WUCHERERIA BANCROFTI ANTIGENEMIA CLEARANCE AMONG MYANMAR MIGRANTS AFTER BIANNUAL MASS TREATMENTS WITH DIETHYLCARBAMAZINE, 300 MG ORAL-DOSE FILADEC TABLET, IN SOUTHERN THAILAND

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Abstract. Using qualitative ICT Filariasis and quantitative Og4C3 ELISA, we assessed a long-term macrofilaricidal effect of two-year biannual mass treatments with a 300 mg oral-dose FILADEC tablet, a reformulation of 6 mg/kg diethylcarbamazine (DEC), on clearance of the *Wuchereria bancrofti* adult worm circulating filarial antigens (CFA) in Myanmar migrants, at risk of emergence of imported bancroftian filariasis in Southern Thailand. Of the 34 antigenemic Myanmar index cases of varying initial CFA levels, who were initially screened out with the ICT Filariasis, 13 index cases were follow-up treated and monitored at the DEC post treatments, 6, 12, and 18 months. At the 18-month post treatment, residual antigenemias (%) in 4 of 5 index cases (group I) with high antigen titers (99.7-181.6 x 10^3 AU/ml) were 54.44%, 33.58%, 27.43%, and 9.97%. Significant decreases of the CFA levels in only 3 out of 5 index cases were affected by the response to DEC treatments ($p < 0.007$). The treatment effects on clearance of the CFA in 8 index cases (group II) with low antigen titers (15.4-37.2 x 10^3 AU/ml) were shown for at least 6 months post DEC treatment and hence had 100% efficacy in the first 6 months of the first year of year round treatment. Group I, was more likely to show an increase of the DEC efficacy after the first 6 months of the second year round treatment, but there was no statistically significant difference ($p = 0.063$). We reemphasized that, for use in the national program to eliminate lymphatic filariasis (PELF) in Thailand, such a DEC regimen had a macrofilaricidal effect on antigenemia clearance, and confirmed its value in evaluating response to the treatment and monitoring the long-term efficacy of the DEC regimen in *W. bancrofti* adult worm burden reductions in Myanmar migrants on a wide scale.

INTRODUCTION

Because of cross-border Myanmar population migration to Thailand due to a "Push and Pull effect" (WHO, 2000), the current situation of emergence of imported bancroftian filariasis, caused by *Wuchereria bancrofti*, nocturnally periodic type, in Southern Thailand has occurred within Myanmar migrants (Filariasis Division, 2000). In regular diagnosis and surveillance, more than 1% microfilarial positive rate (MPR) was observed by longitudinal cross-sectional surveys, during fiscal years 1995-2001 (Fig 1). In cross-sectional surveys among non *en bloc* Myanmar migrants (Swaddhiwudhipong *et al*, 1996; Sitthai and Thammapalo, 1998; Koyadun and Bhumiratana, 2000; Keeratihuttayakorn, 2002), there were possible factors related to the emerging disease in transmission-prone areas: a working group ≥ 15 years of age; having no or less personal protection against mosquitos (particularly at night time); having no bed nets; residing in semi-constructed houses without water disposal drainage. Furthermore, the potential mosquito vector, *Culex quinquefasciatus*, has a host predilection for this parasite (Triteeraprapab *et al*, 2000) and breeding habitats were commonly seen in settlement areas (Sitthai and Thammapalo,

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1998). *W. bancrofti* transmission in Southern Thailand is absent but introduced transmission within the *en bloc* population at risk was considered to be possible (Filariasis Division, 2000; 2001).

Since 1997 (Fig 1), prevention and control of the emerging disease have been straightforward by implementing the mass drug administration (MDA) program with biannual treatments of 6 mg/kg oral-dose diethylcarbamazine (DEC), through levels of health care providers and organizers. Such a DEC regimen was acceptable for country-wide mass treatment since evaluation of efficacy of selective DEC treatment, *ie* a standard regimen of 6 mg/kg oral-dose DEC given once daily for 12 consecutive days (Filariasis Division, 2000; WHO, 1994), was not possible for non *en bloc* microfilaremic Myanmar carriers on a wide scale. Until now, only 30% coverage with DEC mass treatment is postulated (Filariasis Division, 2000; 2001). Little is known about the effective DEC regimen that can suppress the *W. bancrofti* adult worm loads in individuals or exhibit a macrofilaricidal activity. Regardless of the microfilaremic status of the Myanmar migrants in Southern Thailand, an antigen load intensity with a median antigen load of > 14,000 antigen units (AU)/ml, was previously determined (Bhumiratana *et al*, 2003, unpublished data) using quantitative Og4C3 ELISA (More and Copeman, 1990; Chanteau *et al*, 1994). They were generally considered to have an antigen load intensity lower than that of the endemic Karen population (of > 60,000 AU/ml) in border bancroftian filariasis (Bhumiratana *et al*, 2003, unpublished data). Such a lower antigen load intensity of the Myanmar migrants is an indication of the dilution effect of the non *en bloc* Myanmar migrants, who do not acquire naturally prolonged infection exposure. It is possible that treating those with the DEC regimen for a sufficiently long period of delivery could help us to assess a direct effect of its macrofilaricidal activity on clearance of the *W. bancrofti* adult worm circulating filarial antigens (CFA) (Weil *et al*, 1991; McCarthy *et al*, 1995; Eberhard *et al*, 1997; Nicolas *et al*, 1997; Sunish *et al*, 2002). Detailed evaluations of long-term efficacy of such biannual DEC mass treatments are needed for planner's decisions to improve and optimize appropriate regimens for achieving the goal of the national program to eliminate lymphatic filariasis (PELF) (by fiscal years 2002-2006) (Filariasis Division, 2000; 2001).

In the present study, the cross-border Myanmar migrants and local Thai population at risk in transmission-prone study areas in the Phang-Nga Province were screened out with the presence of the CFA, using qualitative ICT Filariasis (Weil *et al*, 1997; Bhumiratana, 2000; Bhumiratana *et al*, 2002), to be representative as antigenemic index cases. We assessed the long-term macrofilaricidal effect of biannual mass treatments with a 300 mg oral-dose FILADEC tablet, a reformulation of 6 mg/kg DEC for use in the PELF in Thailand, on CFA clearance among Myanmar index cases, using both the Og4C3 ELISA and the ICT Filariasis.

MATERIALS AND METHODS

Epidemiological settings

According to lymphatic filariasis control in Southern Thailand in strata (Public Health Regions 11 and 12), regular diagnosis and surveillance for imported bancroftian filariasis (Fig 1) have been done for transmission control by the Provincial Public Health Offices under supervision of the local program manager at the Office of Vector Borne Disease Control (VBDO) 4 (Songkhla), Department of Communicable Disease Control (CDC), Ministry of Public Health (MOPH). Ranong and Phang-Nga Provinces belong to the Public Health Region 11. In the PELF, the MDA campaign at the Phang-Nga provincial level was primarily done by health sectors belonging to the Phang-Nga Provincial Public Health Office, in association with the Vector Borne Disease Control Center (VBDC) 43 (Phang-Nga), belonging to the VBDO 4 (Songkhla).

A longitudinal cross-sectional study in the Phang-Nga Province between 2001 and 2002 (Fig 2) was done to evaluate the long-term efficacy of the two-year biannual mass treatments with the 300 mg oral-dose FILADEC. In cross-sectional community surveys during February-March 2001, cross-border Myanmar migrants as laborers aged ≥15 years (n = 357) were selected from 3 out of 8 districts in the Phang-Nga Province. Three close

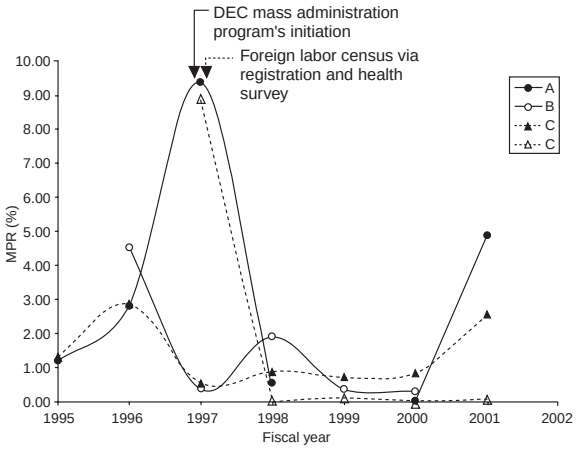

Fig 1-Trends in microfilarial positive rate (MPR) (%) based on regular diagnosis and surveillance (fiscal years 1995-2001) in Southern Thailand in strata: A, Phang-Nga Province; B, Ranong Province; C, Public Health Region 11; D, Public Health Region 12. The DEC mass administration program (solid arrow) has been implemented since 1997, as registration and health survey of foreign laborers at provincial level (dotted arrow) were initially done. No survey data were available at the provincial level: Phang-Nga Province (in 1999); Ranong Province (in 2001).

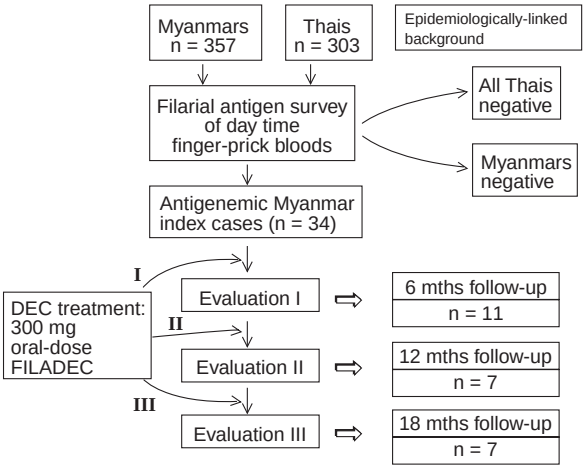

Fig 2-A scheme for study design of screening out the index cases with *W. bancrofti* antigenemic infection and antigenemia evaluation procedure (evaluations I-III) following DEC mass treatments (rounds I-III, 6-month intervals) described in the text.

districts, namely Takua Pa, Takua Thung, and Thai Muang, were the largest workplaces in Phang-Nga Province, where most initially crossed the border or worked in Ranong Province, 226 km north. In each study site criteria for selection of the local Thai population (n = 303) fell into 3 categories: 1) residing for ≥1 year in the same residence areas, within a 2 km radius of an area that is known to have an incidence of microfilaremic Myanmar carriers and stagnant water for breeding *Cx. quinquefasciatus*, 2) having no previous travel history or stay in Myanmar or in endemic areas of *W. bancrofti* nocturnally subperiodic (Bhumiratana *et al*, 2002), and 3) having no history of DEC treatment. Using daytime finger-prick blood samples, all were screened with the ICT Filariasis (AMRAD ICT, French's Forest, NSW, Australia) according to the methods described elsewhere (Bhumiratana *et al*, 2002). Follow-up DEC treatments and *W. bancrofti* antigenemia evaluation among antigenemic index cases were described below.

DEC mass treatment schedule

The DEC dosage schedule was divided into the two-year biannual treatments with the 300 mg oral-dose FILADEC tablet (Pond's Chemical Thailand ROP, Bangkok, Thailand): 1st round, February-March 2001; 2nd round, August-September 2001; 3rd round, March-April 2002; 4th round, August-September 2002. The DEC doses used in this study were supplied by the Filariasis Division, CDC Department, MOPH. The biannual DEC mass treatments were followed according to the guideline for the MDA for the PELF: children under 2 years of age and pregnant women were ineligible for treatment.

***W. bancrofti* antigenemia evaluation methods**

After pre-mass treatment surveys, only 34 Myanmar laborers, as antigenemic index cases, were used for qualitative and quantitative assessment of the CFA levels in individuals at post DEC treatments, 6,12 and 18 months (Fig 2). The antigenemia evaluation for each round of treatment (evaluations I-III) was carried out just before giving the treatment in the next round, using the daytime blood or plasma samples of the index cases prepared from their sites during each of the periods of the scheduled treatments. The

plasma samples were kept at -20°C until use. With the ICT Filariasis, the 100-µl daytime venous blood samples were done at the time of blood collection and the 100-µl frozen plasma samples were done with both the ICT Filariasis, and the Og4C3 ELISA (Tropical Biotechnology, Townsville, Queensland, Australia) for validation of test results as described elsewhere. The plasma samples of the index cases were considered positive with the Og4C3 ELISA if an arbitrary antigen titer was higher than 120 AU/ml.

Data analysis

In the qualitative assessment of *W. bancrofti* antigenemic infection, the epidemiologically related factors of the surveyed populations were presented by descriptive statistics, and in analysis of differences in categorical variables between the groups, the χ^2 test ($p < 0.05$) was used. To test the efficacy of biannual mass treatments with the 300 mg oral-dose FILADEC tablet, changes in the CFA levels or arbitrary antigen titers (AU/ml) of the antigenemic Myanmar index cases as independent subjects in the response DEC treatments were compared. Identical treatment effects on the measured antigen titers of the independent index cases were analysed by the Friedman two-way analysis of variance (χ_r^2) at significant level, $\alpha = 0.05$ (Daniel, 1995). The long-term efficacy of DEC treatments with macrofilaricidal activity was computed as follows: efficacy (%) is equal to $(A_1 - A_k) / A_1 \times 100$; as A_1 is the antigen titer (AU/ml) measured at the initial dependent treatment and A_k is the antigen titer (AU/ml) measured at the response dependent treatment (k). If, on the other hand, the DEC regimen had a beneficial effect on reduction of the CFA in the independent index cases in the first 6 months of the first year round treatment (X_i) and second year round treatment (Y_i), the probability of paired signs of differences ($X_i - Y_i$) in DEC efficacy was one-tailed analysed by the Sign-paired test at $\alpha = 0.05$ (Daniel, 1995).

RESULTS

In CFA screening with the ICT Filariasis, only 34 antigenemic (9.52%) out of the 357 surveyed Myanmar population were screened out, whereas none was the local Thai population. Their epidemiologically related factors tended to have significant differences between the groups (Table 1). Of the 34 antigenemic Myanmar index cases who had the initial CFA levels of 14.746-181.654 x 10^3 AU/ml [geometric mean (GM) = 40,850.24 AU/ml], there were 13 strongly ICT-positive cases (or group I): including 8 males aged 20 to 62 years (mean ± SD = 32.6 ± 13.6 years) and 5 females aged 17 to 25 years (mean ± SD = 21.2 ± 3.4 years). Their antigen titers ranged from 42.204-181.654 x 10^3 AU/ml and the GM antigen load was 93.631 x 10^3 AU/ml (data not shown). There were 21 weakly ICT-positive cases (or group II): including 15 males aged 16 to 37 years (mean ± SD = 25.0 ± 5.9 years) and 6 females aged 19 to 35 years (mean ± SD = 23.8 ± 5.4 years). Their antigen titers ranged from 14.746-46.526 x 10^3 AU/ml, with the GM level of 24.445 x 10^3 AU/ml (data not shown).

Only 13 index cases were followed-up at the 18-month post-DEC treatment evalution (Table 2 and Fig 3). Five index cases (H1 to H5) of the group I had a dramatic decrease in the antigen titers measured at 6, 12, and 18 months. In 3 index cases (H1 to H3), treatment effects on changes in the antigen titers were not identical but had a significant decrease in the CFA levels ($\chi_r^2 = 9.0$, $p = 0.0017$) (Table 2). At 18 months, the residual antigenemias (%) in group I (H1 to H4) were 27.43%, 33.58%, 9.97% and 54.44%, respectively. The treatment effects on clearance of residual antigenemias in 8 other index cases of group II were shown at least 6 month post DEC treatment (Table 2). In other words, the biannual DEC treatments in group II showed 100% efficacy in the first 6 months of the first year of treatment. In the group I (H 1 to H4), there was an increase of the DEC efficacy in first 6 months of the second year of treatment. There was no significant difference in the DEC efficacies between the first and second year of treatments (Sign-paired test, $p = 0.063$). In all cases, the CFA in response to DEC treatments was detected with the ICT Filariasis and the Og4C3 ELISA except for the H3 at 18 months, where it was negative with the ICT Filariasis (Table 2 and Fig 3).

DISCUSSION

In pre-mass treatment surveys, with the ICT

Table 1
Epidemiological related factors of cross-border Myanmars and local Thais at risk in antigenemic infection assessment with the ICT Filariasis in three study areas.

Variable	Surveyed populations		p-value[a]
	Myanmar n = 357 (%)	Thai n = 303 (%)	
Gender			
Male	262 (73.4)	161 (53.1)	< 0.001
Female	95 (26.6)	142 (46.9)	
Age			
< 25 years	185 (51.8)	83 (27.4)	< 0.001
≥ 25 years	172 (48.2)	220 (72.6)	
Marital status			
Single	171 (47.9)	98 (32.3)	< 0.001
Living with a partner	184 (51.5)	187 (61.7)	
Separated/ divorced/ widowed	2 (0.6)	18 (5.9)	
Occupation			
Unemployment	23 (6.4)	73 (24.1)	-
Unskilled labor	327 (91.6)	111 (36.6)	
Fishery	7 (2.0)	0	
Agriculture	0	75 (24.8)	
Others[b]	0	44 (14.5)	
Residency in same study areas			
≤ 2 years	236 (66.1)	56 (18.5)	< 0.001
> 2 years	121 (33.9)	247 (81.5)	
Utilization of bed net[c]	(n = 98)	(n = 297)	
Yes	87 (88.8)	290 (97.6)	< 0.001
No	11 (11.2)	7 (2.4)	
Disposal water drainage in residence area			
Yes	46 (12.9)	143 (47.2)	< 0.001
No	311 (87.1)	160 (52.8)	
Personal protection against mosquitos in night time			
Yes	59 (16.5)	101 (33.3)	< 0.001
No	298 (83.5)	202 (66.7)	

[a]Significant difference for χ^2 test ($p < 0.05$) was shown, as the hyphenation indicated data not available for calculation. [b]Persons including students, housewives, officers, etc. [c]Persons who had bed nets were used for data collection of utilization of bed nets.

Filariasis card test, evaluation of the antigenemia rate in the surveyed Myanmar population showed up to 10% of people were infected, as compared to the local Thai population at risk, which appeared to have a zero baseline. The surveyed Thai population and vulnerability did not reflect the influence of the introduced transmission in urban bancroftian filariasis. A longitudinal cross-sectional survey may be required. Serological, entomological and parasitological evidence shows the infection patterns in sentinel populations under surveillance. In Myanmar, microfilaremia and antigenemia prevalences in the affected Myanmar population show a large number of infected persons as a reservoir (WHO, 1998). In Southern Thailand, such microfilaremia prevalence (Fig 1) represents uncertain point estimates among the non *en bloc* Myanmar migrants. Regardless of clinical status, misclassified persons within the at-risk age group in the population who had the CFA, were taken into account in microfilarial survey (Bhumiratana, 2000; Steel *et al*, 2001;

Table 2
W. bancrofti antigenemia profiles with the Og4C3 ELISA of thirteen Myanmar index cases after follow-up biannual DEC mass treatments.

Index case	Age (yrs)	Sex	Antigen titer [a] (x 10^3 AU/ml) (% residual antigenemia) after DEC treatments (months)				Efficacy (%) in first 6 months of year-round treatments	
			0	6	12	18	1-year	2-year
H1 [b,c]	17	F	172.883 (100)	151.400 (87.57)	126.739 (73.31)	47.416 (27.43)	12.43	72.57
H2 [b,c]	36	M	120.383 (100)	96.230 (79.94)	74.746 (62.09)	40.424 (33.58)	20.06	66.42
H3 [b,c]	25	F	75.255 (100)	53.390 (70.94)	31.653 (42.06)	7.500 (9.97)	29.05	90.03
H4 [c]	30	M	181.654 (100)	167.417 (92.16)	ND	98.899 (54.44)	7.84	45.56
H5	21	F	99.662 (100)	66.102 (66.33)	ND	ND	33.67	ND
H6	25	F	37.246 (100)	0.0 (0)	0.0 (0)	0.0 (0)	100	100
H7	30	M	28.221 (100)	0.0 (0)	0.0 (0)	ND	100	ND
H8	19	M	26.187 (100)	0.0 (0)	0.0 (0)	ND	100	ND
H9	25	M	15.636 (100)	0.0 (0)	ND	ND	100	ND
H10	27	M	15.382 (100)	0.0 (0)	ND	ND	100	ND
H11	30	M	25.678 (100)	ND	0.0 (0)	0.0 (0)	ND	100
H12	37	F	16.526 (100)	0.0 (0)	ND	ND	100	ND
H13	19	F	29.492 (100)	ND	ND	0.0 (0)	ND	100

Abbreviation: M = male, F = female, ND = no data available.

[a]A linear relationship of reciprocal anti-log antigen titers (X) of *Onchocerca gibsoni* standard antigens (numbers 2 to 7) and absorbances measured at 405 nm (A_{405}) (Y) was mathematically expressed by an equation: Y = -0.527 + 0.477X. An arbitrary antigen titer (AU/ml) was computed as follows: sample absorbance minus mean A_{405} of non-endemic Thai populations as negative control (plus 3SD) (or A_{405} cut-off = 0.169) was multiplied by an arbitrary antigen titer of *O. gibsoni* standard antigens (= 1,589 AU) (X) at an A_{405} equal to 1.0 (Y), and by dilution factor (= 80).

[b]Showing significant decreases of the CFA by treatment effects (χ_r^2 = 9.0, p = 0.0017), whereas no significant difference in the DEC efficacies between the first 6 months of 1-year and 2-year round treatments (Sign-paired test, p = 0.063)[c].

Bhumiratana *et al*, 2002). In other words, screening the CFA in daytime finger-prick blood samples in individuals with the ICT Filariasis has been proposed for an initial assessment as part of the PELF (Bhumiratana, 2000; Bhumiratana *et al*, 2002; Filariasis Division, 2000; 2001). Observations were shown that, with commercially available sensitive and specific CFA assays (*ie* the Og4C3 ELISA and the ICT Filariasis) as part of the global program to eliminate lymphatic filariasis (WHO, 1999), detecting and monitoring the CFA levels among the Myanmar index cases, after being given treatment, were well correlated. In the H3 index cases, the CFA level of ≤7,500 AU/ml at 18 months post-treatment was negative with the ICT Filariasis and hence equivalent to a maximum detection limit of the test in this study. We confirmed that qualitative ICT Filariasis played an important role as a rapid, simple-to-use, direct assessment tool for use in the elimination program implementation (Sunish *et al*, 2002; Filariasis Division, 2000; WHO, 1999).

Prior studies demonstrated that a DEC regimen, *ie* one-year or two-year annual treatments with 6 mg/kg single oral-dose DEC, was known to have both long-term microfilaricidal and macrofilaricidal effects on reductions in infection prevalence and intensity in endemic populations (Weil *et al*, 1991; Moulia-Pelat *et al*, 1995; Ismail *et al*, 1996; Eberhard *et al*, 1997; Nicolas *et al*, 1997). An alternative DEC regimen, *ie* one-year biannual treatments with 6 mg/kg DEC, was expected to have the long-term microfilaricidal effect on microfilaremia prevalence reductions

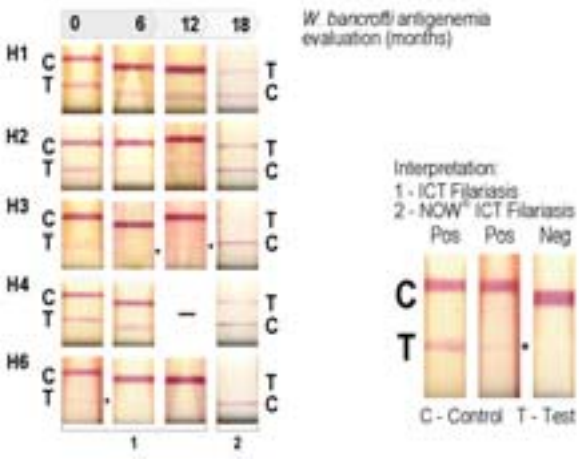

Fig 3-A schematic representation of *W. bancrofti* antigenemia evaluation in five antigenemic Myanmar index cases (H1-H4 and H6). Qualitative assessment with the former ICT Filariasis (used for initial assessment and evaluations I-II) or the latest NOW® ICT Filariasis (Binax, Portland, Maine, USA) (used for evaluation III) was done. Hyphenation indicated no data available for 12-month antigenemia evaluation (H4) during the 3-round DEC treatment. In strong positive or weak positive (as indicated by asterisk) samples, pink line formed in the test line (T), as in negative samples no pink line formed.

(Meyrowitsch *et al*, 1996) but, with no prolonged treatments, recrudescence of *W. bancrofti* transmission within endemic population in Tanzania might have occurred (Meyrowitsch and Simonsen, 1998). In the present study, we demonstrated that, according to our hypothesis, the Myanmar index cases of varying *W. bancrofti* adult worm loads tended to have dramatic changes in antigenemia in the course of biannual DEC mass treatments. Most with low initial CFA had antigenemia clearance after 6- or 12-month follow-ups of the first year DEC treatment, thereby showing 100% DEC efficacy. Another five antigenemic Myanmar cases, of varying antigen titers (≃ 127 to ≃ 4,700 AU/ml), who were DEC-naïve, unregistered and selected from the same study sites during the 3-round DEC treatment, but were negative with the ICT Filariasis (data not shown). In similar fashion, they had antigenemia clearance after a 6-month treatment with the same DEC regimen. The observations suggested that the antigenemia clearance in Myanmar migrants haboring undetectable levels of *W. bancrofti* adult worm burdens with both CFA assays was truly affected by the macrofilaricide (Weil *et al*, 1991; McCarthy *et al*, 1995; Eberhard *et al*, 1997; Nicolas *et al*, 1997). Another five index cases with

Table 3
Results of DEC provocative day test [a] among registered foreign laborers in Phang-Nga Province, February-April 2002.

Hospital	Registered foreign laborers[b]			Persons with *W. bancrofti* microfilaremic infection (%)
	Male	Female	Total	
Phang-Nga	773	364	1,137[c]	0
Thai Muang	1,175	452	1,627[d]	0
Takua Pa	998	199	1,197	0
Takua Tung	1,324	227	1,546[e]	1 (0.07)[g]
Ko Yao	210	99	309	0
Thap Put	321	96	417	0
Kapong	488	229	717	0
Khura Buri	627	152	779[f]	0

[a]Individual venous blood after thirty-minute provocative test with the 300 mg oral-dose FILADEC was used for *W. bancrofti* microfilaria examination. [b]Registered foreign laborers included five Cambodian laborers [c] and Laos laborers (of the same one [d,f] and twelve [e]) who enrolled at the four hospitals, were all negative, whereas the rest was Myanmar laborers and only one male [g] was found to be microfilaremic. The MPR (%) according to population under surveillance was shown in parenthesis.

high initial CFA tended to have reduction of the CFA after the 18-month treatment and, after the first 6 months of the second year of treatment, increase in the DEC efficacy may have occurred. No variation of personal susceptibility to response to the DEC treatments was noted. The biannual DEC mass treatments alone were relatively effective, but the antigenemia clearance relied on the multiple doses during the follow-up period, with no possibility of reinfection in the group. In three index cases (H1 to H3), there was evidence that decreases of the CFA were correlated with the time of the scheduled treatments (Spearman's rho = -0.713, p = 0.009) (data not shown). We had no direct evidence that the levels of the CFA correlated with the adult worm nests or loads. The CFA clearance in those who had high initial levels of the CFA might be correlated with the time required to clear antigenemia, even with different multiple courses of the DEC treatments (Weil *et al*, 1991; McCarthy *et al*, 1995; Eberhard *et al*, 1997; Nicolas *et al*, 1997).

In addition to the 300 mg oral-dose FILADEC, the DEC-provocative day test, as shown in Table 3, resulted in the current status of low microfilaremia prevalence observed in the non *en bloc* Myanmar migrants in Phang-Nga Province. During the period of hospital-based filarial survey in active surveillance for the imported bancroftian filariasis, the seven index cases were given the 3-round DEC treatment (Table 2) and were reconfirmed that they harbored no microfilaremias (data not shown). In Tanzania, there was evidence that, after treatment with a single low dose of 100 mg DEC, the long-term DEC-provocative effect resulted in microfilaremia prevalence reduction (Simonsen *et al*, 1997). If similar response to the treatment occurred within the Myanmar migrants, it is believed that, after treatment with the DEC-provocative regimen, microfilaremia and antigenemia prevalence reductions would likely be seen. For example, after the 2-week treatment, microfilaremic Myanmar cases who had high (161.824×10^3 AU/ml) and low (57.712×10^3 AU/ml) initial CFA tended to have a dramatic decrease in residual antigenemia: 62% in high CFA case and 55% in low CFA case and it was 60% in high CFA case after the 8-week treatment (our unpublished data). This suggests that, along with its combined provocative dose, the long-term DEC efficacy will have a beneficial effect on prevention and control of the emerging disease. Several prior studies showed that the recommended DEC regimen, *ie* single dose combination of 6 mg/kg DEC plus 400 mg albendazole, had more effective macrofilaricidal activity (Ismail *et al*, 1998) and perhaps suggesting the usefulness of the 300 mg FILADEC plus albendazole in the PELF in Thailand (Filariasis Division, 2000; 2001). We reemphasized the macrofilaricidal effect of the biannual oral doses of the 300 mg FILADEC tablet on antigenemia clearance among the Myanmar index cases. We confirmed its value in evaluating the response to treatment and monitoring the long-term efficacy of the DEC regimen in *W. bancrofti* adult worm burden reductions in the non *en bloc* Myanmar migrants in the country-wide mass treatment.

Given the poor prognosis of DEC mass treatment coverage and drug compliance, the DEC regimen evaluated in this study has potential as a principal strategy suitable for the interruption of introduced transmission in urban bancroftian filariasis and elimination of the infection in the non *en bloc* Myanmar migrants in the Phang-Nga Province. This study would allow us to apply an alternatively effective DEC regimen for public health to optimize the elimination program in Southern Thailand. The treatment of border bancroftian filariasis can be demonstrated in endemic parts of Thailand.

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REFERENCES

Bhumiratana A. ICT Filariasis card test as direct assessment tool for evaluation of antigenaemia rate in communities endemic for *Wuchereria bancrofti* in Thailand. *Mahidol J* 2000; 7 (suppl): 17-23.

Bhumiratana A, Wattanakull B, Koyadun S, Suvannadabba S, Rojanapremsuk S. Tantiwattanasup W. Relationship between male hydrocele and infection prevalences in clustered communities with uncertain transmission of *Wuchereria bancrofti* on the Thailand-Myanmar border. *Southeast Asian J Trop Med Public Health* 2002; 33: 7-17.

Chanteau S, Moulia-Pelat JP, Glaziou P, *et al*. Og4C3 circulating antigen: a marker of infection and adult worm burden in *Wuchereria bancrofti* filariasis. *J Infect Dis* 1994; 170: 247-50.

Daniel WW. Biostatic: a foundation for analysis in the health sciences. 6th ed. New York: Molloy Lithographing, 1995.

Eberhard ML, Hightower AW, Addiss DG, Lammie PJ. Clearance of *Wuchereria bancrofti* antigen after treatment with diethylcarbamazine or ivermectin. *Am J Trop Med Hyg* 1997; 57: 483-6.

Filariasis Division, Department of Communicable Disease Control, Ministry of Public Health. Workshop on national programme of the elimination of lymphatic filariasis, Nonthaburi, Thailand, 8 February 2000. Mimeographed document; the 9th Plan of Action for National Programme of the Elimination of Lymphatic Filariasis. 2000.

Filariasis Division, Department of Communicable Disease Control, Ministry of Public Health, Thailand. National Conference on Development of Lymphatic Filariasis Control Planning and Evaluation: the 9th Plan of Action for National Programme of the Elimination of Lymphatic Filariasis, Bangkok, Thailand, 2-3 August 2001.

Ismail MM, Weil GJ, Jayasinghe KS, *et al*. Prolonged clearance of microfilaraemia in patients with bancroftian filariasis after multiple high doses of ivermectin or diethylcarbamazine. *Trans R Soc Trop Med Hyg* 1996; 90: 684-8.

Ismail MM, Jayakody RL, Weil GJ, *et al*. Efficacy of single dose combinations of albendazole, ivermectin and diethylcarbamazine for the treatment of bancroftian filariasis. *Trans R Soc Trop Med Hyg* 1998; 92: 94-7.

Keeratihuttayakorn T. Epidemiological study on *Wuchereria bancrofti* in Ranong. *J Health Sci* 2002; 11: 301-11 (in Thai).

Koyadun S, Bhumiratana A. *Wuchereria bancrofti* infection, environmental and disease prevention behavior factors of Burmese living in Phang-Nga Province. *Commun Dis J* 2000; 26: 219-25 (in Thai).

McCarthy JS, Guinea A, Weil GJ, Ottesen EA. Clearance of circulating filarial antigen as a measure of the macrofilaricidal activity of diethylcarbamazine in *Wuchereria bancrofti* infection. *J Infect Dis* 1995; 172: 521-6.

Meyrowitsch DW, Simonsen PE, Makunde WH. Mass DEC chemotherapy for control of bancroftian filariasis: comparative efficacy of four strategies two years after start of treatment. *Trans R Soc Trop Med Hyg* 1996; 90: 423-8.

Meyrowitsch DW, Simonsen PE. Long-term effect of mass diethylcarbamazine chemotherapy on bancroftian filariasis: results at four years after start of treatment. *Trans R Soc Trop Med Hyg* 1998; 92: 98-103.

More SJ, Copeman DB. A highly specific and sensitive monoclonal antibody based ELISA for the detection of circulating antigenemia in bancroftian filariasis. *Trop Med Parasitol* 1990; 41: 403-6.

Moulia-Pelat JP, Nguyen LN, Hascoet H, Luquiaud P, Nicolas L. Advantages of an annual single dose of ivermectin 400 mg/kg plus diethylcarbamazine for community treatment of bancroftian filariasis. *Trans R Soc Trop Med Hyg* 1995; 89: 682-5.

Nicolas L, Plichart C, Nguyen LN, Moulia-Pelat JP. Reduction of *Wuchereria bancrofti* adult worm circulating antigen after annual treatments of di-

ethylcarbamazine combined with ivermectin in French Polynesia. *J Infect Dis* 1997; 175: 489-92.

Simonsen PE, Meyrowitsch DW, Makunde WH. Bancroftian filariasis: long-term effect of the DEC provocative day test on microfilaraemia. *Trans R Soc Trop Med Hyg* 1997; 91: 290-3.

Sitthai V, Thammapalo S. Epidemiological study on lymphatic filariasis in Burmese labor, Ranong Province. *Malaria J* 1998; 33: 239-52 (in Thai).

Steel C, Ottesen EA, Weller PF, Nutman TB. Worm burden and host responsiveness in *Wuchereria bancrofti* infection: use of antigen detection to refine earlier assessments from the South Pacific. *Am J Trop Med Hyg* 2001; 65: 498-503.

Sunish IP, Rajendran R, Mani TR, *et al*. Resurgence in filarial transmission after withdrawal of mass drug administration and the relationship between antigenaemia and microfilaraemia- a longitudinal study. *Trop Med Int Health* 2002; 7: 59-69.

Swaddiwudhipong W, Tatip Y, Meethong M, Preecha P, Kobasa T. Potential transmission of bancroftian filariasis in urban Thailand. *Southeast Asian J Trop Med Public Health* 1996; 4: 847-9.

Triteeraprapab S, Kanjanopas K, Suvannadabba S, Sangprakarn S, Poovorawan Y, Scott AL. Transmission of the nocturnal periodic strain of *Wuchereria bancrofti* by *Culex quinquefasciatus* : establishing the potential for urban filariasis in Thailand. *Epidemiol Infect* 2000; 125: 207-12.

Weil GJ, Lammie PJ, Richards FO Jr, Eberhard ML. Changes in circulating parasite antigen levels after treatment of bancroftian filariasis with diethylcarbamazine and ivermectin. *J Infect Dis* 1991; 164: 814-6.

Weil GJ, Lammie PJ, Weiss N. The ICT Filariasis: a rapid format antigen test for diagnosis of bancroftian filariasis. *Parasitol Today* 1997; 13: 401-4.

WHO. Lymphatic filariasis infection and disease: control strategies. Report of a consultative meeting held at the Universiti Sains Malaysia, Penang, Malaysia, 22-24 August 1994. Geneva: World Health Organization. *WHO/TDR/CTD/FIL/PENANG/94.1*. 1994.

WHO. Research on rapid geographical assessment of bancroftian filariasis, prepared during a protocol development workshop held at the James Cook University, Townsville, Australia, 22-25 July 1998. Geneva: World Health Organization. *TDR/TDF/COMDT/98.2*. 1998.

WHO. Informal consultation on epidemiologic approaches to lymphatic filariasis elimination: initial assessment, monitoring, and certification, Atlanta, Georgia, USA, 2-4 September 1998. Geneva: World Health Organization. *WHO/FIL/99.195*. 1999.

WHO. Report on the planning meeting: implementation of Roll Back Malaria in the six Mekong countries, Ho Chi Minh City, Viet Nam, 2-4 March 1999. Geneva: World Health Organization. *WHO/MAL/2000.1092*. *WHO/CDS/RBM/2000.15*. 2000.