an important role in shaping and lending authority to technical policies. Regional and inter-regional meetings of tuberculosis workers are useful for disseminating new technical knowledge.

Considerable efforts are made by WHO to induce manufacturers to produce equipment and supplies particularly suitable for use in the developing countries, e.g. X-ray units, built according to radically new concepts, that combine versatility of application, with ease of operation, simplicity of maintenance, and safety from radiation.

4. CO-OPERATION WITH UNICEF AND THE INTERNATIONAL UNION AGAINST TUBERCULOSIS

Throughout the existence of WHO's tuberculosis programme, UNICEF has given very important material assistance to the activities recommended by WHO. In the past, the main support was given to the BCG programmes but, since the review and report made by the Thirteenth UNICEF/WHO Joint Committee on Health Policy, the scope for UNICEF aid has been considerably broadened to include support for comprehensive national tuberculosis control programmes.
The International Union against Tuberculosis supports WHO's efforts in many important ways, e.g., through developing standard terminology for tuberculosis, disseminating information about WHO-assisted activities, and encouraging national tuberculosis associations to support governmental efforts.

5. SUMMARY AND CONCLUSIONS

1. Tuberculosis is a serious public health problem in almost all the developing countries, where one-half to one per cent. of the adult population excrete tubercle bacilli.

2. WHO's research programme in tuberculosis has made important contributions to: the standardization of diagnostic techniques; an understanding of the epidemiological behaviour of tuberculosis; control measures applicable under adverse socio-economic conditions; methodology for public health practice research in tuberculosis.

3. WHO-assisted projects in tuberculosis control have evolved with increasing knowledge from specialized application of independent measures towards integration of all specific antituberculosis measures into one programme within the operational framework of the general health services.

4. The expanding basic health service of almost any developing country has sufficient technical and economic means at its disposal to vaccinate the total susceptible population systematically with BCG at least once every 5-10 years. In addition, it should be able to operate reasonably efficient, simplified, but case-finding and ambulatory treatment throughout the country with a minimum of specialized support. Many serious difficulties, such as traditional budgeting, waning interest in tuberculosis, inadequately functioning health infra-structures, treatment defaults, and drug resistance, need to be overcome, but if application and research are closely geared to these difficulties, global tuberculosis control is bound to make impressive progress during the next decades.