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DIRECTLY OBSERVED TREATMENT SHORT-COURSE : TUBERCULOSIS CURE FOR ALL

Tuberculosis is a major public health problem world-wide and its control continues to elude the brightest minds and to challenge the human and economic resources of countries around the world. Unless urgent action is taken, more than 15 million people including more than 4 million in India will die from tuberculosis in the next decade¹. Tuberculosis can be cured in nearly all patients. Directly Observed Treatment Short-course (DOTS) strategy is the management package that ensures effective diagnosis and treatment of infectious cases. On March 24, 1997, the Director-General of the World Health Organisation declared, "the DOTS strategy for TB control represents the most important public health breakthrough of the decade, in terms of lives which will be saved"². DOTS which cures 8 out of 10 patients treated has now been implemented in more than 110 countries¹. The key strategy followed in the Revised National Tuberculosis Control Programme (RNTCP) in India is DOTS.

History of DOTS

The essential principles of DOTS are the products of India's long and distinguished tradition of

tuberculosis research. From 1955 to 1958, India conducted a national survey, which documented the burden of tuberculosis and the urgent need for a tuberculosis control programme³. In the 1950s and 1960s, studies at the Tuberculosis Research Centre (TRC) in Chennai, demonstrated the efficiency and safety of home treatment of tuberculosis patients without any additional risk of disease to close contacts⁴. The problems of poor compliance to treatment of patients were identified and the necessity and feasibility of supervised administration of every dose of treatment to tuberculosis patients demonstrated. It was also proved that intermittent chemotherapy was as effective as daily treatment^{5,6}. In the 1960s, studies at the National Tuberculosis Institute in Bangalore, documented the efficacy and feasibility of case detection by sputum smear microscopy even at the peripheral health institutions⁷.

Styblo⁸ combined the principles of DOTS into a powerful treatment system that ensured monitoring, supervision, and accountability for every patient started on treatment and demonstrated that this system could provide effective TB treatment, affordable for developing countries. Thus the principles of modern TB control, first developed in India, in the late 1950s

have travelled around the world and finally returned home nearly 40 years later as DOTS (Table I).

Table I. Milestones of DOTS

- 1961 Concept of supervised chemotherapy
- 1993 WHO declared TB a global emergency
- 1995 DOTS strategy defined
- 1999 DOTS expansion in 110 countries (25% global coverage)
- 85% of all TB cases live in 102 DOTS implemented countries
- 50% of global TB cases occur in 5 countries of South-East Asia: India, Indonesia, Bangladesh, Thailand, Myanmar
- Since 1994 the number of new smear positive cases notified by DOTS has increased by an average of 100,000 per year
- By 2005 70% case detection could be reached by DOTS
- DOTS has been successful in a variety of settings:
 - à Africa : Kenya, Tanzania
 - à Asia : Cambodia, Vietnam
 - à Latin America : Peru

Another important element of the DOTS strategy is the innovative recording and reporting system, simple enough to be completed easily, but detailed enough to provide useful information for ongoing evaluation of the progress of both the patient and the programme. This system also makes the health workers accountable for directly observing the TB patients swallow their medicines during treatment.

Principles of DOTS

The DOTS strategy consists of increased commitment, effective diagnosis, standard treatment given under direct observation, secure drug supply and systematic monitoring and evaluation of all patients started on treatment. In the RNTCP patients are the most important component of the programme. The responsibility of treatment completion by patients and the resultant outcome is shifted from the patients to the health system.

Why is DOTS Necessary?

Studies have shown that about one-third of patients receiving self-administered treatment do not adhere to

treatment. It is impossible to predict which patient will take the medicines regularly. Directly Observed Treatment (DOT) is necessary at least in the initial phase of treatment to ensure adherence and achieve sputum smear conversion. The other advantage is that if a patient misses a dose he can be traced immediately and treatment resumed.

The Components of DOTS⁹

The five fundamental principles of the WHO recommended DOTS strategy are:

Effective political and administrative commitment

Governments and other partners must be financially committed to long-term TB control, ensuring that all TB patients have free access to treatment. TB control should be integrated into the existing health care system. A well supported National TB Programme will have a programme manual, a training programme, a plan of supervision, and a development plan.

Case finding primarily by microscopic examination of sputum of patients presenting to health facilities

Tuberculosis patients commonly seek care but are not promptly diagnosed and the challenge is to improve the performance of the health care system. Microscopy, not X-ray must be the primary tool to diagnose tuberculosis. Resources should first be directed towards identifying sputum smear positive cases for treatment, as these individuals are the sources of infection. Chest X-ray is a complementary tool when sputum smears are negative.

Short-course chemotherapy given under direct observation

DOTS make the health system – not the patient – responsible for achieving a cure. This is critical, as most TB patients start to feel better after just a few weeks of medication and often stop taking their pills. Yet it takes at least six months to rid the body of TB bacilli. With DOTS, patients are observed swallowing their medicines by a health worker or trained volunteer. Treatment observers support patients until they are cured. Treatment observation is especially critical during the first two months of treatment. During this phase, the number of tuberculosis bacteria in the body is very high, and missed doses increase the risk of treatment failure and relapse. Patients who do not keep their appointments with the health worker must be immediately contacted and helped to resume treatment.

There can be flexibility and innovation in observing treatment, provided that the observer is accountable to the health services and accessible and acceptable to the patients. DOT can be given in clinics, institutions, the workplace, schools, shelters for the homeless, homes and on the street. Similarly, DOTS providers can be paramedicals, teachers, leaders, friends, colleagues, traditional birth attendants, *etc.* To maximize the potential for the person supervising the therapy and the patient to interact, incentives or legal inducements have been used successfully¹⁰. Such incentives include free bus tokens, free meals, and arrangements for housing and other social services.

Adequate drug supply

The establishment of a dependable, high quality supply of anti-TB drugs throughout the health care system is an essential part of the DOTS strategy. The correct combination and dosage of anti-TB medicines known as short-course chemotherapy must be used for the right length of time (Table II). These drugs – which include isoniazid, rifampicin, pyrazinamide, streptomycin and ethambutol kill TB bacilli rapidly and make the patients non-infectious in a short period thus cutting the chain of transmission in the community. In India, the drugs in

RNTCP are supplied in blister packs in patient-wise boxes containing the entire course of treatment. In this way patients are assured of drugs availability until cure and no patient will be started on treatment unless the full supply of drugs is available.

Systematic monitoring and accountability for every patient diagnosed

TB patients must be provided complete treatment and be monitored to ensure cure. Sputum is examined during and at the end of treatment to ensure that a patient is free of TB bacilli. The recording and reporting system rigorously monitors and evaluates progress made while treating and curing each patient. Thorough analysis of each group of patients enables the health services to quickly identify districts and communities not achieving 85 per cent cure rates and intervene with additional support and training.

The Indian Scenario

Burden of TB in India

In India it is estimated that more than 40% of the adults are infected with TB bacilli and every year 2 million people develop tuberculosis and nearly 500,000 die from

Table II. Treatment regimens followed in India in Revised National Tuberculosis Control Programme

Category of treatment	Type of patients	Alternative TB treatment regimens	
		Initial phase	Continuation phase
Category I	New smear positive PTB		
	New smear negative PTB with extensive parenchymal involvement	2H ₃ R ₃ Z ₃ E ₃	4H ₃ R ₃
	New cases of severe forms of extra-pulmonary TB		
Category II	Sputum smear positive:		
	- Relapse		
	- Treatment failure	2S ₃ H ₃ R ₃ Z ₃ E ₃ /1H ₃ R ₃ Z ₃ E ₃	5H ₃ R ₃ E ₃
- Treatment after interruption			
Category III	New smear negative PTB (other than in category I)	2H ₃ R ₃ Z ₃	4H ₃ R ₃
	New less severe forms of extra pulmonary TB		

PTB : Pulmonary tuberculosis

H : Isoniazid; R : Rifampicin; Z : Pyrazinamide; E: Ethambutol; S : Streptomycin.

The prefix indicates the duration of drugs administration in months. The subscript indicates number of doses per week

it. By any measure, the burden of suffering caused by tuberculosis is mind boggling¹¹. The incidence of TB has changed little in the past 30 years, despite having had a tuberculosis control programme. The human immunodeficiency virus (HIV) is estimated to have infected 3.5 million people in India¹². HIV-associated TB and the emergence of multidrug resistant TB (MDRTB) will further increase the magnitude and severity of the TB epidemic. Further, TB is a major barrier to economic development, costing India approximately Rs.13,000 crores (US \$ 3 billion) a year¹³. In addition, TB patients spend more than Rs.645 crores (US\$180 million) on private TB care¹⁴. Tuberculosis has devastating social costs as well – data suggests that each year, more than 300,000 children are forced to leave school because their parents have TB and more than 100,000 women with TB are rejected by their families¹⁵. This continued burden of disease is particularly tragic because TB is nearly 100% curable. Untreated patients can infect 10-15 persons each year, poorly treated patients develop drug-resistant and potentially incurable TB. Given this burden, a substantially increased political commitment at all levels to control the disease is necessary.

DOTS implementation and its implications in India

In India, the Revised National Tuberculosis Control Programme was launched in 1997 with phased coverage in various states¹⁶. It is expanding rapidly, covering more than 313 million population. India now has the second largest DOTS programme in the world. Today more than 30% of the population of India has access to DOTS. More than 200,000 patients have been treated, with cure rates of about 75-80%. The pace with which the expansion of the RNTCP occurs will determine the number of cases and deaths from TB as well as the magnitude of drug resistance. DOTS has also been shown to be highly cost effective and it doubles cure rates.

If India expands the RNTCP, to cover the entire country by 2005 and meets global targets for TB control, then over the next 20 years, the best estimates are that the Programme will cumulatively cure more than 25 million cases of TB, prevent more than 15 million additional cases of TB, prevent nearly 6 million deaths and save more than Rs.115,000 crore (US\$27 billion)¹⁷. However, for each year of delay in national expansion beyond 2005, the human and economic costs over the next 20 years will be high; 800,000 preventable cases of TB, 280,000 avoidable deaths – 700 per day and direct and indirect costs of Rs.5700 crores (US \$ 1.3 billion).

Unless the Programme is given a much higher priority at the central, state and district levels, it will not be able to expand as planned to cover more than 500 million people within the next 2-3 years and the entire population by 2005. If global targets are met by 2005, it can be expected that deaths from TB and prevalence of the disease can be reduced by approximately 50% in 5 years, with incidence being reduced by approximately 50% in 10 years.

The RNTCP has important implications for the health and development of India. Not only can the RNTCP save million of lives and hundreds of millions of dollars, it can also promote a culture in which decisions are based on data. This can provide a solid and lasting foundation for continuous improvement in India's health services.

Successful implementation of this Programme in India could save more lives than any other public health intervention over the next 10 years. This would also greatly reduce the burden on children and families. The diagnostic and treatment principles of DOTS can easily be adapted to infants and children. Success will require active communication, collaboration, and participation on the part of governmental and non-governmental sectors.

Global Applications of DOTS

The DOTS strategy has been implemented successfully in many countries. In the United States, Baltimore demonstrated a marked reduction in case rates with use of DOTS¹⁸ despite a high rate of HIV infection. In New York city, by 1991, half of the TB patients were HIV infected and one in five had multidrug resistant tuberculosis, but DOTS resulted in a rapid decrease in both tuberculosis and in multidrug resistance^{10,19}. Murraay *et al*²⁰ reviewed experiences in Malawi, Mozambique and Tanzania, documenting cure rates of 86-90%. Effective programmes have been established and have continued to function well even in the context of civil war. Application of universal DOT and subsequent adoption of short-course chemotherapy were associated with a substantial decline in tuberculosis in Cuba, to a level below that of many industrialized countries²¹. In Beijing, DOT was implemented in 1978 and short course chemotherapy was introduced in 1988²². Prevalence of smear-positive tuberculosis in Beijing decreased from 127 per 100,000 in 1979 to 16 per 100,000 population in 1990, a decrease of 17% annually²³. More recently, a World Bank assisted project in China has had remarkable success²⁴. More than 3 million patients have undergone sputum examinations and more than 515,000 smear positive patients have been

treated, with cure rates of more than 93%. The failure rate in previously treated patients fell progressively from 18 to 6% in the initial years of the programme. The programme in China currently covers a population of 800 million. In the South-East Asia Region, Bangladesh had had excellent success in DOTS implementation, with coverage of more than two-thirds of the country and cure rates above 80%²⁵. The impact of TB control programme was quite considerable in Peru. After a decade of implementation of DOTS, the TB morbidity dropped down by 35%, the incidence by 42%, the incidence of smear positive cases by 40% and the mortality rates from 21 to 11% (Personal communication).

DOTS and HIV

It has been demonstrated that DOTS can prolong the life of HIV infected individuals and improve their quality of life and can stop the spread of TB by making them non-infectious in a short time²⁶. It can prevent the emergence and also reverse the trend of MDRTB. On the other hand, failure to use DOTS in the face of HIV can lead to explosive spread of TB, with cases tripling and drug resistance increasing rapidly²⁷⁻²⁹.

Other Measures in TB Control

The measures that were believed to be useful in the control of tuberculosis were improved socio-economic development, environmental improvement, vaccination and preventive therapy. However, these measures were found to be not very useful. Styblo³⁰ demonstrated that the decline in the annual risk of infection due to socio-economic development and environmental improvement was limited to about 4% per year. Adding effective chemotherapy increased the rate of decline by 14% per year. BCG vaccination and preventive chemotherapy were not useful in TB control³⁰.

As against all these measures DOTS produces high cure rates, prevents new infections by curing infectious patients and prevents the development of drug resistant TB by ensuring that the full course of treatment is taken¹⁵. The World Bank ranked the DOTS strategy as one of the most cost-effective of all health interventions²⁰.

Acceleration of TB Control

This requires the highest level of Government commitment and provision of adequate human and financial resources. Several groups have enormous potential for improving the RNTCP. These include private

practitioners, non-governmental organizations (NGOs) and employees health services¹. The spirit of partnership and collaboration will be key for an effective, sustained TB control programme in future years in India, particularly with the threat of HIV and MDRTB on the horizon. In addition, there should be strong training institutions for human resource development. Advocacy to political leaders and bureaucrats is absolutely essential for sustainability of the programme¹⁷.

What Should be Done Now?

There is a pressing need to accelerate the expansion of DOTS, take the DOTS to specialized settings and forge partnership with multiple sectors¹. There is a need to do more operational research to improve the performance and also consider DOTS-plus for countries with high proportion of MDRTB. Operational research provides programme managers the tools needed to analyse their programmes and provide continuous quality improvement. The goal is to improve the diagnosis, care and access for TB patients by translating the results of that research into policy and practice. Local programme managers should analyse and evaluate resources available in their community. The goal is to identify facilities and means by which TB patients can be diagnosed earlier in the course of their disease and resources by which patients can be given observed treatment more conveniently. DOTS is the best treatment strategy available today, but it does not and cannot remain static. DOTS have evolved through decades of research and it must continue to evolve as it adapts to local situations and emerging scientific data.

Conclusions

Key findings from the Tuberculosis Research Centre, Chennai and the National Tuberculosis Institute, Bangalore have changed treatment practices all over the world. Application of these findings in other countries has led to sustained decrease in tuberculosis. DOTS is a classic example of research findings not being applied where they are most needed and where they were discovered. Forty years after the discovery of the principles of DOTS in India, DOTS is being applied on a mass basis in our country. Fostering an atmosphere of enquiry and analysis strengthens programmes by continuously identifying areas, which need improvement, as well as the means to improve the programme in these areas. Policy makers need to be aware of research findings and of the implications of these findings for programme decisions. It is essential that DOTS is rapidly and effectively implemented and quality of

services ensured before MDRTB and HIV convert an already serious situation into a massive and potentially uncontrollable epidemic. A poorly implemented programme is worse than no programme at all.

Tuberculosis does not merely reflect the socio-economic status but perpetuates and exacerbates poverty. Hence RNTCP is highly effective anti-poverty programme as well. TB patients must be clearly and repeatedly informed that treatment is free of charge, and must be given the option of receiving treatment under observation either through governmental or non-governmental channels. In the public and private sectors, improved interpersonal communication, standardized treatment, direct observation at a time and place convenient to patients, and systematic monitoring and accountability are needed urgently.

DOTS in South-East Asia has prevented more than 200,000 TB cases, saved more than 100,000 lives, and saved more than US\$500 million. In India, more than 500,000 patients have been put on treatment, more than 80,000 lives have been saved (4500 lives every month) and more than 1 million infections have been prevented (Personal communication). To achieve this, more than 150,000 health workers including more than 10,000 doctors and 3000 laboratory technicians underwent modular training, more than 7,500,000 microscopic examinations were performed for TB and about 15,000,000 directly observed doses of anti-tuberculous treatment were administered. In the past 3 years, 20-fold expansion of DOTS has been achieved in India covering more than 350 million population by early 2001. It now has the second largest DOTS programme in the world. Today more than 33% of the population has access to DOTS. All these findings suggest that DOTS is succeeding in India.

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