BACKGROUND DOCUMENT
BASED ON SUMMARY REPORTS RECEIVED FROM COUNTRIES
for reference and use at the
TECHNICAL DISCUSSIONS
"RECENT ADVANCES IN TUBERCULOSIS CONTROL"
FOURTEENTH WORLD HEALTH ASSEMBLY

February 1961
## CONTENTS

<table>
<thead>
<tr>
<th>Chapter</th>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>INTRODUCTION</td>
<td></td>
<td>3</td>
</tr>
<tr>
<td>GENERAL CONSIDERATIONS</td>
<td></td>
<td>4</td>
</tr>
<tr>
<td>1.</td>
<td>Epidemiology of tuberculosis</td>
<td>7</td>
</tr>
<tr>
<td>2.</td>
<td>Case-finding</td>
<td>7</td>
</tr>
<tr>
<td>2.1</td>
<td>Tuberculin testing</td>
<td>8</td>
</tr>
<tr>
<td>2.2</td>
<td>Photofluorography of the chest</td>
<td>10</td>
</tr>
<tr>
<td>2.3</td>
<td>Bacteriological examination</td>
<td>13</td>
</tr>
<tr>
<td>2.3.1</td>
<td>Atypical mycobacteria</td>
<td>14</td>
</tr>
<tr>
<td>3.</td>
<td>Tuberculosis in domestic animals</td>
<td>15</td>
</tr>
<tr>
<td>4.</td>
<td>Prevention</td>
<td>16</td>
</tr>
<tr>
<td>4.1</td>
<td>BCG vaccination</td>
<td>16</td>
</tr>
<tr>
<td>4.2</td>
<td>Chemoprophylaxis</td>
<td>18</td>
</tr>
<tr>
<td>4.2.1</td>
<td>Primary chemoprophylaxis</td>
<td>18</td>
</tr>
<tr>
<td>4.2.2</td>
<td>Secondary chemoprophylaxis</td>
<td>19</td>
</tr>
<tr>
<td>5.</td>
<td>Chemotherapy</td>
<td>20</td>
</tr>
<tr>
<td>6.</td>
<td>Non-institutional treatment</td>
<td>21</td>
</tr>
<tr>
<td>7.</td>
<td>Organization of a tuberculosis control programme</td>
<td>24</td>
</tr>
<tr>
<td>7.1</td>
<td>Assessment of the tuberculosis problem</td>
<td>25</td>
</tr>
<tr>
<td>7.2</td>
<td>Case-registers</td>
<td>26</td>
</tr>
<tr>
<td>7.3</td>
<td>Role of the hospital</td>
<td>26</td>
</tr>
<tr>
<td>7.4</td>
<td>Social assistance and rehabilitation</td>
<td>27</td>
</tr>
<tr>
<td>7.5</td>
<td>Integration of tuberculosis control services</td>
<td>27</td>
</tr>
<tr>
<td>8.</td>
<td>Health education in tuberculosis</td>
<td>28</td>
</tr>
</tbody>
</table>
INTRODUCTION

In June 1960 a document outlining the technical aspects of certain important problems in tuberculosis control and indicating some subjects which might usefully be discussed was forwarded to Members and Associate Members. This document was intended to help governments to start national discussions on the situation of tuberculosis control in their countries in preparation for the Technical Discussions on "Recent Advances in Tuberculosis Control" to be held by the Fourteenth World Health Assembly in February 1961. The suggestions made in the preliminary document have met with considerable interest and more than fifty countries have made summary reports on national meetings on tuberculosis control available to the Organization. In the present "background document" many of the points raised in the national commentaries are considered in the general framework of the whole subject.

During 1960 tuberculosis control was also the subject of special meetings of a regional character. Thus a tuberculosis seminar organized by WHO in Sydney discussed tuberculosis control in the light of recent advances and the Regional Committee for the Eastern Mediterranean held technical discussions on "Tuberculosis control, with particular reference to domiciliary treatment". In addition, the International Union against Tuberculosis, at meetings of its technical committees, reviewed several problems of tuberculosis control, using the preliminary document distributed by WHO as a basis. Reports on these various meetings will be available at the Technical Discussions.
GENERAL CONSIDERATIONS

Very little reference was made by any country to the ultimate objective of tuberculosis control - the eradication of tuberculosis. On the other hand, there was some discussion of the definition of when tuberculosis ceases to be a public health problem. The WHO Expert Committee on Tuberculosis at its seventh session had stated that "the elimination of the disease as a public health problem could not be considered to have been achieved in most instances until the prevalence of natural reactors to tuberculin among children in the 14-year age-group had become less than one per cent. (a natural reactor being defined as a person showing a significant reaction to a standard dose of tuberculin)". To some countries, e.g., India, this standard was not acceptable because of the prevalence of non-specific tuberculin sensitivity. It was recommended that under these conditions a search be made for some other appropriate index.

In practically all countries the tuberculosis control programme seems to be established on a nation-wide basis. It is universally recognized that the main objective of this control programme is to find the infectious tuberculous persons (and animals) and render them non-infectious. Whether the case-finding survey commences with community-wide tuberculin testing or with mass photofluorography of the chest depends very largely on the prevalence of infection and the age-groups to be included. Tuberculin testing is considered valuable in dividing the members of the population into those who are probably not infected and those who almost certainly are infected. Photofluorography of the chest serves to screen out those who have evidence of "pulmonary pathology". Bacteriological examination will determine who has infectious tuberculosis.

---

1 Also called mass miniature radiography, radiophotography, R.P., etc.
The ability of BCG vaccination to increase the immunity of the uninfected members of a community is widely recognized. In areas with a high prevalence of infection it can be used on a mass scale for selected age-groups and where the prevalence is low it is valuable for the protection of those who are "living and working at risk".

The highly effective antituberculosis drugs play a valuable part in prophylaxis as well as in therapy. While primary chemoprophylaxis\(^1\) has a very limited place in the control programme, secondary chemoprophylaxis\(^2\) is considered of value in preventing dissemination or the development of disease in some who are already infected.

The introduction of effective drugs has made the treatment of individual patients one of the most important health measures in the control of tuberculosis. By preventing non-infectious disease from becoming infectious and by rendering infectious cases of tuberculosis non-infectious the antituberculosis drugs considerably reduce the public health problem. Whether the tuberculous patient is treated in hospital (sanatorium) or on a domiciliary or ambulatory basis depends largely on local conditions.

In the economically less developed countries much of the treatment will have to be given on a domiciliary or ambulatory basis. In them as in the more developed countries inexpensive hostels will have to be provided for some of the patients who do not respond to modern treatment and who remain infectious.

\(^1\) Primary chemoprophylaxis is usually defined as the administration of antituberculosis drug(s) to a person who is not infected with tubercle bacilli (i.e. who does not react to the tuberculin test), the aim being to prevent infection (infection chemoprophylaxis).

\(^2\) By secondary chemoprophylaxis is generally meant the use of an antituberculosis drug(s) to prevent the development of disease in a person who is already infected with tubercle bacilli, as evidenced by a positive reaction to the tuberculin test (disease chemoprophylaxis).
In the economically more developed countries also much of the treatment will be given on a domiciliary basis. This mode of treatment will be used mainly for patients who have already had an initial period of treatment in hospital. Chemotherapy, to be successful, must be taken in adequate doses and used continuously for long periods. Frequently hospitalization during the whole period of treatment is not feasible, and the drugs will then have to be self-administered. Under these circumstances supervision by specially trained home visitors is essential as is intensive health education to ensure the fullest co-operation of patients and of their families.

It appears to be widely recognized that a tuberculosis control programme should be carefully planned, and implemented as the necessary trained staff and equipment become available. It should form part of the general public health service of a country. Case-finding should be followed by effective treatment and "disposal". At regular intervals an "audit" should be taken of all available information so that the methodology of the control programme can be evaluated. Assessment of the progress of the control programme may be greatly aided by the keeping of "live" case registers, i.e. registers which are currently kept up to date.

By integration of tuberculosis control into the general public health services duplication of personnel and of effort is avoided and expenditure is reduced. In planning control measures their financial implications must be related to the cost of the whole public health service. The extent to which the plans can be implemented depends on the availability of trained personnel, of funds and of equipment.

As an infectious disease concerns the entire community and not only the individual patient the success of a control programme will, to a very large extent, depend on the ready co-operation of the members of the public among whom the control measures are to operate. Health education of the public therefore plays a decisive role as it promotes a high level of health consciousness and thus ensures a high participation rate by the population in recommended control measures.
1. Epidemiology of tuberculosis

Prevalence surveys including tuberculin testing, mass photofluorography and bacteriological examination and associated with the study of mortality and morbidity rates are valuable if immediate action is taken on the cases found. Those that are infectious or potentially infectious should be treated and their contacts should be fully investigated.

It is recognized that in some of the economically and technologically more developed countries the epidemiological pattern has changed during the last few years. Thus in Canada "the average age of a new active case of tuberculosis is 40 years and over. The incidence among males is higher in all age-groups over 30 ... Over the age of 25 a disquieting feature is the high incidence of tuberculosis among the single, widowed and divorced males. The rates for these groups are from two to four times higher than among the married males".

Socio-economic conditions are considered to have a definite effect on the prevalence of tuberculosis. Various deleterious factors are mentioned: overcrowding, especially in the cities; unfavourable habits and customs as for instance in French Somaliland where young children sleep with tuberculous adults and where the abuse of khat is widespread; malnourishment which is prevalent in many countries and perhaps plays a larger part than undernourishment. Thus, it appears that animal proteins (which are scarce in many parts of the world) rather than vegetable proteins contain the amino-acids which are thought to be needed in the overcoming of tuberculous infection. Another aspect of this problem is the possible role of endogenous factors. It is reported for instance that ascorbic acid which is needed for the proper metabolism of amino-acids is either destroyed or not absorbed by tuberculous subjects. Also, it is thought that in the tuberculous subject the normal fat metabolism is affected by toxic products of the bacilli.

2. Case-finding

As it is the infectious cases who spread tuberculosis in a community the main objective of a tuberculosis control programme must be to find them and to ensure that they are rendered non-infectious. In other words the purpose of case-finding
and of its follow-up is to "interrupt the epidemiological chain: patient - contact - new case".

Case-finding should be conducted on a community-wide scale. It is usually based on three diagnostic procedures - the tuberculin test, photofluorography of the chest and bacteriological examination. The order in which these examinations are made depends largely on the prevalence of infection in the area being surveyed.

In areas where the prevalence of infection is low the photofluorographic examinations are frequently, even usually, preceded by tuberculin testing and only the tuberculin reactors are X-rayed. In high prevalence areas all members of the community above the age of 15 years are X-rayed. In most countries, be the prevalence of infection high or low, members of the age-groups below 15 years are not included in community-wide photofluorographic surveys unless they are positive reactors to tuberculin.

2.1 Tuberculin testing

Although WHO has drawn up standards for an intradermal tuberculin test which include the dose and product, the technique of injection and the method of reading the test, this standardized tuberculin test is far from being universally adopted.

Because they are painless and easily applied the jelly tests are preferred for young children in several countries, for instance Finland and Eire; in the Argentine the patch test is used for sucklings, as well as routinely by general medical practitioners and in Austria it is preferred for young children, because it requires less personnel and because the parents' consent is more easily obtained than for an intradermal test. When the object of the tuberculin test is to separate the infected from the non-infected members of a community many countries find a percutaneous method, such as the multipuncture test, to be satisfactory. The multipuncture method is widely used for this purpose in New Zealand, the United Kingdom, Nepal and Australia to mention only a few countries, and it is growing in popularity in the United States of America, Canada, El Salvador and France. In Venezuela, the percutaneous methods are recommended for use in rural areas while the Pirquet test
A14/Technical Discussions
page 9

is used for testing young children in the Netherlands. The BCG skin test is not widely used but its value is being investigated.

The intradermal Mantoux test, using a standardized tuberculin, is the most widely employed method and appears to be a most efficient single test. It is certainly the most useful test in areas where non-specific sensitivity is being investigated such as in Malaya and Nepal and in many other countries.

The question how the reactions to a low-dose intradermal test should be interpreted was discussed by the WHO Expert Committee on Tuberculosis at its seventh session in 1959. The Committee held that "in areas where small reactions are infrequent i.e. where there is probably little or no non-specific sensitivity to tuberculin, the criterion for a "tuberculin reactor" recommended in its sixth report - namely, a reaction of 5 mm or more in diameter - may still be used to separate the tuberculous infected from the non-infected ..... However, with regard to areas where small reactions are common (probably indicating the presence of non-specific infections producing reactions to the tuberculin test) it can only be stated (1) that a reaction of less than 5 mm indicates in all probability that the person is not infected with M. tuberculosis; (2) that a reaction of 10 mm or more indicates in all probability that the person is so infected and (3) that a reaction measuring 5-9 mm indicates that the person may or may not be infected ....."

These views are supported, for instance, in the United States of America. In that country the dose generally used for the intradermal test is 5 TU of PPD-5, a dose which according to comparisons made is approximately two times stronger than that recommended for the WHO standard test, viz. 1 TU of RT23, with Tween.

As regards the use of the low-dose intradermal test for determining who should be excluded from BCG vaccination it has been proposed by the WHO Expert Committee that "in an area in which reactions of less than 5 mm are common - probably indicating the presence of non-specific infections producing reactions to the tuberculin test - the criterion for a "positive" reaction might be set at 10 mm or more .....". While this course of action is supported in the Philippines where non-specific sensitivity is widespread it is not supported by the Netherlands authorities because
it is their opinion that low-grade tuberculin sensitivity indicates a certain degree of protection against tuberculosis. The effect of this naturally acquired low-grade tuberculin sensitivity on the efficacy of BCG vaccination is being studied in several areas.

Repeated longitudinal-tuberculin surveys are considered valuable in the Netherlands, in Canada, Chile, Guatemala and France, to mention just a few of the countries who conduct such surveys at intervals varying from one to five years. Sometimes these surveys are confined to the most exposed groups as in the Argentine, where the age-groups exposed to primary infection are tested annually. These surveys enable the trend of tuberculosis to be followed and assist in the assessment of the effect of the tuberculosis control programme. Information on the percentage of reactors to tuberculin at given ages, for instance at the age of school entrance and/or school leaving, is useful for following the trend of the tuberculosis problem in a country or even in different population groups. In fact, the percentage of reactors at a specified age might become a most valuable index for international comparisons of the tuberculosis problem.

2.2 Photofluorography of the chest

There is almost universal agreement on the value of photofluorography as a case-finding procedure in tuberculosis control. It is very frequently used on a community-wide basis and in many countries, such as Sweden, the majority of new cases are found by this method. Only in a few countries is mass photofluorography not considered practicable, e.g. in French Polynesia. The interval at which the mass X-ray case-finding should be repeated varies from country to country and extends from one to five years. In areas where the prevalence of tuberculosis is low repeated mass X-ray case-finding is considered uneconomical. It is suggested that in such areas the X-ray case-finding programme should be selective, i.e. confined to groups of the population in which prevalence is known to be relatively high.
While the value of initial tuberculin testing - preceding photofluorographic examination - is appreciated for areas where the prevalence of tuberculous infection is low, it is considered impracticable in many of these, except for children under 15 years of age. Young children and pregnant women are usually excluded from mass X-ray programmes.

In some countries, X-ray examination of the chest is compulsory; in Finland, for example, it is compulsory for all over 15 years of age and in Austria for all over 14 years, excluding pregnant women. In France it is pointed out that the co-operation of the public can be secured either by intensive health education - or by compulsion. In the Netherlands, X-ray examination is compulsory for selected groups, such as nurses, teachers, staff of maternity and child care clinics, midwives and student midwives. In some countries it has been noticed that photofluorography is very popular with members of the general public, e.g. in South Viet Nam and in Dahomey where it is reported to have a fascination for the people which tuberculin testing lacks.

It is recognized that there are certain professional and other groups which should be examined more frequently than the general population. These groups may be broadly divided into (i) high prevalence groups (contacts of known cases, patients admitted to general hospitals); (ii) high-risk groups (persons exposed to more than average risk of infection, e.g. staffs of hospitals, sanatoria and clinics), and (iii) danger groups (i.e. persons who by virtue of their occupation may constitute a special danger to others should they develop infectious tuberculosis - teachers, children's nurses, food-handlers, etc.).

Radiation hazards to the technical staff, as well as to the population examined, have been given much consideration during recent years. They have not, however, given rise to any problems, nor have they affected attendance at surveys. There is general agreement that fluoroscopy should not be employed in mass case-finding and its use is now mostly limited to certain forms of investigation, e.g. to routine check-up of cases receiving collapse therapy.
The measures required for the protection of the staff and of the public are well known; they include careful location and alignment of the equipment, adequate tube housing and shielding, optimum kilovoltage, the use of aluminium filters, fast films and fast screens, restriction of the beam to the smallest reasonable field, conversion to the mirror-optics system, the use of gonad drapes and correct use of protective screens. It is stressed that persons awaiting their turn for examination should not be allowed to stand near the X-ray apparatus.

The reading of chest X-ray films is usually done by radiologists or by chest physicians. While technicians can be trained to operate the photofluorographic equipment under the supervision of qualified radiographers, it is in general not considered advisable to use them for the reading of films. In France, such reading is only entrusted to medically qualified staff. In South Viet Nam, however, some reading is done by specially trained technicians as it is in India. They divide the films into "normal" and "probably abnormal", the final classification being made by medically trained personnel.

Dual independent reading is rarely practised. A very frequent reason is that shortage of qualified personnel makes this procedure impracticable. However, in Taiwan, for instance, dual reading is the normal procedure. In Eire 10 per cent. of the photofluorograms are read twice, mostly to check the standard of interpretation.

The finding of radiological evidence of pulmonary pathology is usually, but not invariably, followed by complete investigation before the diagnosis of tuberculosis is made. In the rural areas of Korea, for example, the diagnosis is often made on X-ray evidence alone. In a number of countries, such as France and Belgium, a large film is usually included in the follow-up examination.

It is widely recognized that it is important to keep under observation those cases where the photofluorogram shows evidence of pulmonary pathology but where there is no bacteriological proof that tuberculosis is the cause. In Scotland the period of observation is three months and in India these subjects are re-X-rayed some time after the first radiophotograph. There is wide support for giving chemotherapy to the positive reactors to the tuberculin test among this group of people.
2.3. Bacteriological examination

Direct microscopic examination of the sputum is used in almost all areas and under most conditions. Specimens of the sputum are obtained either by the voluntary cough method or by swabbing the larynx. Where facilities are available examination by culture and/or animal inoculation are used to check the results of the direct microscopy. In most rural areas, however, the opportunities for culture tests are few; usually the necessary facilities are confined to central laboratories in the larger cities. In some countries, e.g. the United States of America, it is held that only a presumptive diagnosis can be made on the result of a direct microscopy and until the result of the culture is known the cases are classified as suffering from "suspect tuberculosis". However, as stressed by the International Union against Tuberculosis, direct microscopy is of value for detecting the patients for whom treatment is urgently needed. In India the health authorities do not consider examination by culture practicable in their public health programme. Culture both for diagnosis and before patients are discharged from hospitals or sanatoria is considered necessary by some countries, e.g. El Salvador. The experience in Nepal has been that patients whose sputum is positive on direct microscopy are six times as infectious as those whose bacilli are only demonstrable on culture. From Romania it is reported that culture brings to light 30 to 35 per cent. more "positives" than direct microscopy.

The training of laboratory technicians varies within very wide limits. In New Zealand the training period is five years, and in many countries a three-year course is required. On the other hand, some countries hold that technicians and assistants can receive enough training in three to six months, part of this period being spent in special laboratories and part in the field.

Transportation of sputum is not regarded as causing many difficulties but some countries, e.g. India, report that growth of contaminants may occur in the specimens; in Malaya contaminating organisms are observed in 10 to 15 per cent. of the specimens. In that area it has been found that the early morning specimen of sputum, rather than a 24 hours' specimen, is the most suitable for examination. To prevent contamination malachite green is added to the specimens. Saturated solutions of tri-sodium
phosphate and two per cent. Désogène have also been found satisfactory in reducing the growth of most contaminants.

2.3.1 Atypical mycobacteria

The so-called atypical mycobacteria present a problem in many parts of the world. Relatively little is known about their epidemiology and their clinical importance. Infection with atypical mycobacteria has been reported to produce sensitivity to tuberculin and thus to be a source of non-specific reactions to the tuberculin test. This problem is being widely investigated, one reason being that non-specific reactions are important in the diagnosis of tuberculous infection in both animals and man. From some countries where the prevalence of tuberculosis is very low, e.g., the United States of America, it is reported that sensitization to tuberculin caused by infection with atypical organisms is more common than sensitization caused by infection with the mammalian tubercle bacillus.

It is thought that infection with atypical mycobacteria, besides giving rise to skin sensitivity to tuberculin, might interfere with the effect of BCG vaccination.

The problems posed by the atypical mycobacteria are being studied in many countries, including Canada, United States of America, Chile, the Philippines, India, Venezuela and the Netherlands. In the last mentioned country, for instance, 36 strains of the "yellow bacillus" have been isolated from male patients in two distinct regions, one with mining industry, the other with steel industry.

Selected problems, such as the identification and classification of atypical strains, their geographical distribution, etc. are also the subject of co-operative studies conducted under the auspices of WHO.

At the present state of our knowledge it is difficult to assess the importance of atypical mycobacteria to tuberculosis control. The results of further investigations will have to be awaited. Of interest in this connexion is the opinion expressed by Dr Rist, Chairman of the Committee on Laboratory Methods of the International Union against Tuberculosis. While agreeing that the problem of the
role of atypical mycobacteria is of great scientific and epidemiological interest. He stresses that this problem should in no way throw doubt on the value of the classical methods of the diagnosis and treatment of tuberculosis.

3. Tuberculosis in domestic animals

If tuberculosis is to be controlled in man it must be eradicated from animals which might be sources of infection in man. Tuberculin testing is the most reliable method of detecting infection with the tubercle bacillus in animals as it is in man. But in neither case is it infallible.

From the United States of America it is reported that "the problem of the NVL (no visible lesions) reactor in cattle and other farm animals is becoming increasingly important. Not infrequently veterinarians make routine tuberculin tests in farm animals only to find a number of positive reactors in herds once free from tuberculosis; at slaughter these animals may reveal "no visible lesions", whereas the microscopic examination of certain lymph nodes may indicate the presence of acid-fast bacilli. If this is going to be one of the "atypical" problems in the United States of America, then it seems necessary for veterinarians to resort to multiple tuberculin testing of cattle using more specific PPDs instead of the currently used OT which we now know from human trials to be much less specific than PPD. Where these "atypicals" come from and how they are spread are problems which are still under investigation.

In some countries tuberculosis in domestic animals presents a more serious problem as shown, for instance, by the following statement from Kuwait: "A huge number of sheep and cattle are imported from other countries, most of which have no law for tuberculin testing these animals. There is no doubt many are tuberculous. The veterinary division examines all animals slaughtered in the municipality's slaughterhouse, but many others are killed outside and escape inspection. Most of the milk consumed in Kuwait is of the dried, pasteurized type, but most of the Bedouins, and some of the poorer classes, are still using fresh unboiled milk".
During an investigation of the source of "atypical tuberculosis" occurring in human subjects in Western Australia "anonymous mycobacteria" were found in the mesenteric and submaxillary lymph glands of pigs. These mycobacteria were "completely indistinguishable from the mycobacterium causing the new disease in man" in that geographical area.

It is reported that bovine tuberculosis has been eradicated in some countries in Europe and North America. In these countries as well as in other countries where bovine tuberculosis is nearly eradicated non-specific tuberculin reactions in animals become of increasing importance. The development of a more specific test for domestic animals, as suggested by the United States of America, would ensure large financial savings since the destruction of cattle reacting non-specifically to the present tests but with no detectable tuberculosis could be avoided.

4. Prevention

4.1 BCG vaccination

The tuberculin test permits a division to be made of the members of the community into those who are probably already infected with tubercle bacilli and those who are unlikely to have been so infected. In order to increase the resistance of the latter, uninfected, group vaccination with BCG may be used. The value of this preventive method is widely recognized. Some countries, e.g. Canada and Belgium, drew attention to the results of controlled trials carried out in England, in Canada and among North American Indians which show that BCG vaccination is about 80 per cent effective. Other countries, such as Eire, Taiwan, and French Polynesia, reported that they continued to use BCG because of the marked reduction, in fact almost total disappearance, of tuberculous meningitis and miliary disease observed in successfully vaccinated infants.

Both the intracutaneous and the percutaneous methods of vaccination are widely used. In many countries the oral method is preferred especially for the younger age-groups. Thus, in the USSR, Romania, Venezuela, the Argentine, France and South Viet Nam the oral method is used for new-born and young children. To vaccinate
new-borns by the intracutaneous method is difficult and complications are more frequent than in other age-groups. However, in some countries such as Canada, Belgium and Bulgaria the oral route has been abandoned and the intracutaneous and percutaneous methods have been adopted. In a number of countries BCG vaccination is compulsory by law. In Bulgaria, for instance, vaccination is compulsory for all subjects up to 30 years of age. In the Argentine, it is compulsory for all non-reactors to the tuberculin test, including new-borns, while in Finland it is compulsory for hospital and laboratory staffs.

Although the value of BCG vaccination in a tuberculosis control programme is widely recognized, it has been pointed out, for example by the Philippines, that "BCG vaccination is a supplement and not a substitute for other recognized control measures". There is very general agreement as to the population groups in which it should be used. In low prevalence areas, especially in such areas where the infection rate is falling, as in the United States of America, Canada, Great Britain and Australia, there is no justification for mass BCG vaccination. Under these conditions its use should be confined to those who are living and working "at risk". In Great Britain, except under special circumstances, BCG vaccination is used for school-leavers (adolescence being considered a "high-risk" period) and so the diagnostic value of tuberculin test is preserved up to the age of vaccination, i.e. up to 13 or 14 years. In areas where the prevalence is high, there is very strong support for its mass use for new-borns, especially in the maternity hospitals, and for school-entrants and for school-leavers.

While there is less need for BCG vaccination in areas of low prevalence, the French authorities drew attention to the growing mobility of people from the more highly-developed countries (with a presumably low prevalence) and their entry into areas of high prevalence. In these circumstances, it might be wise to vaccinate with BCG the non-reactors to tuberculin, as is done in Australia for those officials going to overseas posts.
The value of, and need for, re-vaccination appears to depend on local conditions. It is not recommended in the United States of America, where the requirement is said to be very small. The interval between vaccination and re-vaccination varies, on the whole, between three (e.g. in the Philippines) and five years (e.g. in Eire). In countries where the oral method is used, as in Romania, re-vaccination is done at 18 to 21 months, three to four years, seven years, 14 years and 17 to 20 years. In many tropical countries it has been found that the post-vaccination skin hypersensitivity is appreciably lower than that following natural infection. This observation has increased in importance since the introduction of the "international" batch of purified tuberculin RT23 with Tween 80. The use of 3TU instead of the currently recommended dose of 1TU of this product is under trial. Some countries, e.g. the Republic of the Niger and two provinces in Canada, prefer the intradermal BCG test for post-vaccination testing.

4.2 Chemoprophylaxis

4.2.1 Primary chemoprophylaxis, i.e. the administration of antituberculosis drugs (e.g. isoniazid) to prevent infection in those not already infected, has not been practised to any large extent. In some countries, such as the Philippines, the Republic of the Niger, Dahomey and Venezuela, it is used only under very special circumstances, e.g. when newly-born and young children have to remain in contact with tuberculous parents and the use of BCG vaccination is not practicable. In France, an infant is rarely left in contact with an infectious parent but if it is, the use of both BCG and isoniazid is recommended, and this may be an occasion for the use of BCG vaccine prepared from isoniazid-resistant organisms. This type of vaccine is currently being studied, e.g. in Bulgaria.

There seems to be no experience of the use of primary chemoprophylaxis in the other situations in which it has been suggested it might be useful: the household associates of persons receiving chemotherapy for tuberculosis in an infectious stage; all the uninfected inhabitants of whole villages with a high prevalence of tuberculous infection; and laboratory accidents involving the implantation of tubercle bacilli in a human being who is a non-reactor to tuberculin.
That primary chemoprophylaxis should not replace BCG vaccination was the opinion in most countries; in areas with a very low prevalence of tuberculosis this form of chemoprophylaxis was not considered necessary. The value of giving isoniazid prophylactically to special groups, such as silicotics, is being studied in Australia.

4.2.2 Secondary chemoprophylaxis is generally defined as the use of antituberculosis drugs to prevent the development of disease in persons already infected.

By preventing the dissemination of infection, by controlling the progress of such disseminations into active disease processes or by diminishing the likelihood of re-activation of old infections, this form of chemoprophylaxis should have a very definite place in any tuberculosis control programme.

There is general agreement that chemoprophylaxis should be used for young infected children. The upper age limit varies from country to country, being two to three years in Nepal, for instance, and seven years in Romania.

The value of chemoprophylaxis in primary tuberculosis in children has been demonstrated in a controlled trial carried out by the United States Public Health Service. A daily dose of INH was shown to prevent nearly all extra-pulmonary complications such as bone and joint disease, tuberculosis of the kidneys and meninges, etc. In most countries, for example in Nepal, Malaya, New Zealand, the Philippines, the Netherlands, Chile and Bulgaria to mention only a few, chemoprophylaxis is used for all recent tuberculin converters.

Contacts of infectious patients who are reactors to the tuberculin test are given chemoprophylaxis in most countries (for instance, French Somaliland, Taiwan and New Zealand). In Guatemala, in certain pilot areas, isoniazid is given to all contacts of infectious cases up to the age of 15 years, be they reactors or non-reactors. Chemoprophylaxis is also being used for adolescents and young adults who show marked hypersensitivity to the tuberculin test. Furthermore, in Romania, chemoprophylaxis is given to persons who are convalescent from pleurisy with effusion.
While Canada reports that the use of secondary prophylaxis is being extended, e.g. to children under four years of age, contacts and nurses, India would like to wait until more studies have been made of this method. Such studies are being conducted in the Argentine and in other countries.

5. **Chemotherapy**

It is recognized that if treatment with antimicrobial drugs (e.g. isoniazid, p-amino salicylic acid, streptomycin, etc.) is to be effective, it must be prolonged, uninterrupted and given in adequate doses and in the correct manner, e.g. using a combination of at least two drugs during the infectious stage and when there is evidence of cavities of over 2 cm in diameter. These points were stressed by France, Belgium, the Argentine and Bulgaria, as well as by several other countries.

Because these requirements were not always met, many cases remained chronically infectious. Most countries have found that chemotherapy does reduce the infectiousness of chronic excretors, but some, such as New Caledonia keep their infectious chronics in institutions to ensure segregation and the prolonged, uninterrupted taking of the correct drugs. In India, chemotherapy is thought not to affect the infectiousness of "therapeutic failures". In both France and the Argentine attention is drawn to the problem of drug resistance, which should not be disregarded or underestimated. In France, it has been reported that some chronic excretors, but only relatively few, can be rendered non-infectious by using the newer drugs (pyrazinamide, cycloserine and α-ethyl thiomidole).

Primary bacterial resistance to the usual antituberculosis drugs is not regarded as constituting a public health problem in the United States of America or in the United Kingdom. On the other hand it is reported from Canada that primary resistance is increasing in frequency. In the Philippines, primary drug resistance has been found to occur in about 0.5 per cent. of new cases and in Romania, the reported frequency is about 3.4 per cent. for adolescents and adults and 3.7 per cent. for children. In both Eire and Malaya the occurrence of primary resistance is recognized, but, as elsewhere, its presence is regarded as not yet causing a public health hazard.
The importance of drug resistance to both the individual patients and to the community was stressed by India and France as it presents a double problem. Reduction in the therapeutic effectiveness of the drugs in the case of an individual patient is important but not nearly so important as the implications of the spread of drug-resistant mycobacteria in a community. So far, such organisms have only rarely been isolated from primary infections in children. McDermott is of the opinion that "at the moment the prevalence of isoniazid-resistant tubercle bacilli in various communities does not appear to represent a threat".\(^1\) He does, however, consider that these bacilli cause some public health hazard but points out that more people have died because they did not receive INH than have been seriously affected by INH-resistant tubercle bacilli. In both the Argentine and in Belgium drug-resistant organisms are thought to be a danger to the public health. In the former, cases of primary drug resistance are not widely seen, but in the latter, as in Canada, they are becoming more common and are causing some anxiety.

The question of whether chronic excretors of INH-resistant mycobacteria cause a public health problem has not been studied long enough or sufficiently widely for many countries to be able to express an opinion. In both Eire and Malaya chronic excretors of such organisms are not yet regarded as presenting any risk to the health of the public. In Chile it is thought that isoniazid-resistant mycobacteria, through mutation, might become more pathogenic. In some countries, for instance, in the Republic of the Niger and in Dahomey, it is believed that these bacilli will cause a public health problem in a few years.

6. Non-institutional treatment

The importance of non-institutional, i.e. domiciliary and ambulatory treatment in tuberculosis control is widely recognized. In the economically less-developed countries with their usually very limited hospital resources, this mode of treatment

\(^1\) Unpublished working document WPR/TB/4 presented at the WHO Tuberculosis Seminar, Sydney, 23 May-3 June 1960
will have to be used for the majority of patients. And non-institutional treatment is also gaining ground in the economically more favoured countries where it is used for instance for long-term continuation of hospital treatment.

Where hospital beds are available, there is general agreement as to how they can most efficiently be used. Newly-discovered infectious patients are admitted for a few months during which they are fully investigated, the correct treatment is commenced and the patient and his family are educated concerning the disease. When the patient has ceased to be infectious, his or her transfer to domiciliary or ambulatory care is arranged.

Besides the newly-discovered infectious cases, there are other tuberculous patients who are in need of hospital care, for example, those who are acutely ill, those with tension pneumothorax, large pleural effusion or haemoptysis and those requiring surgical treatment.

If treatment can be given on an ambulatory basis, very few problems arise. The patients can attend out-patient departments of hospitals, dispensaries or clinics for their daily injections, if these are necessary, and their behaviour and progress can be easily supervised. It is when the treatment has to be commenced on a domiciliary basis, as in areas where hospital beds are not available, and/or continued on this basis for long periods that the difficulties of supervision become greater. The condition of the homes, the possibility of isolation, the presence of young children and adolescents, the availability of transport and the possibility of arranging the necessary frequent visits by trained health visitors, nurses, etc., are of paramount importance.

In South Viet Nam, it has been found that the organization of domiciliary care is often very difficult because the necessary transport is not always available, and the services of a large number of home visiting nurses are required. Chemotherapy, to be successful, must be given for long periods in adequate dosage and the drug or combination of drugs prescribed must be taken continuously. It has been found in France and in other countries that those patients who commenced their treatment in
hospital were, on the whole, more co-operative than those whose whole period of
treatment had to be given on a domiciliary basis.

For chemotherapy in the home to be successful, the drug or drugs prescribed
must be acceptable to the patients; otherwise they are taken irregularly and for
too short a time. This has been reported as the experience with farmers in France.
In Alaska, much supervision is given by so-called chemotherapy aides, who are
selected in each village and trained by the public health nurses. In Malaya and
in the Philippines, much of the supervision in the homes is done by the staff of the
rural health centres. Trained home visitors called tuberculosis health aides are
found in Taiwan to be able to supervise between 150 and 200 open cases when they can
operate from health centres. But where no such centres are available, e.g. in the
areas remote from the large towns, it is difficult to provide adequate supervision.
A different problem, stressed by the Swiss health authorities, is the greatly
increased difficulty of providing satisfactory supervision when the patients
frequently change their address.

However, where satisfactory supervision is available, it has been found that,
as a general rule, the patients do take their drugs quite regularly. This has been
the experience in the Netherlands, in Guatemala, Burma and in many other countries;
also it has been noticed that the regularity with which the drugs are collected and
taken is proportionate to the amount of supervision given. From New Caledonia, as
from many other countries, it is reported that isoniazid is taken quite regularly,
while PAS (para-aminosalicylic acid) is not nearly so acceptable to the patients.
Even when complaints are not made about the unpleasant taste and "side effects" of
PAS, the large quantity in each dose, and its expense, cause difficulties in some
areas.

The incidence of infection among the contacts of patients treated on a
domiciliary basis has not yet been very extensively studied. From Belgium, it has
been reported that family contacts are more often infected by patients under
domiciliary care, and that they need adequate prophylaxis. This is not the experience
in Burma and in those parts of India where this important aspect of domiciliary care has been thoroughly investigated. While recognizing that many problems remain to be solved, the Indian authorities stress the very high place domiciliary treatment must take in their tuberculosis control programme; they are of the opinion that social factors are more important than drug acceptability.

Few comparisons have been made so far between the relapse rates in patients treated in hospital and on a domiciliary basis. Because it is the infectious patients who are treated in hospital, the authorities in some countries, e.g. the Netherlands, expect more relapses in the hospital patients than in those who have been treated in their homes. In Bulgaria, on the other hand, it is felt that there is no clear-cut demarcation between cases which receive domiciliary and hospital care, and so it is not possible to comment on the frequency of relapse and contact infection. Further studies will have to be made of patients who, of necessity, have received nothing but domiciliary treatment, i.e. in areas where hospital beds are not available or not available in adequate numbers.

The question of financial assistance, or assistance "in kind", is of importance. In some areas, drugs are supplied free to patients only while they are receiving treatment in hospital. In Canada it has been found necessary to continue the issue of free drugs to patients who have been discharged from hospital and who continue chemotherapy on a domiciliary basis. In Switzerland, tuberculosis insurance assistance is not available to patients who are being treated out of hospital, except for those suffering from minimal non-infectious disease.

7. Organization of a tuberculosis control programme

Today the tuberculosis control programmes are increasingly being organized on a community-wide or public health basis. This extension of the scope of the attack on tuberculosis has been made possible mainly by four factors:

(1) The discovery of highly effective and relatively non-toxic antituberculosis drugs and the accumulation of experience in how to administer them.
(2) The development of simple and inexpensive methods for photo-
fluorography of the chest and increased experience in how to apply
them on a community-wide basis under all possible conditions.

(3) Improvements in methods and products for tuberculin testing
and BCG vaccination.

(4) The efficacy of well-supervised domiciliary care.

7.1 Assessment of the tuberculosis problem

The control of tuberculosis is a problem for the public health administrator. In planning such a programme he would want information on the extent and on the nature of that problem. Having formulated a control plan and put it into operation he would want later to be able to assess the efficacy of the control measures.

For many years morbidity and mortality rates have been used to gauge the extent of this problem and where these are accurately recorded, as, for instance, in the United States of America and in Canada, prevalence surveys are not considered necessary. However, reliable data indicating its extent are rarely available in those countries where the need to organize a tuberculosis control programme is greatest.

It has been stated that the most reliable index of the tuberculosis problem for local use and for international comparison is the prevalence of persons excreting tubercle bacilli. Whether the prevalence of significant shadows in chest X-ray films or that of natural reactors to tuberculin skin tests is the more important as a second index has not yet been decided.

It has been recommended that future prevalence surveys should include all three diagnostic procedures: tuberculin testing, photofluorography and bacteriological examination of the sputum - of those showing radiological evidence of pulmonary pathology. The results of these prevalence surveys should be based on a complete follow-up. Such surveys should, in the first instance, be conducted in and around the larger centres of population and should form part of so-called national pilot area
projects. These should include the training of national personnel, health education of the public, case-finding and treatment and such preventive measures as BCG vaccination and chemoprophylaxis.

7.2 Case registers

If notification of cases of tuberculosis is satisfactory, the maintenance of a "live" case register is helpful, if not essential, for the public health administrator in his task of operating an effective tuberculosis control programme. Whether this registration is done centrally or locally makes little difference. While some countries, such as Taiwan, New Caledonia, Austria and the Netherlands, regard central registration as necessary or essential, others, such as the Argentine and Chile, report that, while a central registry is valuable, the local or provincial register is even more important. When they are kept at the local level, they assist both patient supervision and local programme planning. If the tuberculosis control programme is planned and/or financed on a national basis, the essential statistical data can be forwarded from each local register to the national centre, as is done in Bulgaria and in Canada.

7.3 The role of the hospital

The "clinical" role of the hospital in a tuberculosis control service has already been described in a previous chapter (see under 6). Where hospital beds are available all infectious cases of pulmonary tuberculosis should be admitted for a period during which necessary investigations are carried out and suitable therapeutic measures initiated. During this period of hospitalisation the patient and perhaps members of his family also will be given instruction in how to avoid the spread of infection. Patients presenting such complications as tension pneumothorax, massive haemoptysis and massive pleural effusion will need a period in hospital. In addition many patients suffering from extra-pulmonary disease such as tuberculous meningitis, tuberculous bone and joint disease, etc., are unsuitable for domiciliary treatment.
Not only does the hospital provide isolation of the infectious persons and an opportunity for health education, but in some countries, e.g. Chile, the hospital authorities also undertake public health activities and in others, such as the Argentine, they provide rehabilitation services. In the report from Belgium attention is drawn to the important part hospitals play in the training of nurses and of general medical practitioners. A special problem, stressed by the health authorities of Venezuela, is that in areas where a large part of the population lives under difficult socio-economic conditions, many patients who could be treated ambulatorily may have to be hospitalized as the necessary isolation and subsistence cannot be provided at home. One solution of this problem, it is pointed out, might be the construction of inexpensive hostels.

7.4 Social assistance and rehabilitation

In most countries, some form of social assistance is available to tuberculous patients and/or their families. That special aid is necessary for the aged and the indigent is recognized, for instance, in New Caledonia. Rehabilitation of the tuberculous ex-patient is not as difficult as it used to be, except for those aged 50 years and over, especially if they are unskilled. In Bulgaria, re-employment of the ex-patient is obligatory, if possible with easier conditions and without any loss in earnings. That country also reports on the value of night sanatorium care. In some countries, e.g. New Zealand and Australia, there is a generous special pension for tuberculous patients and their dependants. If the patients are breadwinners for the family, this provision does much to remove financial anxiety while undergoing treatment.

7.5 Integration of services

In some countries, not all the control measures are handled by the tuberculosis control service. The school medical service, as for instance in Switzerland, may be responsible for the tuberculin testing and for the BCG vaccination of schoolchildren. In order to ensure that there is effective follow-up of the tuberculin testing, it is necessary to have the closest co-operation between the two services.
In practically every country it is agreed that the tuberculosis control division should be planned and operated as an integral part of the public health service. It is widely held that such integration produces the most efficient service, though some countries, as, for instance, Switzerland, consider it difficult to generalize since local conditions vary so greatly.

3. Health education

Just as the prescribed treatment must be acceptable to the patient if it is going to be successful, so there must be the fullest co-operation between members of the general public and the public health services if the plan to control tuberculosis and eventually eradicate it is to succeed. In planning a control programme, it is essential, as pointed out by the French authorities, not to exclude the valuable part which can be played by private initiative and by the voluntary tuberculosis associations and the Red Cross, etc. In some countries (e.g. the United States of America) health education of the public is largely the responsibility of special "health educators" who operate in both official and voluntary agencies.

Often, mass actions such as mass X-ray campaigns or BCG vaccination campaigns are used as occasions for a special health education drive; this approach has been very successful, for instance, in Romania, Bulgaria and El Salvador. In Venezuela, the national annual celebration of "The Day of the Tree" is combined with propaganda for tuberculosis control, appeals being made both for the conservation of natural resources (the tree) and for public co-operation in tuberculosis control. Similarly, in many countries the annual campaign for the sale of Christmas seals is used as an opportunity for intense educational activity. In the Netherlands, much health education is done by the private organizations which put emphasis on self-help of the people and encourage co-operation between the public, the medical and nursing professions and the public health authorities. An important factor in the success of health education campaigns may be the help of the religious authorities, as is stressed by the health authorities of South Viet Nam. The success of these education drives can be judged by the public's response to mass campaigns.