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REPORT ON THE TUBERCULOSIS SITUATION IN THE EASTERN MEDITERRANEAN REGION

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1. INTRODUCTION

This paper, presented to the Regional Committee for review at its Thirty-sixth Session, describes the tuberculosis situation and the development of control programmes in the Eastern Mediterranean Region of WHO.

It outlines constraints encountered and endeavours made in recent years to pursue the reorientation of policies and strategies towards the application of tuberculosis control as an integral component of primary health care, in accordance with WHO technical guidelines and World Health Assembly and Regional Committee resolutions on the subject. In this connection, it is to be noted that the last time the Regional Committee considered tuberculosis control in detail was in 1970, at its Twentieth Session, when it adopted a resolution on the subject, EM/RC20/R.12.

Based on this current review and the discussions which will take place, the Regional Committee may consider adopting a resolution to reflect the needs for national strengthening of approaches and activities for control and for further WHO collaboration in this regard.

2. BACKGROUND

The present situation of tuberculosis control in the WHO Eastern Mediterranean Region, and in fact all over the world, seems to constitute a paradox; tuberculosis (TB) represents a serious disease with a known natural history, and against which an effective control technology has been developed, yet the application of this technology is far from satisfactory and the disease continues to be a major public health problem for many countries, particularly the developing ones.

It is already four decades since the essentials of a comprehensive policy for tuberculosis control programmes were laid down by WHO. During these forty years, nine expert committees were convened for the purpose of elaborating recommendations on technical policy concerning the control of tuberculosis. The objectives of tuberculosis control have been stated in social and epidemiological terms: socially, to relieve human suffering by reducing morbidity and mortality caused by the disease, and epidemiologically, to reduce progressively the tuberculosis problem in the community by breaking the chain of transmission of infection with tubercle bacilli.

The WHO policy on tuberculosis control is based on the concept of a comprehensive national tuberculosis programme (NTP) implemented on a country-wide scale through the network of existing general health service institutions particularly at the primary health care level. This concept was formulated for the first time in the Eighth Report of the Expert Committee on Tuberculosis in 1964 and, after critical review ten years later, reaffirmed and enlarged in the Ninth Report of the Expert Committee on Tuberculosis in 1973 and more recently in the Report of a Joint IUAT*/WHO Study Group in 1982.

Full implementation of a comprehensive national tuberculosis control programme implies a commitment by the government concerned to give tuberculosis control its deserved importance in the national health plan and ensure availability of necessary budgetary allocations.

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* IUAT = International Union Against Tuberculosis.

Although the current policy on tuberculosis control, as well as the basic principles of formulating and implementing an effective national programme, were laid down some twenty-five years ago, many countries of the Region have not yet achieved a satisfactory level of programme implementation. In addition to inadequate networks of health care institutions and shortage of financial and material resources, there has been, and still is, a shortage of trained manpower aggravated by its inequitable distribution.

In such situations the national tuberculosis programmes, whether or not they were well-formulated technically, could only have been partially implemented. It is important to record that the available trained staff, mainly clinically oriented, did their best to relieve the human suffering caused by tuberculosis within available resources, but their efforts have had limited impact on the overall problem, due to the fact that a great proportion of the existing cases are not being detected or treated.

In planning for the future, the reasons for the shortcomings in applying the recommended strategy must be carefully considered. These reasons apply in fact not only to tuberculosis but to many other health problems, particularly those that require programme activities efficiently sustained over a long period of time. Planning and application of tuberculosis control activities must be guided by a clear understanding of the epidemiological, technical and operational aspects of the problem.

3. THE TUBERCULOSIS PROBLEM IN THE REGION

Tuberculosis in the Eastern Mediterranean Region continues to be a major public health problem for many Member States. Although there are countries with low prevalence of both disease and infection they represent less than 5% of the population of the Region. On the other hand, one 6th (1/6) of the Region's population lives in countries with very high prevalence of the disease and have a rather limited access to tuberculosis services.

3.1. Official morbidity statistics

Although some statistics are available on the incidence and prevalence of tuberculosis yet, as in many other health information systems, these figures are far from being complete or reliable. To a large extent they refer only to bigger cities or tuberculosis institutions.

In order to obtain more accurate information on the subject, two questionnaires were sent in 1988 to all 23 Member States. Due to the weakness of national recording and reporting systems, the information obtained, though very useful, indicated that there is much left to be desired in their completeness and reliability. Data are also difficult to compare between Member States due to (a) different criteria used for diagnosis, reporting and counting cases; (b) lack of information on bacteriological confirmation of reported cases; (c) failure to diagnose as many as two thirds of smear-positive cases and inability to diagnose smear-negative cases (including some extrapulmonary cases and cases in children) due to lack of bacteriological culture and X-ray facilities; and (d) lack of information from large sectors of populations for which extrapolation from reported data could be risky to some extent.

Notwithstanding all the above limitations, the officially reported data on tuberculosis in the Eastern Mediterranean Region indicate that

approximately 40 000 new smear-positive cases are detected each year, and that about 350 000 patients (diagnosed mostly on clinical grounds, without bacteriological confirmation) are currently under treatment. These figures, which constitute probably only a fraction of the estimated true number of new cases, nevertheless represent a considerable case-load for the health services.

3.2. Estimation of the "true" magnitude of tuberculosis in the Region

As the officially reported figures on tuberculosis in the Region are, with few exceptions, incomplete and to some extent unreliable, the best single indicator for evaluating the magnitude of tuberculosis and its trend is the annual risk of infection, which is an expression of the attacking force of tuberculosis within the community. Unlike morbidity and mortality notifications, it has the advantage of being an objective and a reliable indicator, since data for its calculation are collected independently of the routine reporting procedures. They are derived from tuberculin surveys of representative population samples and indicate the proportion of the population which has been infected (or reinfected) with tubercle bacilli in the course of one year.

There appears to be a relatively constant ratio between the annual risk of tuberculosis infection and the incidence of smear-positive tuberculosis in developing countries: every 1% of the risk of infection corresponds to about 50-60 new smear-positive cases of pulmonary tuberculosis per 100 000 general population.

Some tuberculin surveys have been conducted in a few countries of the Region during the past decade, mainly among unvaccinated schoolchildren. Extrapolation of the results of these limited surveys allows some assessment to be made of the probable annual risk of infection.

There are six countries in the Region with low prevalence of infection and disease; their situation may be compared to that of the industrially developed countries of the world. They comprise less than 5% of the Region's population. The annual infection rate is in the range of 0.1-0.2%. More than three quarters (78%) of the Region's population lives in 12 countries with moderate or high prevalence of tuberculosis, with the estimated annual risk of infection in the range of 0.5-1.5%. The rest (17%) of the population of the Region lives in five countries with very high prevalence of tuberculosis; the annual risk of tuberculosis infection in this latter group is in the range of 2-3%.

The estimated total number of smear-positive pulmonary tuberculosis cases developing each year in the Region is presented in Table 1. Giving full regard to possible error in assessing the risk of infection, it may be estimated that each year approximately 250 000 new smear-positive cases of pulmonary tuberculosis appear in the Region (Table 2).

It is known that the number of new smear-negative pulmonary tuberculosis cases (especially among children) and of extrapulmonary cases is usually of the same order as the number of smear-positive cases. It may be estimated, therefore, that the total annual number of new cases of tuberculosis of all forms appearing in the Region is in the range of about half a million. As the prevalence of cases is at least twice the incidence this means that about one million or more cases of tuberculosis (all forms exist) in the Region.

TABLE 1. ESTIMATED NUMBER OF SMEAR-POSITIVE PULMONARY TUBERCULOSIS CASES DEVELOPING EACH YEAR IN THE EASTERN MEDITERRANEAN REGION

Countries grouped according to prevalence of tuberculosis	Estimated level of the risk of infection	Population at risk in millions	Estimated incidence per 100 000 *population*	Estimated number of new cases per year
1. Low-prevalence countries (Bahrain, Cyprus, Kuwait, Lebanon, Libyan Arab Jamahiriya, Jordan).	0.1 - 0.2%	13	15	2 000
2. High-prevalence countries (Republic of Afghanistan, Democratic Yemen, Somalia, Sudan, Yemen).	2.0 - 3.0%	60	120	72 000
3. Intermediate level prevalence countries: all the rest	0.5 - 1.5%	280	60	168 000
Regional Total		353		242 000

TABLE 2. REPORTED AND EXPECTED NUMBER OF TUBERCULOSIS CASES IN THE EASTERN MEDITERRANEAN REGION

Cases of tuberculosis	Number reported	Number expected	Ratio of reported to expected
Number of smear-positive cases per year	40 000	250 000	1:6
Number of cases under treatment	350 000	1 000 000	1:3

Comparing these figures with those officially reported it appears that probably one in every three cases of tuberculosis is under treatment, but only one in six of bacteriologically positive cases is diagnosed. (Table 2)

4. PROGRAMME SITUATION

All Member States of the Region have endorsed, as a formal policy, the integration of tuberculosis control into the basic health infrastructure. However, the scope of integration is still limited by the level of development of basic health services and the inefficiency, or lack, of a laboratory network. Although the majority of countries indicate achieving at least a partial integration, the tuberculosis control services are in practice still delivered mainly through specialized institutions, which are few and accessible to only a small fraction of the population. This is simply because integration is far from being an administrative reality. It requires considerable organization and reallocation of resources to be successful. For example, it requires that health units have the facilities (manpower and equipment) to provide bacteriological diagnosis and treatment.

4.1. Tuberculosis control activities

The most powerful weapon in tuberculosis control is the combination of case-finding and chemotherapy, considered as one entity, as case-finding is a prerequisite for diagnosis and cure. Bacteriology plays a key role in diagnosis. Examination of direct smears is of first importance, as it is simple, inexpensive and detects those cases of pulmonary tuberculosis that are the most infectious. A target in all developing countries should be to provide microscopic examination of sputum at all levels of the basic health services and on a large enough scale to permit accurate bacteriological diagnosis of every smear-positive case of tuberculosis. Sputum microscopy for patients with respiratory symptoms is, in fact, the method of choice in all developing countries, and should be available at the level of the basic health services. A central laboratory with facilities for culture examination is a desirable addition to programme activities, provided that one of its main responsibilities is to supervise the performance of all the peripheral laboratory services for sputum microscopy.

The implementation of this policy in the Region has progressed very slowly. The network of peripheral laboratories with facilities for sputum microscopy is far from satisfactory and, where they do exist, they are often under-utilized, due to poor referral of symptomatic patients by physicians or other health personnel. They are frequently left without any supervision, may not be regularly provided with stains and supplies and their technicians are inadequately trained. As a result a great proportion of patients seeking care are diagnosed by X-ray examination or even on a clinical basis alone, while the great majority of true smear-positive cases are not detected at all.

As far as treatment of tuberculosis is concerned most Member States are fully aware of the importance of providing adequate chemotherapy to every diagnosed patient, since it meets the expressed needs of patients, saves lives, and reduces transmission of infection in the community. Ambulatory treatment is by far the most common treatment in the Region, but its organization in many countries leaves much to be desired. It is usually based on self-administration of drugs, even the most potent drugs, without proper supervision.

Standard regimens of 12 months' duration, using isoniazid, streptomycin and one other accompanying drug are still basic for use in most national programmes. Recently, however, a short-course chemotherapy regimen of 6-9 months' duration, with rifampicin, pyrazinamide, isoniazid and ethambutol, is being introduced in an increasing number of countries, and became in fact "standard treatment" in economically advanced countries of the Region where, however, the prevalence of tuberculosis is low.

Annex I provides information on the recommended treatment schedules for newly diagnosed tuberculosis cases on: (a) standard regimens of 12 months, and (b) short-course chemotherapy of eight months. The cost of drugs for short-course chemotherapy is about US$40 per patient, and for the standard regimen about US$20 per patient.

In almost all countries the main problem is the irregularity of drug intake, resulting in a high rate of defaulters. Besides, there is also almost complete lack of bacteriological monitoring of treatment results, hence a prolonged drug administration to patients who are no longer bacteriologically positive, not to mention a great number of patients put in treatment without bacteriological proof of the disease.

4.2. BCG vaccination

BCG vaccination has become entirely the responsibility of the Expanded Programme on Immunization. It is carried out in infancy in all but two Member States with coverage of infants ranging from 13% to almost 100%. Apart from low coverage in many countries, a commonly observed problem in connection with BCG vaccination is a low post-vaccinal tuberculin allergy which may be due to either improper handling of BCG vaccine or faulty vaccination technique.

Since BCG vaccination remains the most important control measure in preventing severe forms of tuberculosis and death in children, particularly in developing countries with high prevalence of the disease, national tuberculosis programme managers should pay due attention to the quality of vaccine, its handling, techniques of application and training of personnel, as well as coverage achieved under programme conditions.

The importance of the above points is particularly relevant for some Member States in the Region where an increasing rate of side reactions to BCG has been observed recently. It has been well established that the rate of complications after BCG vaccination is generally related to (a) the dose of vaccine administered, (b) the strain of BCG vaccine used, particularly if there is a change of strain, and (c) faulty technique in vaccine administration.

5. CONCLUSIONS AND PROSPECTS

The review of the tuberculosis situation in the Eastern Mediterranean Region indicates that the disease is still an important public health problem in most countries and, population-wise, it is a problem for more than 90% of the Region's people. It is encouraging to note, however, that in recent years almost all Member States have become more aware of the importance of this problem and have started to intensify their efforts to extend tuberculosis control services to their entire populations.

It is, for example, increasingly accepted that a basic tuberculosis control programme, providing microscopic diagnosis, ambulatory chemotherapy as affordable, and BCG vaccination as part of an expanded programme on immunization, is within the capabilities of all health care systems if the strategy of Health for All is successfully put into practice. The cost of meeting the social target of alleviating human suffering from tuberculosis can be largely achieved by the year 2000; this cost can be around US$0.10 - 0.20 per head of the total population, assuming that diagnosis is made only by microscopy and that the standard chemotherapy regimens of one year's duration are applied. This is compatible with the financial resources for primary health care of even the least developed countries. It must be noted that neglecting tuberculosis control for many years results in the build-up of the problem and its aggravation.

It must be noted also that for many Member States of the Region the shortage of financial resources is not the major constraint in tuberculosis control. Most often it is a reluctance to change traditional and outmoded orientation in tuberculosis control, coupled with maldistribution of trained manpower and exacerbated by lack of managerial skills.

What is important and encouraging is the fact that a comprehensive national tuberculosis control programme has been formulated by all Member States in the Region. Although progress in implementation has been slow in some countries, these programmes are being gradually implemented on a country-wide scale and gradually integrated into existing health infrastructures. This means in practice that in most countries in the Region a population-based approach to tuberculosis control with drug treatment at home instead of a traditional clinical, hospital-oriented approach, is gaining ground. It is a known fact, however, that the overall success of any national tuberculosis control programme depends on efficient implementation of all programme components simultaneously, i.e. case-finding, case-holding and chemotherapy, and not just one or the other component separately.

An example of such success has recently been observed in the Region, namely in the AGFUND-sponsored tuberculosis control programme among Afghan refugees in Baluchistan Province, Pakistan, for which WHO has been the executing agency. Proper implementation of case-finding by sputum smear examination of all symptomatic patients, proper supervision of case-holding and treatment of cases and appropriate administration of BCG has yielded very encouraging results. During the short period of a few years several thousand new smear-positive cases have been diagnosed and put on treatment, and the defaulter rate among patients under treatment has come down from 60% at the beginning of this period to only about 2% at present.

During the last two years eight Member States requested WHO's collaboration in the form of consultants, and a Regional Scientific Meeting on Tuberculosis Control, held in September 1988 in Sana'a, Yemen, was attended by representatives of national tuberculosis programmes from 14 Member States, and provided a forum for exchange of information and experience between the countries.

In terms of budgetary figures the Regional budgetary allocations for tuberculosis control in the Eastern Mediterranean for the biennium 1988/1989 were US$880 000 and for the biennium 1990/1991 US$834 500. In relation to the total Regional budget this represents 1.4% in the current biennium and 1.2% for 1990/1991. These figures must be considered as too low in relation to the importance of the tuberculosis problem in the Region.

There is a need for continued WHO support, especially through the provision of experts (mainly on a short-term basis) to assist Member States in further development of national control programmes, including the strengthening and expansion to the periphery of proven control measures and also in training personnel. Major collaboration is needed in twelve countries (Republic of Afghanistan, Democratic Yemen, Islamic Republic of Iran, Jordan, Lebanon, Morocco, Pakistan, Saudi Arabia, Somalia, Sudan, Syrian Arab Republic and Yemen) while the other countries of the Region are increasingly able to continue their tuberculosis control programmes without WHO participation except for periodic consultations.

WHO's collaboration in strengthening national tuberculosis programmes must be considered a legitimate expectation of all Member States, but it is of the utmost importance for countries with high or very high prevalence of tuberculosis. Its direction would be toward defining the epidemiological situation and determining specific conditions and circumstances that characterize each country (and sometimes different parts of the same country).

Collaboration can also be effective in setting clear objectives and targets of the national tuberculosis programmes, based on a sound combination of internationally known facts as well as on the integration of tuberculosis control services into the existing components of the basic health services.

As stressed in the Regional Medium Term Programme on Tuberculosis for the years 1990-1995, to improve programme efficiency there is a need to further strengthen the managerial aspects of the programme, and particularly programme monitoring, including continuous analysis of data collected at the service delivery level (this implies the introduction of an appropriate recording and reporting system), the on-going supervision of programme activities, and training and re-training of personnel engaged in the implementation of the programme.

Due attention must be paid to training of professional personnel performing managerial duties, microbiologists and laboratory personnel from all laboratory levels dealing with tuberculosis bacteriology, medical doctors working in all types of health facilities who carry out direct clinical care with regard to individual cases, as well as types of auxiliary personnel and primary health care workers who are usually responsible for first-line contact with patients and should be able to identify all patients with respiratory symptoms who are eligible for sputum microscopy.

Evaluation of both the programme operation and its impact has to be built into the active management of the programme and must be applied on a continuing basis, so that the programme's effectiveness and impact can be regularly, at least annually, assessed to indicate any need for replanning of one or more components of the programme.

Annex I

SUITABLE REGIMENS OF CHEMOTHERAPY FOR TUBERCULOSIS IN NATIONAL CONTROL PROGRAMMES (1987)

Duration in months	Regimens[1]	Failures/ relapses (%)	WHO drug cost[2]	
			US$ (1987)	Ratio[3]
12	2 STH/TH	5-10	7.2	1.0
	1 SH/SH_2	5-10	9.0	1.2
	2 SEH/EH	5-10	13.2	1.8
8	2 SRHZ/TH	0-3	31.1	4.3
	2 SRHZ/H	0-3	30.0	4.1
	2 SRHZ/SHZ_2	0-4	43.7	6.0
6	2 SRHZ/RH	0-2	69.4	9.6
	2 ERHZ/RH	0-2	67.6	9.4
	2 RHZ/RH	0-2	66.1	9.1
	2 RHZ/RH_3	0-2	43.3	6.0
	2 RHZ/RH_2	0-2	37.5	5.2

Key

(1) The drugs utilized in these regimens are conventionally represented by the following letters: E = ethambutol; H = isoniazid; R = rifampicin; S = streptomycin; T = thioacetazone; Z = pyrazinamide.

The number preceding the first letter indicates the duration in months of the initial intensive phase; the number which follows the last letter represents the number of weekly doses in the continuation phase if the regimen is intermittent.

(2) The prices are average prices for adults, calculated on the basis of prices paid by WHO to producers in 1987. They are not the actual price of the drugs on the shelf of the pharmacy of the health unit. It is necessary to add the cost of transportation
and distribution which represents an increase of 50 to 100% over the WHO price.

(3) The ratio or relative cost of regimens is based on their cost relation to the less expensive regimen, to which a value 1 was assigned.

1. STANDARD DRUG REGIMENS

The essential drugs available today allow us to compose highly efficient chemotherapy regimens: the potential efficacy of these drug regimens, when regularly followed, is virtually 100%, as demonstrated in different controlled clinical and comparative field trials in many countries.

These regimens share the following characteristics:

- they have two phases: an initial intensive phase, usually of eight weeks, with three or four essential drugs and a subsequent continuation phase with generally two drugs given daily or intermittently, three or two times a week;
- they are well tolerated;
- they are of low toxicity.

These drug regimens differ in two main respects: their duration (12 months for the longest and six months for the shortest regimen) and their price.

In the tuberculosis programme of a country, two alternative regimens could be adopted: one, a daily drug regimen, fully supervised during the initial intensive phase, if possible, and then self-administered in the continuation phase; the other initially daily in the intensive phase and subsequently intermittently, both phases fully supervised. These two regimens can guarantee efficient chemotherapy of all newly diagnosed patients, wherever they live (urban or rural), whatever their way of life (sedentary or nomadic), their medical problems (other diseases) or behavioural problems (psychopaths or drug addicts).

The categories of standard drug regimens based on different durations, but all highly efficient, are as follows:

1.1. Twelve-month drug regimens

The 12-month drug regimens have been widely used in the world after the Eighth Report of the WHO Expert Committee on Tuberculosis, published in 1964.

All these regimens have a potential efficacy of more than 90% and over 95% if streptomycin is given daily for at least the first eight weeks. The risk of major toxicity which implies the discontinuation of at least one drug is variable but it is not higher than 4%.

These regimens are still used in many developing countries because of their low cost. Their effectiveness under programme conditions is always inferior to their potential efficacy, which entails the need for retreatment of a large proportion of patients, 20% or more.

1.1.1. 2 STH/TH

The regimen associating 12 months of daily isoniazid and thioacetazone with an initial supplement of daily streptomycin (from four to eight weeks), is the least expensive regimen. The association of three drugs in the initial intensive phase quickly reduces the number of bacilli and makes it useless to continue up to 18 months.

Moreover, this association considerably reduces relapses from pre-treatment drug resistance, whether primary resistance to streptomycin and/or to isoniazid, or a natural resistance to thioacetazone, which is common in West Africa, where strains of *Mycobacterium africanum* are prevalent.

When streptomycin cannot be given to all patients, due to financial constraints, the use of this regimen should be restricted to sputum-positive cases.

1.1.2. 2 SEH/EH (and 2 SThH/ThH)

In some countries, isoniazid and ethambutol are associated for one year in a daily regimen (ethambutol thus replacing thioacetazone). This regimen SEH/EH is comparable in efficacy to the former one: it is better tolerated but always more expensive.

In other countries, thioamides (Th = ethionamide or prothionamide) are utilized instead of thioacetazone. Wherever applied, this regimen seems efficient, but there are no controlled trials that compare the efficacy of this regimen to STH/TH: moreover, optimal daily dosages of thioamide in association with 300 mg of isoniazid are not yet clearly determined. Usually 500 mg of thioamides are prescribed as the daily dose, but some studies suggest that lower doses could be equally effective.

Tolerance to thioamides is variable in different countries, and the association of isoniazid and thioamide is always more expensive than the combination isoniazid and thioacetazone.

1.1.3. 1 STH/SH_2 or 1 SH/SH_2

This 12-month alternative drug regimen has the advantage of being a fully supervised one and the disadvantage of having 124 to 136 intramuscular injections of streptomycin, which may not be welcome. After an initial intensive phase of daily chemotherapy, the continuation phase comprises fully supervised twice weekly isoniazid (at higher doses, 12-15 mg/kg) and streptomycin.

It is also possible to give a fully intermittent regimen (SH_2) for one year with comparable efficiency. Intermittent drug regimens with thioacetazone and isoniazid or isoniazid and ethambutol have lower efficacy and should not be used.

1.2. Nine-month regimens

The nine-month regimens - 2 RHE/RH or 2 RHS/RH - have been widely used in developed countries since 1976. They are based on a daily administration of isoniazid and rifampicin during nine months, with the addition of a third drug - ethambutol or streptomycin - during the first two months. Now they are being gradually abandoned because, having the same efficacy, they are longer and more expensive than the 6-month regimens which contain pyrazinamide in the first phase.

1.3. Eight-month regimens

In the eight-month regimens, rifampicin is given only during the first two months. Therefore they are less expensive than 6-month regimens in which

rifampicin is present throughout the full course. To compensate for the lack of rifampicin in the second phase a total duration of eight months is required with these regimens.

1.3.1. 2 SRHZ/TH or 2 SRHZ/H

This drug regimen combines in the initial intensive phase of two months (eight weeks) four essential drugs: isoniazid, rifampicin, pyrazinamide and streptomycin, daily; in the continuation phase of six months, isoniazid and thioacetazone (or isoniazid alone) are given daily. The regimen is well tolerated and has over 98% efficacy. The risk of toxicity is very low, even during the initial four-drug intensive phase. The regimen 2 SRHZ/H should be used only in countries where the initial mycobacterial resistance to isoniazid is low.

The use of four drugs in the initial intensive phase makes it possible to achieve 90% culture negative results in two months: therefore, drug consumption under strict supervision is imperative during this phase, whether in hospital, in the health centre or at home. The six-month continuation phase of thioacetazone and isoniazid (or isoniazid alone) is self-administered daily.

The advantages of these regimens are shortening of duration of treatment and supervision, high efficacy, low toxicity and a fairly large possibility of applicability, even in rural areas of developing countries, because of their relatively low cost.

1.3.2. 2 SRHZ/SHZ_2

If there is a need for a fully supervised eight-month regimen it is possible to give isoniazid, streptomycin and pyrazinamide, twice a week, during the second phase. The total duration of this regimen should be eight months, since its discontinuation after the sixth month reduces the efficacy.

1.4. Six-month regimens

These are the shortest regimens that can be applied in tuberculosis programmes. They are also the most effective regimens; their potential efficacy is more than 98%. The combination of isoniazid, rifampicin and pyrazinamide has the highest bactericidal and sterilizing activity against tubercle bacilli.

1.4.1. 2 RHZ/RH

This regimen is based on the association of daily isoniazid and rifampicin for six months, with the supplement of daily pyrazinamide during the first two months. The use of tablets combining the three drugs of the first phase and the two drugs of the second phase makes compliance easier to the patient, and reduces the risks of toxicity and failure due to errors in the dosage.

This regimen is effective in the treatment of pulmonary and extrapulmonary tuberculosis, in children and in adults.

If fully supervised treatment is desirable, isoniazid and rifampicin can be given either three times or twice a week during the continuation phase - regimens 2 RHZ/RH_3 and 2 RHZ/RH_2.

1.4.2. 2 SRHZ/RH or 2 ERHZ/RH

In countries with high prevalence of initial mycobacterial drug resistance it is desirable to add a fourth drug - ethambutol or streptomycin - in the first phase of treatment of smear-positive pulmonary tuberculosis. Ethambutol is a good fourth drug choice because primary resistance to it is still quite rare. However, streptomycin is generally preferred because the need for the injection offers the best opportunity to the health personnel to fully supervise the first phase of intake of oral drugs.

In these two regimens, isoniazid and rifampicin can be administered intermittently, three or two times a week during the continuation phase. The regimens can also be administered intermittently throughout, three times a week.

2. CHOICE OF STANDARD DRUG REGIMENS

One of the most important decisions is the choice of drug regimens to be applied in a national programme.

Many factors should be taken into consideration when taking a decision:

(a) Wrong prescribing habits (e.g. intermittent monotherapy with daily isoniazid and streptomycin twice weekly, systematic addition of tonics and pyridoxin, too long treatments, fanciful associations) or drug consumption habits within the country (complete disregard for pyrazinamide, but widespread use of thioamides; free sale of antituberculosis drugs by chemists, even without prescription);

(b) the insufficient competence in tuberculosis control of those in charge of training health personnel (medical and nursing students). The inadequate knowledge of the teachers often poses considerable obstacles to a modern policy of chemotherapy, as it contributes to perpetuating schemes which are archaic or scientifically unfounded;

(c) the direct or indirect influence of drug manufacturers.

This list of constraints is not exhaustive, but it shows possible causes of failure if obstacles are not removed before a good chemotherapy programme is to start.

2.1. Criteria of decision

Three objective criteria should be applied in decision-making:

(a) the money which is available for antituberculosis drugs at national level;

(b) the number of patients to treat, taking into consideration the number of cases that can realistically be diagnosed and kept under treatment for an appropriate period;

(c) the state of development of health services, present coverage of the population and level of training of health personnel who have to deliver and supervise chemotherapy at the peripheral level.

The amount of money spent on antituberculosis drugs in the country is not only the drugs budget of the public health services; one should also find out the consumption of such drugs in the private and social security systems and compare the information with national pharmaceutical production figures (when drugs are manufactured locally) and the quantities imported. The analysis of the amount spent for each of the essential or subsidiary drugs consumed in the country makes it possible to identify erroneous or excessive prescribing, to detect whether financial resources under public services that were meant for the purchase of antituberculosis drugs are being diverted to other purposes, and to determine how the available money could be spent in a wiser and more useful way. Obviously, the cost of antituberculosis drugs on the world market is an important criterion for planning a more rational policy for the purchase of drugs.

In this respect, the list of prices paid by WHO for essential drugs is a valuable indication to estimate the basic price of the drugs (price FOB, excluding transport to destination and distribution within the country).

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Report on the Tuberculosis Situation in the Eastern Mediterranean Region

Summary of Recommendations

It is recommended that Member States, particularly those where tuberculosis is a major problem:

1. Develop and strengthen national Tuberculosis control programmes,
2. Strengthen microscopic examination through development of peripheral laboratories to ensure the provision of microscopic examination of sputum at all levels of health care services and ensure satisfactory supervision to this basic need,
3. Ensure provision of adequate chemotherapy to every diagnosed patient until complete cure is achieved,
4. Maintain BCG vaccination within EPI and ensure high vaccine quality and trained vaccinators to limit complications.