NTP - control strategies

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Principles of IUATLD Collaborative Tuberculosis Progammes[1-2]

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Abstract : The success of IUATLD-assisted National Tuberculosis Programme developed by Dr. Karel Styblo is dependent on a number of important principles. The most important step is the organization of the basic components of the National Tuberculosis Programme. This first step requires 1) a political commitment on the part of the Government, 2) a secure supply of drugs and materials, including a reserve stock, 3) a network of microscopy centres with a system of quality control and 4) proper recording and reporting of cases. These conditions can result in significant improvement in case-finding and treatment results but rarely results in a cure rate of smear-positive cases in excess of 55 per cent. To obtain the levels of cure necessary to achieve an epidemiologic impact, it is necessary to employ short-course chemotherapy. Additional conditions must be met for this to be successful : 1) adequate supervision of drug-taking in the initial intensive phase, 2) proper training of staff prior to commencement of the treatment and 3) step-wise introduction throughout the country. Several factors may adversely affect the outcome of treatment programmes. These are drug resistance, a high rate of relapse and HIV infection. To date, the IUATLD-assisted programmes have shown sustained success.

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Key words Tuberculosis programmes, treatment results, short-course chemotherapy, programme evaluation

Introduction

Although tuberculosis is a curable and, to a great extent, a preventable disease, successful programmes to combat it in developing countries have been disappointing. Whereas in most technically advanced countries the disease has declined very rapidly over the 4 decades since the introduction of effective chemotherapy, in most developing countries it continues to be a very large problem and shows very little sign of disappearing. Indeed, it has been shown that, to some extent, programmes designed to hasten the disappearance of the disease may have, themselves, had a negative impact (1). Programmes using «standard» chemotherapy under «mass» treatment conditions, while dramatically reducing fatality from tuberculosis, have, in some instances, resulted in an increase in the prevalence of infectious tuberculosis cases in the community (Fig. I).

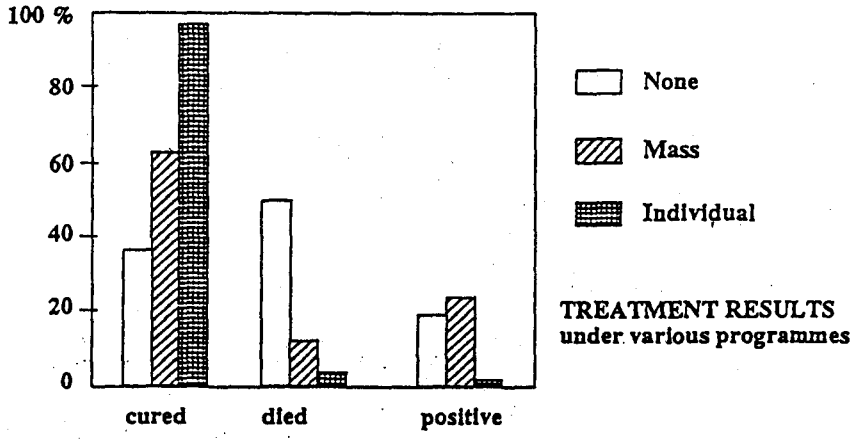

Figure I. Fate of cases of pulmonary tuberculosis under various treatment programmes (1)

Over the past decade, a style of National Tuberculosis Programme (NTP) has been developed by Dr. Styblo within the context of the Mutual Assistance Programme of the International Union Against Tuberculosis and Lung Disease (IUATLD) which has shown results which will be likely to have an impact on the transmission of tuberculosis within the community. While these programmes were commenced using «standard» chemotherapy (consisting of 12 months of isoniazid and thiacetazone with an initial 2 months of streptomycin), the results were really no better than had been observed previously (figure 2), with a documented cure rate just over 50 %. With the introduction of a «cheap» regimen of short-course chemotherapy for new smear-positive cases of pulmonary tuberculosis (consisting of 2 months of fully supervised isoniazid, streptomycin, rifampicin and pyrazinamide (SHRZ) followed by 6 months of unsupervised isoniazid and thiacetazone (TH), accompanied by a special regimen for the retreatment of previously treated cases of smear-positive pulmonary tuberculosis (3 months of fully supervised HRZ plus ethambutol (E), supplemented in the first 2 months with S, E, followed by 5 months of three times weekly, unsupervised HRE), treat-

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ment results have been shown to improve to the point where a positive epidemiological impact would be expected (greater than 75 % of cases are cured, Fig. II and III). The expansion of short-course chemotherapy to most new smear-positive cases throughout a country can be accomplished rather quickly (Fig. IV).

These results have been obtained under programme conditions in whole countries, under all the constraints existing in those countries (including poverty, nomadism, and war). Nevertheless, this accomplishment has occurred under rather precise conditions (2, 3, 4).

Conditions required for an NTP

Prior to successful introduction of an NTP, certain conditions must be met in order for the NTP to be a success.

Political commitment on the part of government

The first condition to be met prior to the introduction of an NTP is a political commitment on the part of the government. As the NTP is the responsibility of the government, and NGO input is accomplished only in partnership with the government, the government must indicate its priority for the establishment of such a programme. The commitment of the government is indicated by the establishment of an adequate structure for the programme, including a central unit for supervision, material management, and training, consisting of a qualified full-time coordinator who is idealistic and enthusiastic, as well as logistical support in the form of administrative assistance and transport facilities. The NTP is carried out within the primary health care system at the district level, usually in conjunction with the district hospital and its associated health centres. At each location where tuberculosis diagnosis and treatment is carried out, an individual within the existing health structure must be identified to take responsibility for the activities of the NTP. Such a person is termed the District Tuberculosis Coordinator (DTC) and undertakes this function as one of a number of health responsibilities within the district under the direction of the District Medical Officer. The district serves a population, on average, of about 100,000. Finally, and very importantly, the intermediate level consists of a Regional Tuberculosis Coordinator (RTC). Like the DTC, the RTC is an officer within the existing health structure. The RTC is responsible to see that the NTP functions well within the region. To accomplish this, the RTC makes regular supervisory visits to the districts and is responsible for training of the staff at the district level.

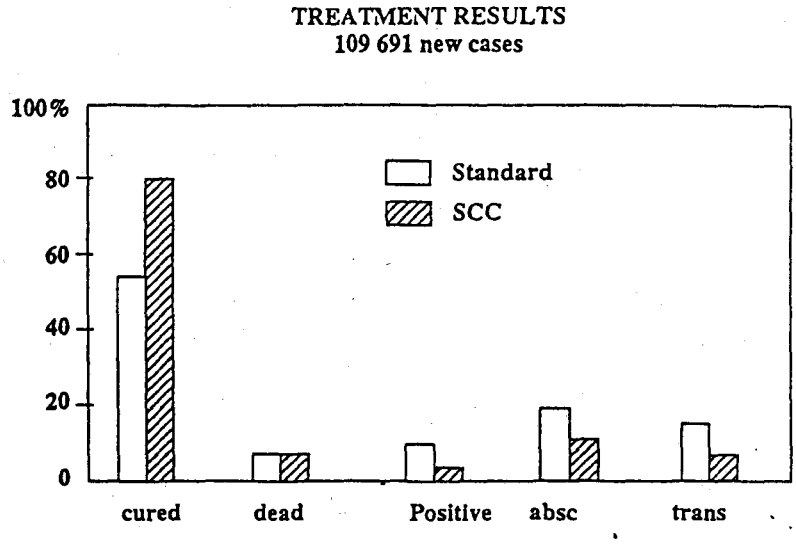

Figure II. Evaluation of treatment results at the completion of chemotherapy of new smear-positive cases of pulmonary tuberculosis in Tanzania, Malawi, Mozambique, Nicaragua and Benin, 1979-1989. Standard chemotherapy consisted of 2STH/10TH in 56,851 cases ; SCC represents short-course chemotherapy consisting of 2SHRZ/6TH in 52,840 cases.

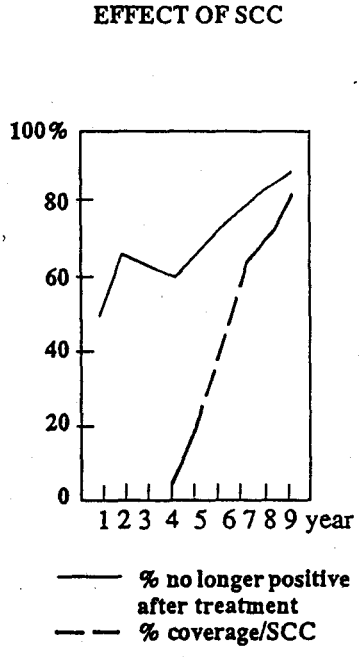

Figure III. Introduction and expansion of short-course chemotherapy (SCC) for new smear-positive cases of pulmonary tuberculosis in Tanzania and its effect on treatment results.

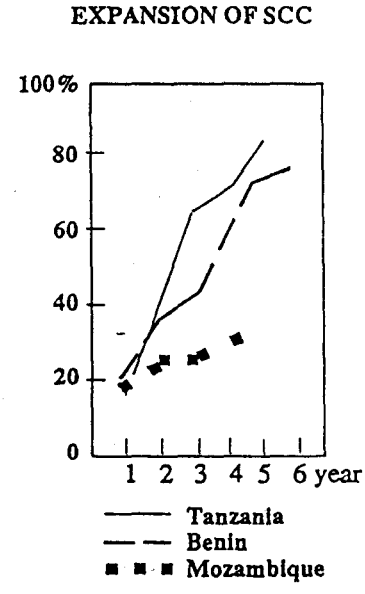

Figure IV. Rate of expansion of short-course chemotherapy (SCC) for new smear-positive cases of pulmonary tuberculosis in Tanzania, Benin and Mozambique. Per cent refers to the proportion of all new smear-positive cases of pulmonary tuberculosis who have been placed on SCC.

A secure supply of drugs and materials.

Prior to the introduction of an NTP, it must be determined that the drugs and materials required for the diagnosis and treatment of tuberculosis patients are available at each location of diagnosis/treatment throughout the country. To accomplish this, it is necessary to deter-

mine the number of cases requiring treatment. At the outset, this number may be difficult to determine and may need to be estimated. It should be estimated from the number of known cases in the country on treatment at the outset of the programme. The precise determination of the number of cases (and therefore the amount of the supplies required) will subsequently be made by the regular recording and reporting of cases as described below. To determine the amount of diagnostic supplies needed, it should be estimated that for every case diagnosed, each requires 3 examinations and approximately 10 will have been examined as suspects in order to diagnose a single case. Moreover, it is necessary to plan to use diagnostic materials in the evaluation of treatment, each patient requiring an additional 4 examinations for this purpose. In addition to the amount of supplies required for consumption, a further amount required for stocks must be planned. The amount of stocks required within a country should be equal to a full year's requirements for consumption : 6 months equivalent stocks at central level, 3 months equivalent stock at regional level and 3 months equivalent stock at district level. Only in this way can treatment proceed uninterrupted.

When the amount of supplies required has been estimated, the cost can be determined. This amount of money must be available prior to embarking on an NTP, as it is unethical and harmful to diagnose cases if it is not possible to offer them treatment. When costs have been estimated, it is possible to determine whether the resources required are available within the country or whether external assistance should be requested. Finally, the method of distribution of supplies must be specified. This should normally be through the existing health care structure.

A network of microscopy centres with quality control

The diagnostic network should consist of microscopists capable of performing sputum examination for acid-fast bacilli on direct microscopy. This network should exist within the present health structure and usually is situated within the general purpose laboratory of the district hospital. The laboratory is under the direct supervision of the individual responsible for diagnostic facilities within the general health structure and the laboratory technician has other responsibilities within the laboratory. In addition, the technician should relate to the DTC and RTC for purposes of communication and supply.

The microscopy service must have a regular system of quality control to ensure the diagnostic accuracy of its activities. This is usually accomplished by selecting a random sample of examinations for review at the central/regional level and the retention of all specimens from diagnosed cases for a period of at least 6 months at the microscopy centre in order that they may be reviewed in the normal course of supervision by either the regional laboratory personnel responsible or the RTC. Finally, regular review of the examinations performed for the evaluation of treatment and systematic comparison of the laboratory and district tuberculosis registers, provide an additional check on the accuracy of the examinations. Where deficiencies are detected, a plan for the upgrading of skills of the laboratory technician must be elaborated.

Proper recording and reporting of cases

This activity is one of the most essential of all for the operation of the NTP, and it is one that is frequently neglected. It is quite straightforward. It is the only means of evaluation of case-finding and treatment and forms the basis for ordering of supplies and medications. Recording of cases and their treatment is done at the district level within the District Tuberculosis Register. This is the only level at which registration of patients should take place in order to provide accurate account of all patients without duplication. All patients from the relevant district are recorded in the register in numerical order as they come to the attention of the DTC, regardless of where they were diagnosed or started their treatment. Numbering of patients begins newly at the commencement of each new year. At the completion of each calendar quarter, each quarterly «cohort» is complete for purposes of evaluation of case-finding and of treatment. No cases may be added to the cohort after the completion of the quarter.

Each patient entered in the register should be correctly assigned to the appropriate treatment category (new smear-positive, new smear-negative, extra-pulmonary, or retreatment) and have sputum smear examination at the commencement of treatment and, in those positive at the outset, at 2 (or 3 months for retreatment cases), 5, and 8 months (as well as 12 for those on standard treatment). Quarterly reports of case-finding, indicating the relevant diagnostic categories, are then submitted immediately at the close of the quarter. Quarterly reports of evaluation of treatment results are completed 15 months after the end of the quarter for the results of short-course and 18 months after the end of the quarter for the results of standard chemotherapy. The results of treatment are as follows : cured (smear-negative), treatment completed (no bacteriologic examination), smear-positive, died, absconded or transferred to another region.

The reports, when complete, are sent to the RTC who reviews them and forwards them to the Central Unit. When this has been completed, a composite report on a half-yearly basis of all case-finding and treatment results can be prepared by the Central Unit.

Additional requirements for the introduction of short-course chemotherapy

Short-course chemotherapy, although theoretically better than standard chemotherapy, can be operationally superior only under certain programme conditions. Before short-course chemotherapy is introduced, all the requirements for the commencement of an NTP should be met. In addition, several other requirements should be met.

Adequate supervision of drug taking during the initial intensive phase

The success of short-course chemotherapy is closely linked with its ability to rapidly remove visible bacteria from the sputum of smear-positive patients. Thus, the initial intensive phase is the most important and, if it is not completed correctly, the results will deteriorate.

To accomplish this requirement, it is necessary to observe every dose of medication taken by the smear-positive case of pulmonary tuberculosis until such time as the sputum smear is negative on direct microscopy (in the majority of instances, by the end of the second month of treatment.

If the smear remains positive, the intensive phase should be continued and

the sputum re-evaluated weekly until the smear becomes negative, at which time the patient may be transferred to the continuation phase. In order to ensure drug-taking, the patient must either attend the outpatient clinic for every dose of medication or, where this is not possible, be admitted to hospital where the directly observed treatment can be given. The adequate completion of the initial intensive phase of chemotherapy is the single most important activity to ensure success of short-course chemotherapy.

Proper training and supervision of NTP staff

The continued success of short-course chemotherapy within the NTP is dependent on the adequate knowledge and performance of the staff assigned to carry it out. This necessitates an initial period of training immediately preceding the introduction of short-course chemotherapy followed by regular refresher training and by regular (at least quarterly) supervision by senior staff members. The regular supervisory visits should concentrate on quality assurance of sputum microscopy, complete and correct registration and reporting of patients and their treatment as well as correct identification of patients for treatment regimens (whether new or retreatment). The visits, therefore, must focus on the Laboratory Register, the District Tuberculosis Register as well as interview with a random selection of patients.

Step-wise introduction of short-course chemotherapy

The success of short-course chemotherapy in improving treatment results depends upon its initial sucessful introduction into a country. This can only be accomplished by a step-wise introduction into the country (and not a generalized institution throughout the country at one point in time). The programme is first introduced into a single region which has the highest likelihood of success (there is an enthusiastic RTC, logistical problems are minimal, there are good facilities for diagnosis and strict supervision of the initial intensive phase of treatment). The successful introduction of the programme into one region allows the expansion to other regions using the initial region as a model. Moreover, the success of short-course chemotherapy quickly becomes known among the general population who then are more inclined to cooperate fully with its institution (including the requirement for initial strict supervision). Once the programme is successfully introduced into a region, fairly rapid expansion to other regions should follow.

Factors which might reduce the success of an NTP

The NTP described above will be successful if patients are correctly diagnosed, they satisfactorily complete their treatment (especially the initial intensive phase of short-course chemotherapy), they are usually initially sensitive to the medications, they have no concomitant, complicating illnesses and they do not relapse after completion of chemotherapy. The results of the programme may not be as good if these conditions are not met. Moreover, if the programme adversely affects these conditions (for example, produces drug resistance), it may deteriorate the tuberculosis situation.

Drug resistance

The institution of short-course chemotherapy under programme conditions might worsen the tuberculosis situation if it promotes resistance to antituberculosis drugs. If short-course chemotherapy is given as described above and there is not a high rate of initial resistance, there is no reason to suspect that this should occur. The powerful antituberculosis agents (especially rifampicin and pyrazinamide) are given only under strict supervision and in the form of combination tablets. Thus the opportunity for incorrect use of these medications is minimized. Moreover, such patients as are enrolled, almost always respond to retreatment (Fig. V). They fail to do so virtually only when they are resistant to both isoniazid and rifampicin, which is fortunately very uncommon (5). This is illustrated for Tanzania in Table 1.

Relapse after chemotherapy

The occurrence of a high rate of relapse after chemotherapy would pose a problem with the NTP by increasing the number of patients to be retreated. Nevertheless, such patients would still be curable using the retreatment regimen, although at an increased cost. A follow-up study of patients who completed treatment with short-course chemotherapy in Nicaragua has been reported (6). The results are illustrated in Table 2. Of 187 patients followed, on average, approximately one and one-half years, only two relapses were noted.

The advent of HIV infection and its impact upon tuberculosis

The introduction of HIV infection into the general community has had a measu-

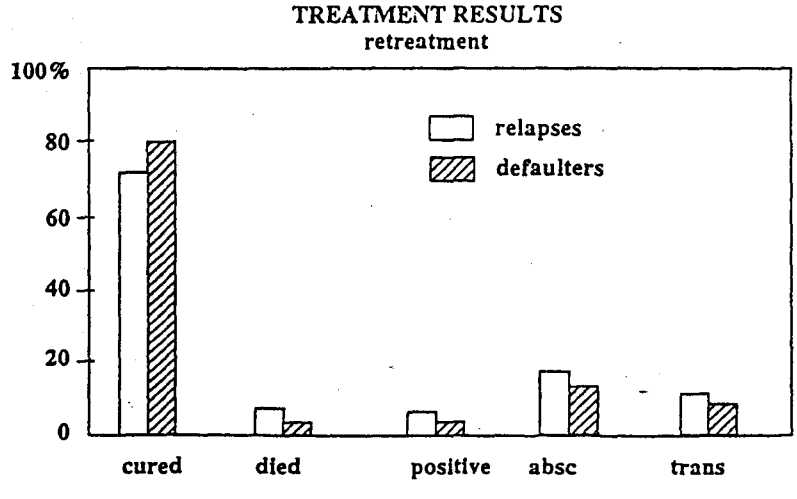

Figure V. Results of short-course chemotherapy in the retreatment of smear-positive cases of pulmonary tuberculosis (relapses and cases returning smear-positive after default) in Mozambique in 1988. The retreatment regimen consists of 2SHRZE/1HRZE/5H$_3$R$_3$E$_3$.

Table 1. Primary (initial) resistance to antituberculosis drugs in a sample survey, Tanzania, 1968, 1978 and 1988 (3).

Year	Proportion of cases resistant to				
	H	S	R	S+H	S+H+R
1968	5	3	0	1	0
1978	8	2	0	1	0
1988	6	3	0	2	0

Table 2. Relapse after short-course chemotherapy for new smear-positive cases of pulmonary tuberculosis in Nicaragua, 1986-1988*

Follow-up (months)	Number treated	Relapses N	(%)
18-24	93	2	(2,1)
15-21	94	0	-

* 2SHRZ/6TH

rable impact on the occurrence of tuberculosis within several of the NTPs assisted by the IUATLD. This has been precisely recorded in Malawi (7) and in Tanzania (6) (Fig. VI). Although the number of tuberculosis cases has been rising since the entry of HIV infection into the community in the early 1980s, the results of short-course chemotherapy among the larger number of cases remain very similar (only the fatality rate has risen ; the cure rate is not adversely affected, Fig. VII).

Conclusion

It is now clear that tuberculosis can be successfully treated under programme conditions even under severe constraints existing in developing countries. Diagnosis and cure of smear-positive cases of pulmonary tuberculosis form the most important and practical method of preventing tuberculosis cases in the future. Moreover, tuberculosis programmes are among the msot cost-effective of all health interventions (9). Even with the increase in the number of cases associated with the advent of HIV infection into the community it is possible to achieve good results if the conditions for the application of short-course chemotherapy are met. ■

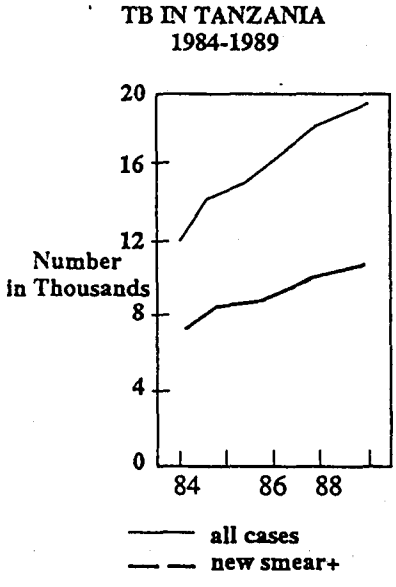

Figure VI. Trend in tuberculosis case-finding in Tanzania, 1984-1989

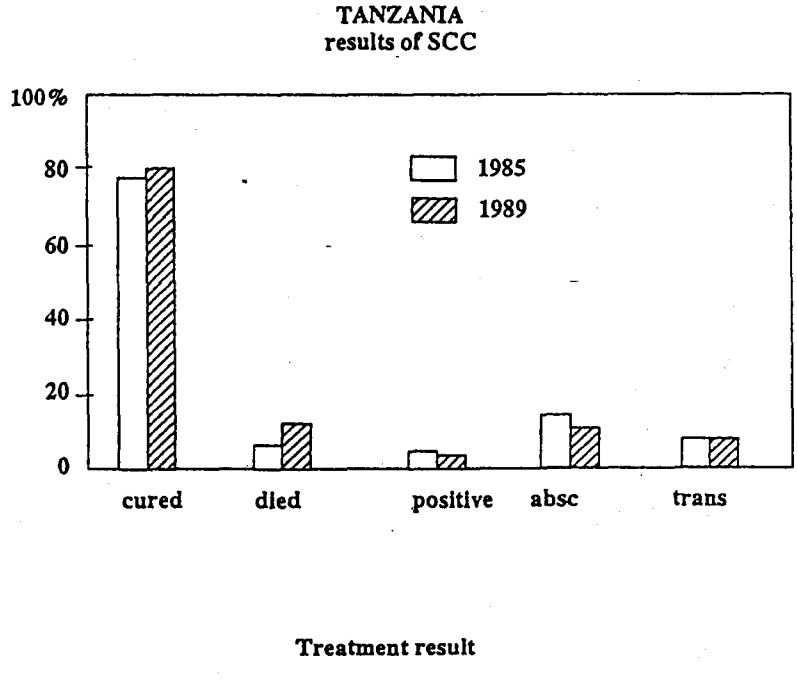

Figure VII. Trend in results of treatment of new smear-positive cases of pulmonary tuberculosis in Tanzania, 1985 and 1989.

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