REVIEW

STATUS OF TUBERCULOSIS CONTROL IN THAILAND*

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Abstract. The national tuberculosis control program (NTP) was implemented in Thailand as integrated with the privincial general health services since 1967, with BCG vaccination successfully introduced from the beginning, but progress in expansion of case-finding and chemotherapy had only been achieved following the establishment of hospitals at the district level since the late seventies. At present, case-detection and treatment have operated in more than 95% of the 600 district hospitals and 87 hospitals at provincial and regional levels, with patient follow-up by health centers, logistically supported and technically supervised by 12 zonal TB centers. The trend of the disease has shown noticable decline as indicated by the three national surveys in 1962, 1977 and 1991, that is, morbidity rate as suspected by x-ray of 2.1%, 1.4% and 1.01%; infectious case rate of 0.5%, 0.31% and 0.24% respectively, a reduction of about 2-3% per year. The infection rate of children 0-14 years of age was found to be 15.2% in 1977; 8.9% in 1983; and 5.18% in 1987, giving the annual risk of infection (ARI) of 4.9%, 2.3% and 2.0% respectively.

Currently the program detects and treats about 31,000 smear-positive TB cases plus an equal number of smear-negative cases per year. Short-course chemotherapy was introduced since 1985 and expanded to cover all the former by 1991, resulting in improvement of the treatment success rate from less than 50% when using the old standard 18-24 months regimen to 70-80%. As the coverage of case detection and treatment is still only about 60% of the incidence or 30% of the prevalence, trials of primary health care approach have yielded substantially increased case detection coverage as well as improved cure rates. BCG vaccination as part of the Expanded Program on Immunization has reached 90-100% coverage of infants. HIV infection surveillance in TB patients has revealed rapidly rising prevalence, particularly in Chiang Mai of up to 14.8%, followed by 6.67% in Bangkok. Thus there is an urgent necessity to intensify the TB control activities, by integration of case-finding and treatment into primary health care to improve and expand the population coverage as well as undertaking operational and technical research relevant to the situation.

HISTORICAL PERSPECTIVE

The campaign against tuberculosis in Thailand was pioneered as early as 1920 by HRH Prince Mahidol of Songkla, who as a physician wrote a health educational booklet "Tuberculosis" and had it published for distribution to the general public. In 1935, the Antituberculosis Campaign Association was founded by the Medical Association of Siam as its affiliate. With the help of the Siamese Red Cross in using the latter's premises, the new Association, which later separately became the present Anti-Tuberculosis Association of Thailand, opened a TB clinic in Bangkok, the first service of its kind in the Kingdom. In 1941, the first tuberculosis hospital was erected by the government in Nonthaburi Province north of Bangkok.

After the end of Second World War, tuberculosis was recognized by the government as a major public health problem, ranking second only to malaria as one of the most important causes of death of the population. The first attempt to control the disease was started by the Department of Health in late 1949 by opening a chest clinic equipped with a static mass miniature radiographic unit in central Bangkok to render diagnostic and ambulatory treatment services. With assistance from WHO and UNICEF starting in 1951, the chest clinic became a TB demonstration and training center, raised to divisional status and working in close coordination with the already existing TB

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hospital which was being developed mainly as a thoracic surgical center.

A national mass BCG vaccination campaign, with pretuberculin testing, was launched during 1953-1956, concentrating in school children, followed by consolidation phase operated by mobile vaccination teams visiting every province every 3-4 years.

With the advent of chemotherapy, the policy decided upon was to concentrate on expansion of ambulatory treatment service, instead of building more TB hospitals. As a result, begining in 1959 more TB centers had been set up in other regions of the country, thus operating and expanding primarily as a specialized program.

The first national epidemiological survey conducted during 1960-1964 revealed morbidity averaged for all age groups at 2.1% as suspected by x-ray and 0.5% infectious tuberculosis (Sunakorn, 1969). The morbidity and infection rates in rural areas were much lower than in urban areas, but since 85% of the population was in the former, obviously the main bulk of the tuberculosis problem was in the medically under-served rural population.

Thus, following the WHO recommendation, the National Tuberculosis Program (NTP) was conceived and implemented by the Ministry of Public Health (MOPH) by integration of the program into the existing general medical and health services since 1967 (WHO, 1964), in order to expand the population coverage on a countrywide and a permanent program basis, as the disease cannot be successfully controlled by one time endeavor or temporary mobile operational campaigns because TB cases will continue to develop from the large pool of infected individuals.

During the first decade of NTP implementation, the direct BCG vaccination of pre-school children was working well by the provincial general health services in achieving better coverage than when operated by specialized vaccination teams (Sunakorn, 1973). However, the symptomatic case-finding by sputum microscopy and ambulatory chemotherapy, which were initiated by posting two or three trained health workers at a first class health center or at the provincial health office in each province, working under supervision and logistic support of the zonal centers, made almost no progress by way of expansion, because of low utilization of the peripheral health services, together with the Patters' limited capability in having to undertake integration with several other specialized health projects.

The second national epidemiological survey conducted during 1977-1979, although indicating 38% overall reduction in the prevalence of infectious tuberculosis, down from 0.5% found by the first survey of 1962 to 0.31%, found almost no such change in the rural areas (Daramas *et al,* 1981), confirming that integration was still far from satisfactory. Nevertheless, the policy and strategy of the integrated tuberculosis program, reaffirmed to be epidemiologically and economically sound (WHO, 1974), was to be further pursued as the NTP.

PROGRESS AND PRESENT SITUATION

BCG vaccination: This has been included in the Expanded Program on Immunization (EPI) since 1977 for the primary target age of under one year with revaccination at school entrance. The vaccination coverage of infants had steadily increased from 38% in 1977 to 91-100% in 1989, as confirmed by countrywide assessment survey (Anonymous, 1990). A study in children contacts of TB cases in Bangkok revealed 53% overall protection (Padungchan *et al,* 1986); another study by case control method found 83% protective efficacy of neonatal BCG vaccination (Sirinavin *et al,* 1991), and also TB meningitis in children appeared to be much reduced during the last 20 years (Expert Committee, 1989).

Case-finding and treatment: The policy of the government to provide hospitals at the district level for the whole country gave a new impetus to the integration. From the 4th Five-Year National Economic and Social Development Plan (1977-1981) on, the integration effort had been shifted from health centers to the district community hospitals, which were staffed by doctors and other health personnel as well as equipped with laboratory and x-ray facilities to be the district focal point in symptomatic case-finding and treatment, while health centers were assigned an auxiliary role.

With additional cooperation of the provincial level general hospitals and regional hospitals, and training of doctors and key staff members jointly

by the TB Division and the Anti-TB Association of the NTP. Moreover, patients found to be negadetection and ambulatory chemotherapy was achieved in accordance with the standard procedures of the NTP. Moreover, patients found to be negative on microscopic examination of sputum also benefit from diagnosis with the use of x-ray and from treatment as well. By 1990, out of the total number of about 784 districts in 72 provinces of the whole country, 98% of the already established 600 district community hospitals, plus 94% of the 87 provincial general and regional hospitals had been cooperating in the NTP (Expert Committee, 1992).

By 1985 the number of smear-positive TB cases detected by the integrated provincial health services had increased from an average of only about 1,000 cases, which was about one-tenth of those detected by all the TB centers per year during 1967-1976, to over 22,000, more than twice as many as detected by the specialized TB service (Fig 1). The number of TB patients under care at the latter also steadily decreased, while the number of those being treated by the district and provincial level hospitals increased to more than four times of those attending the TB centers (Tuberculosis Division, 1977-1991).

Under the technical supervision, logistic support of anti-TB drugs and microscopic supplies, monitoring and assessment by the 12 zonal TB

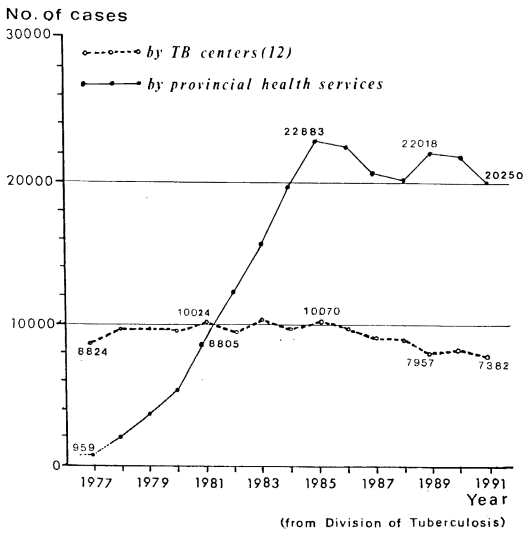

Fig 1—Progress of integration: smear-positive TB cases detected, National Tuberculosis Program.

centers, standard procedure in case-detection and ambulatory chemotherapy services with better level of treatment compliance have been established for the integrated health service units, particularly at the community and general hospitals.

Currently, 57.5% of a total of about 31,000 smear-positive TB cases discovered a year are detected by the provincial health services while about 42.5% are diagnosed by the TB centers and then some are referred by the latter to be treated by the community or general hospitals near the patients' homes. Thus the integrated provincial health services now account for the treatment of about 76% of TB cases detected, while the specialized TB services (TB centers and chest hospital) account for only 24% (Expert Committee, 1992). In addition, about the same proportion of smear-negative active TB patients a year are also registered for treatment.

IMPLEMENTATION OF SHORT COURSE CHEMOTHERAPY (SCC)

Formerly, the standard basic drug regimen used in the NTP since 1967 up to 1985 was isoniazid plus thiacetazone for both smear-positive and smear-negative tuberculosis, with streptomycin added to the intensive phase for the former; PAS and later on ethambutol were used to replace thiacetazone in case of intolerance to the latter. Because of the considerable degree of toxicity and side-effects of thiacetazone and the fact that the regimen requires 18-24 months of continuous treatment, only about 50% of patients were able to complete the treatment with an even lower success rate (Chunhaswasdikul, 1981).

After successful field trials (Kechararanta *et al*, 1983) some selected short-course drug regimens, containing rifampicin and pyrazinamide in combination with the old drugs isoniazid, streptomycin and thiacetazone, of 6 and 8 months' duration were adopted for use in the NTP, firstly for smear-positive cases since 1985 (Table 1). By 1991 the short course chemotherapy (SCC) had been expanded to cover practically all smear-positive cases detected. A countrywide assessment through the 12 zonal TB centers by cohort analysis of smear-positive cases registered for SCC, which was concerned with self-administered drug treatment (or unsupervised therapy) during 1989-1990 revealed a much better treatment completion and

Table 1

Short-course regimens used in the NTP 1986-1992.

Period	Bacteriological status	Regimen	Treatment completion	Efficacy	Cure rate
1986-1991	smear+	**Primary treatment**			
		2HRZ/4HR 2HRZ/4H_2R_2 2SHRZ/6HT	70-80%	98%	68-78%
		Retreatment			
		2HRZE/4HRE 2HRZC/4HRC 2SHRZ/6HT	70-80%	95%	69-78%
	smear−	12HT/or 12HE	58-61%	NA	NA
1992-	smear+	**Primary treatment**			
		2HRZS/4HR or 2HRZE/4HR	NA	NA	NA
	smear−	2HRZ/2HR-4HR	NA	NA	NA
		Treatment failure/ relapse			
		2HRZE/4HRE	NA	NA	NA

S = streptomycin; H = isoniazid; R = rifampicin;
Z = pyrazinamide; T = thiacetazone; C = cycloserine
Number preceding alphabets denotes number of month; alphabets without subscript denote daily drug administration; alphabet with subscript number denote number of intermittent administration per week, all regimens are given by self-administration.

cure rate of 70-80% (Table 2) (Expert Committee, 1992), as compared with the results of using the old standard regimens. From 1992 the SCC has been extended to smear-negative, x-ray active suspects as well, and thiacetazone was dropped from the revised short course regimens.

Table 3 shows the results of drug susceptibility tests through many years since 1967 (Nuchprayoon *et al,* 1969; Supcharoen *et al,* 1984) with more recent ones conducted by the Tuberculosis Division. The initial drug resistance to isoniazid appeared to be not much changed around 11%; there has been some increase of sensitivity to streptomycin. A point of concern is that resistance to rifampicin appeared to increase from 1% to 3% in recent years.

A joint study by the Ministry of Public Health and Chulalongkorn University was made on the cost analysis of the short-course chemotherapy implemented in the NTP in comparison with the standard drug regimen of isoniazid and thiacetazone which had been used for the past 20 years. Analysis showed that the three short-course regimens, in spite of considerably higher prices of drugs, had lower costs than the standard regimen from the health service provider perspective (Chunhaswasdikul *et al,* 1992).

Thus significantly, progress in the integration, as well as the introduction of the short-course chemotherapy, has been achieved mainly by the upgrading the quality of the peripheral health services, and by provision of sufficient budget for the cost of the more expensive but much more efficacious SCC drug regimens, a result of the fair share accorded from the gain of economic growth of the country.

TREND OF THE TUBERCULOSIS PROBLEM

The trend of tuberculosis is expressed through various epidemiological indices in Table 4.

Tuberculosis mortality rate had steadily de-

Table 2

Treatment completion rate and cure rate of short course chemotherapy (year 1989).

Health service type	Number treated	Treatment completion %	Cure rate %	Reported as no sputum/no sputum exam
1. Specialized service				
1.1 Bangkok Chest Clinic	1,050	87	78	5%
1.2 Central Chest Hospital	692	76	74	0.6%
1.3 Zonal TB Centers (11)	3,161	83	76	6.9%
Subtotal 1	4,903	83	76	5.7%
2. Integrated service				
2.1 Community hospitals (547)	12,105	77	68	9%
2.2 General and regional hospitals (82)	3,758	71	50	29%
Subtotal 2	15,863	75	64	13.8%
Grand total	20,766	77	67	12%

Of smear-positive TB, based entirely on self-administered treatment (from Expert Committee Report, MOPH, 1992)

Table 3

Trend of initial drug resistance.

	1966-1967	1977-1980	1986-1987	1989	1991
	(1)	(1)	(2)	(2)	(2)
Isoniazid%	14.6	18.0	11.6	4.1	11.6
Streptomycin%	10.2	16.3	6.6	7.7	10.1
Rifampicin%	-	-	1.6	2.1	3.4
Ethambutol%	-	-	1.0	2.1	1.6

(1) from Anti-TB Association of Thailand
(2) from Division of Tuberculosis, (including resistance to more than one drug)

creased from 31.9 per 100,000 population in 1962 down to 6.8 in 1990, when it still ranked among the top 10 leading causes of death and the first among the infectious diseases of the general population (Health Statistics Division, MOPH, 1962-1990).

From the first national epidemiological survey in 1962 to the second one in 1977, it appeared that the trend of tuberculosis morbidity had already been slowly declining from 0.5% prevalence of infectious tuberculosis (bacteriologically confirmed by microscopy and culture) to 0.31% at the rate of 2.5% per year.

Since frequent full-scale longitudinal epidemi-

Table 4

Trend of tuberculosis, Thailand 1962-1991.

Epidemiological index	1962	1977	1983	1987	1991/92
a. **Prevalence rate** pulmonary tuberculosis					
- suspected by x-ray%	2.1(S1)	1.4(S2)	-	-	1.01(S3)
- bacteriologically confirmed% (smear + culture)	0.5(S1)	0.31(S2)	-	-	0.24(S3)
- smear + only%	0.3(S1)	0.2(S2)	-	-	0.17(S3)
b. **Prevalence rate** infection in children 0-14 yrs%	(12.7)*	15.2(S2)	8.9(T)	5.18(T)	4.7(S3)
c. **Annual risk** of infection (ARI)%	(3.8)**	4.9	2.3	2.0	1.73(P)
- Annual incidence of smear + TB per 100,000 pop	-	245	115	100	87(P) 85(S3)

(S1)-(S3) = National epidemiological survey;
(T) = Tuberculin/BCG scar survey only
(P) = Projection based on the reduction of the risk of infection 3.5% per year
* estimated from the survey (SI)
** reported as "incidence of infection"
(From Division of Tuberculosis)

ological surveys are generally not feasible because of resource constraints, a tuberculin survey in BCG-unvaccinated children for infection rate was therefore conducted by the Tuberculosis Division in 1983 (Konjanart *et al,* 1984) and 1987 (Konjanart and Permsak, 1988) to calculate the annual inicidence, or the annual risk of infection (ARI), from which the incidence of smear-positive tuberculosis can be estimated to be about 50 cases per 100,000 population for each 1% of ARI (Styblo, 1985).

The two tuberculin surveys also showed decrease in the infection prevalence : 8.9% and 5.18% respectively as compared with 15.2% from the national survey of 1977. The annual risk of infection for 1977, 1983 and 1987 was 4.9%, 2.3% and 2.0%, respectively, and 1.73% as projected for 1991, from which the annual incidences of smear-positive cases/100,000 were estimated to be 245, 115, 100 and 87, respectively.

Table 5 shows the total incidence of smear-positive cases as estimated from the ARI for the whole country; the actual number of smear-positive cases detected and its coverage on the incidence and prevalence (= incidence × 2; Styblo, 1985) by year from 1983 to 1991. The detection coverage appeared to range from 45.8 to 63.6% of the incidence and 22.9% to 31.8% of the prevalence only.

For smear-positive cases detected during 1989-1990 at the provincial towns and districts, most were in the age group of 45 years and over, while those detected in Bangkok were highest in the age group 25-34 (Fig 2). This is because there have always been a very large number of migrants

Table 5

NTP case detection coverage of smear-positive tuberculosis Thailand, 1983-1991.

Year	Population × 1,000	ARI	Incidence rate smear+ cases per 100,000	Incidence no. smear+ cases	Prevalence no. smear+ = Incidence × 2	Total no. smear+ cases detected	% coverage of	
							Incidence	Prevalence
1983	49,730	2.3*	115	57,190	114,380	26,204	45.8	22.9
1984	50,710	2.22(1)	111	56,288	112,576	29,604	52.6	26.3
1985	51,680	2.14(1)	107	55,298	110,595	32,953	59.6	29.8
1986	52,650	2.07(1)	104	54,756	109,512	30,486	55.7	27.8
1987	52,895	2.00*	100	52,895	105,790	29,930	56.6	28.3
1988	54,465	1.93(1)	97	52,831	105,662	29,010	54.9	27.4
1989	55,538	1.86(1)	93	51,650	103,300	28,975	56.1	28.0
1990	56,303	1.80(1)	90	50,673	101,346	30,085	59.4	29.7
1991	56,923	1.73(1)	87	49,523	99,046	31,482	63.6	31.8

1991/92 Third National Survey, prevalence of smear positive cases = 0.17% or = 96769 cases; The coverage being about 32.5% only.

* from BCG scar/tuberculin survey

(1) based on reduction of 3.5% per year

(from Division of Tuberculosis)

from all the other parts of the country working in Bangkok and vicinity because of better income opportunity (Expert Committee, 1992).

The Third National Epidemiological Survey conducted during 1991-1992 (Tuberculosis Division, 1993) revealed an overall morbidity prevalence of 1.01% as detected by x-ray and 0.24% bacteriologically confirmed, which included 0.17% smear-positive only, about 22.6% lower than the bacillary case prevalence found in the 2nd survey of 1977. The infection rate of all ages was 29.47%, also down from 40.6% found in the latter. The prevalence of smear-positive TB cases as worked out from the proportion of 0.17% of the 1991 total population, is 96,769 cases. This prevalence figure divided by 2 makes for an incidence of 48,385 cases (Styblo, 1985) or 85 per 100,000, which compares closely with 87 as estimated from the projected ARI (Table 5).

RECOMMENDATIONS IN THE SITUATION OF THE RISING AIDS EPIDEMIC

Following the first report of AIDS in Thailand in 1984 and the rapid spread of HIV infection (Epidemiology Division, 1992), the disease has now become the most urgent and important national health problem.

HIV infection prevalence in tuberculosis patients has been studied by 9 zonal TB Centers, Bangkok Chest Clinic, Tuberculosis Division, and the Chest Hospital, by serological testing of attending TB patients every six months since 1989. In summary (Fig 3) up to the end of 1991, the highest prevalence with the most rapid rise of HIV seropositive rate has been observed at TB Center 10 in Chiang Mai, followed by the rate found in Bangkok; at the former it increased from 5.1% to 14.8% (Akarasewi, 1992), and at the latter from 2.4% to 6.67% within two years and is still rising thereafter. High prevalences of 5.6% and 4.3% were also reported by the end of 1991 by centers in Chon Buri (East central) and Yala (Southernmost). However, neither the country figure of the morbidity prevalence of pulmonary tuberculosis as found by the Third National Survey (1991-1992) nor the epidemiological surveillance reports (Fig 4) has so far showed any definite unusually high rate.

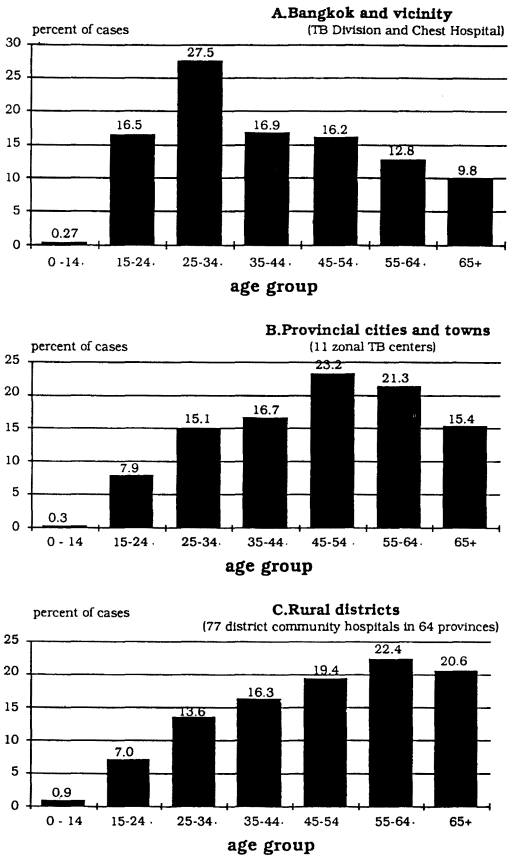

Fig 2—Age distribution of smear-positive tuberculosis detected at different levels of localities (Thailand, 1989).

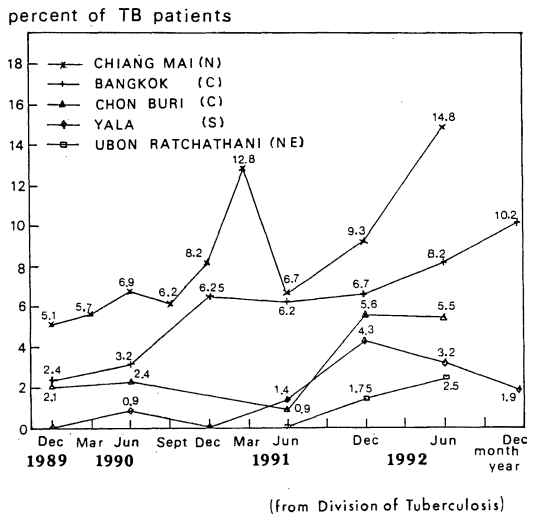

Fig 3—HIV seropositive prevalence in tuberculosis patients in different regions.

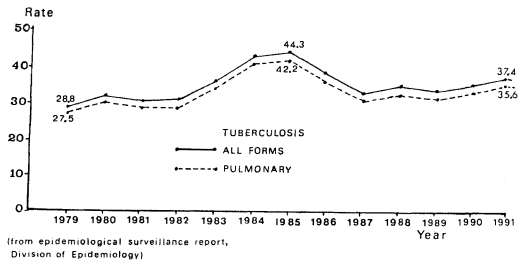

Fig 4—Reported tuberculosis morbidity rate, Thailand (per 100,000 population).

In the early period of serological study of tuberculosis patients, those HIV-infected were mostly intravenous drug users, but later on the sharp increase was mainly due to heterosexual transmission through commercial sex practice.

Two consecutive Expert Committees appointed by the MOPH during 1989-1991, the first to assess the NTP and the second to advise on the intensification of the NTP case-finding and short-course chemotherapy in the situation of HIV epidemic (Expert Committee, 1992) have recommended the following actions:

In view of the fact that tuberculosis, usually regarded as low priority, has now become an urgent problem which will be adversely affected by the HIV epidemic in the very near future (WHO and IUATLD, 1989), there is an immediate need to accelerate and intensify tuberculosis control particularly in case-finding and treatment for the following objectives:

- to reduce the source of and protect against tuberculosis infection in the population, about 70% of which is still uninfected.

- to find methods to prevent tuberculosis disease in persons with dual HIV and TB infection.

Hence it is recommended that:

(1) As a trial of the primary health care approach in some districts/provinces had shown that with community participation in helping to seek out patients with relevant symptoms for arrangment of sputum examination and support in treatment,

from 27% to over 100% more cases could be detected and treatment cure rate of over 80% could also be obtained (Lumphun Provincial Health Office, 1989; Chanachaiviboonwat *et al,* 1992; Sriyabhaya *et al,* 1992), case-finding and treatment should be integrated into primary health care nationwide to expand population coverage (WHO, 1988).

(2) The role of health centers should be revised and re-introduced to complete the network with the district community/general hospitals and community in case-finding, treatment and follow-up.

(3) Operational objectives and targets as recommended by WHO (Kochi, 1991) should be set toward the goal of Health for All by the Year 2000, thus:

- to improve the cure rate of smear-positive cases with short-course therapy to 85% of cases detected by providing sufficient budget for the SCC drugs for treatment free of charge; improving drug distribution and effective follow-up of patients by the treatment services and community/ family members.

- to expand the coverage of case-detection to 70% of the smear-positive prevalence.

(4) Research should be directed mainly towards improving tuberculosis control operation, and studies relevant to the intensification of the tuberculosis programs in the situation of rising HIV epidemic such as preventive therapy in HIV/TB dually infected individuals should be undertaken.

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