# **Comparison between Different Methods of Monofilament Test in Multibacillary Leprosy**

Saranjit Wimoolchart MD\*, Penvadee Pattanaprichakul MD\*\*, Onjuta Chayangsu MD\*\*, Kamonpan Lertrujiwanit BSc\*\*, Pacharee Iamtharachai BSc\*\*, Suteeraporn Chaowattanapanit MD\*\*\*

\* Raj Pracha Samasai Institute, Department of Disease Control, Samut Prakan, Thailand \*\* Department of Dermatology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand \*\*\* Division of Dermatology, Department of Medicine, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand

**Background:** Leprosy or Hansen's disease predominantly affects skin and peripheral nerves; therefore, can cause visible deformities from sensory and motor impairment. Early detection of sensory deficit has been of great benefit in a vigorous preventive role.

**Objective:** To compare the result of sensory evaluation in multibacillary leprosy (MB) patients using Semmes-Weinstein monofilament (SWM) and conventional monofilament technique used in Thailand and to observe the course of neuritis detected during the study period.

**Material and Method:** MB patients from Hansen's clinic at the Department of Dermatology, Siriraj Hospital, and Leprosy clinic at Raj Pracha Samasai Institute were evaluated for sensory impairment using monofilament test by both SWM and conventional technique for two consecutive follow-up visits. The patients' demographic data, clinical and laboratory findings, and course of disease were recorded.

**Results:** Seventy MB patients were enrolled. Two-third of the patients were male (71.4%) and a mean (SD) age was 43 (15.75) years with a range of 19 to 85-years-old. The results from SWM and conventional Thai technique were not statistically different for ulnar, median, and posterior tibial nerve distribution excluding heel area (p = 1.00). Twenty-eight (40%) patients who mentioned of numbness at either palms or soles had impaired sensation detected by SWM technique (p = 0.014). **Conclusion:** Using SWM with less tested points can minimize the time spent on sensory evaluation in MB patients; hence, we encourage the application of the present SWM technique to shorten the time in each follow-up visit and to improve the follow-up practice for better services of leprosy patients in Thailand.

Keywords: Monofilament, Leprosy, Hansen's disease, Sensory impairment

## J Med Assoc Thai 2015; 98 (11): 1124-32 Full text. e-Journal: http://www.jmatonline.com

Leprosy patients can develop various irreversible deformities from motor and sensory impairment, in the absence of any apparent signs or symptoms called 'silent neuritis', which may occur before, between, or after multi-drug therapy (MDT)<sup>(1,2)</sup>. Approximately 10% of the new leprosy cases demonstrate some degree of motor, sensory, or autonomic neuropathy at first registration<sup>(3)</sup>. In Thailand, 18% of the new cases were documented to have nerve function impairment<sup>(4)</sup>.

Variety of tests had been used to establish early symptoms of nerve function deficit for prevention of disability in leprosy<sup>(5,6)</sup>. Sensory assessment included nerve conduction velocity (NCV), quantitative thermal

Correspondence to:

sensory testing, vibrometry, ballpoint-pen technique, and monofilament testing (MFT). The motor function evaluation consisted of dynamometry and voluntary muscle testing (VMT)<sup>(1,3,7)</sup>.

In Thailand, we have been using a ballpointpen technique for screening of sensory impairment and follow-up the leprosy cases during the past few decades. However, MFT is preferred over the ballpoint pen technique due to its higher sensitivity<sup>(8,9)</sup>. While NCV is considered a good tool to detect earliest neuropathy, the gold standard tools for motor and sensory screening remain to be VMT and MFT respectively<sup>(3)</sup>.

The standard MFT technique used worldwide is Semmes-Weinstein monofilament (SWM), which consists of 200 mg, 2 gm, 4 gm, 10 gm, and 300 gm fibers with test sites as shown in Fig.  $1^{(1)}$ . The sensitivity of this technique was 26%, reported by van Brakel et al<sup>(3)</sup>. In Thailand, we have been using

Pattanaprichakul P, Department of Dermatology, Faculty of Medicine Siriraj Hospital, Mahidol University, 2 Prannok Road, Bangkoknoi, Bangkok 10700, Thailand. Phone: +66-2-4194332, Fax: +66-2-4115031 E-mail: penvadee.pat@mahidol.ac.th

either ballpoint pen or monofilament with more test points as shown in Fig. 2, following the guideline for leprosy care promoted by the Leprosy Organization of Thailand, to achieve higher sensitivity for sensory impairment screening and the treatment goal for prevention of disability<sup>(8)</sup>. However, this method takes more time to complete.

To the best of our knowledge, there was no previous study in Thailand to compare the efficacy between Semmes-Weinstein MFT and Thai conventional monofilament technique. Therefore, we aimed to compare the result of sensory evaluation using Semmes-Weinstein MFT and Thai conventional technique in multibacillary leprosy (MB) patients, and to observe the clinical course of neuritis during the study period.

## Material and Method Population and study design

This cross-sectional study was approved by the Siriraj Hospital Institutional Review Board (SIRB). We recruited the patients who were literate, age more than 18 years old, and were diagnosed as MB leprosy according to World Health Organization (WHO) criteria<sup>(10)</sup>. The patients with diabetes, chronic alcoholism, and peripheral neuropathy from other causes were excluded. The patients were tested for sensory impairment by both Semmes-Weinstein and Thai conventional monofilament techniques for two consecutive periods, the first date of study enrollment, and the next follow-up visit.

The patients' demographic data, disease activity (categorized into new case, during treatment, and surveillance), present illness, physical examination (cutaneous lesions and neuropathy), laboratory investigation (slit skin smear reported as initial Bacteriological Index (BI) at first-time clinic visit and skin biopsy result prior to MDT), leprosy reaction (type I and II), location and onset of neuritis, grading of deformities, and the result of both MFT were recorded.



Fig. 1 Semmes-Weinstein monofilament testing points.



Fig. 2 Thailand conventional monofilament testing points.

#### Grading of deformities

As indicated by WHO, disability grading 1998 demonstrated in Table  $1^{(10,11)}$ .

#### Monofilament methods

Semmes-Weinstein MFT method is composed of six test-points at each hand and four points at each foot (Fig. 1). The conventional technique consisted of 10 test-points for each hand and 12 points for each foot (Fig. 2). The MFT kit (TNT Velcro Box design<sup>®</sup>) used in the present study was demonstrated in Fig. 3. Sensory assessment was performed by using 5-color graded monofilaments with different weight, 200 mg (blue), 2 gm (purple), 4 gm (red), 10 gm (orange), and 300 gm (pink). Normal controlled threshold used in the study were 200 mg for hand and 2 gm for foot. Cutaneous sensation supplied by ulnar, median, and posterior tibial nerve of both hands and feet were evaluated respectively. The patients were asked to point to where they felt the monofilament was applied (Fig. 4). The tests were performed while the patients

Grade	Hands and feet	Eyes
0	No anesthesia or visible deformity	No eye problem due to leprosy; no evidence of visual loss
1	Anesthesia present without visible deformity	Eye problems due to leprosy present, but vision not severely disturbed (vision: 6/60 or better; can count fingers at 6 m)
2	Visible deformity or damage present	Severe visual impairment (vision: worse than 6/60; inability to count fingers at 6 m) includes lagophthalmos, iridocyclitis and corneal opacities

Table 1. WHO grading of disability 1998<sup>(10,11)</sup>

kept their eyes closed. At each test site, one score was given for every level of monofilament threshold increase from the normal control. We considered positive or abnormal MFT result when the scores were 3 or more.

#### Statistical analysis

Descriptive statistics, including numbers and percentage for categorical data and mean with standard deviation (SD) for continuous data, were used to describe the demographic data, disease activity, symptoms, signs, laboratory findings, deformity grading, and monofilament results. Unpaired student's t-test was applied to compare the means of continuous variables. Pearson Chi-square or Fisher's exact test was performed to analyze the association between different contributing factors, categorized BI groups, and MFT result. Multiple logistic regressions were used to test the association between BI groups and



Fig. 3 Monofilament kit used in the study.



Fig. 4 C-shape monofilament technique.

multiple factors simultaneously. McNemar's test was applied to compare the result of different MFT technique and the result between first and second evaluation in each patient. All statistical analyses were performed using PASW statistics 18.0 (IBM Corporation, New York, USA). A *p*-value <0.05 was considered to be statistically significant.

#### Results

#### Demographic data

Twenty MB patients from Siriraj Hansen's clinic and 50 cases from Raj Pracha Samasai Institute were enrolled in the present study during their hospital visits between May and December 2012. Two-third of the patients in this study was male (71.4%). The mean (SD) age of the population was 43 (15.75) with a range of 19 to 85-years-old. The majority of cases were from the central (51.4%) and the northeastern (37.1%) region of Thailand. Fifty-one cases (72.9%) denied family history of leprosy. Approximately 90% of the patients had been on treatment or surveillance period. Most of the cases (74.3%) were diagnosed as borderline tuberculoid (BT) and lepromatous (LL) leprosy (Table 2).

#### Physical examination

The physical examination on the day of enrollment was shown in Table 3. The data were categorized into two groups, low BI ( $\leq 2.5$ ) and high BI (>2.5) groups according to the mean (SD) BI of 2.5 (1.88) in our study population. Most of the patients presented with erythematous plaques/papules (67.1%) and the lesions were bilaterally distributed (95.7%) of more than five lesions (88.6%). Likewise, we found that 68.6% of the cases demonstrated enlarged peripheral nerves. Deformities were detected in only 37.1% of the cases. Most of the patients in the high BI group experienced type II leprosy reaction (76.5%), in contrast to the low BI group, which developed more of type I leprosy reaction (47.2%).

From univariate analysis, the factors found to associate with high BI were the lesion of erythematous plaques/papules (crude OR 17.44, 95% CI 2.03-150.04, p = 0.009), absence of anhidrosis (crude OR 3.29, 95% CI 1.23-8.78, p = 0.018) and presence of type II leprosy reaction (crude OR 46.22, 95% CI 8.30-257.41, p<0.001). Multiple logistic regression or multivariate analysis was analyzed only for the factors found to have significant or borderline significant association with high BI, as demonstrated in Table 3, type II leprosy reaction was the only robust factor for high BI profile

CharacteristicsNumber of cases (%)GenderMale $50 (71.4)$ Female $20 (28.6)$ Age (years) $\leq 40$ $\leq 40$ $35 (50.0)$ >40 $35 (50.0)$ >40 $35 (50.0)$ Mean (SD) $43 (15.75)$ Hometown (region) $Central$ Central $36 (51.4)$ Northeast $26 (37.1)$ Others (North, South, and East) $3 (4.3)$ Family history of leprosy $Presence$ Presence $19 (27.1)$ Absence $51 (72.9)$ Occupation $3 (18.6)$ Unemployed/students $12 (17.1)$ Disease activity $New$ caseNew case $4 (5.7)$ During treatment $39 (55.7)$ Surveillance $27 (38.6)$ Type of multibacillary leprosy (MB) leprosyBorderline tuberculoid (BT) $26 (37.1)$ Borderline lepromatous (BL) $15 (21.4)$ Lepromatous (LL) $26 (37.1)$	study (II 70)	
GenderMale $50 (71.4)$ Female $20 (28.6)$ Age (years) $\leq 40$ $\leq 40$ $35 (50.0)$ >40 $35 (50.0)$ Nean (SD) $43 (15.75)$ Hometown (region) $Central$ Central $36 (51.4)$ Northeast $26 (37.1)$ Others (North, South, and East) $3 (4.3)$ Family history of leprosyPresencePresence $19 (27.1)$ Absence $51 (72.9)$ Occupation $3 (18.6)$ Unemployed/students $12 (17.1)$ Disease activityNew caseNew case $4 (5.7)$ During treatment $39 (55.7)$ Surveillance $27 (38.6)$ Type of multibacillary leprosy (MB) leprosyBorderline tuberculoid (BT) $26 (37.1)$ Borderline lepromatous (BL) $15 (21.4)$	Characteristics	Number of cases (%)
Male $50 (71.4)$ Female $20 (28.6)$ Age (years) $\leq 40$ $\leq 40$ $35 (50.0)$ >40 $35 (50.0)$ >40 $35 (50.0)$ Mean (SD) $43 (15.75)$ Hometown (region) $(6 (51.4))$ Central $36 (51.4)$ Northeast $26 (37.1)$ Others (North, South, and East) $3 (4.3)$ Family history of leprosy $Presence$ Presence $19 (27.1)$ Absence $51 (72.9)$ Occupation $45 (64.3)$ Officers/merchants $13 (18.6)$ Unemployed/students $12 (17.1)$ Disease activity $New case$ New case $4 (5.7)$ During treatment $39 (55.7)$ Surveillance $27 (38.6)$ Type of multibacillary leprosy (MB) leprosyBorderline tuberculoid (BT) $26 (37.1)$ Borderline lepromatous (BL) $3 (4.3)$	Gandar	
Female $20 (28.6)$ Age (years) $\leq 40$ $35 (50.0)$ $\geq 40$ $35 (50.0)$ $\geq 40$ $35 (50.0)$ Mean (SD) $43 (15.75)$ Hometown (region) $(Central)$ Central $36 (51.4)$ Northeast $26 (37.1)$ Others (North, South, and East) $3 (4.3)$ Family history of leprosy $Presence$ Presence $19 (27.1)$ Absence $51 (72.9)$ Occupation $45 (64.3)$ Officers/merchants $13 (18.6)$ Unemployed/students $12 (17.1)$ Disease activity $New case$ New case $4 (5.7)$ During treatment $39 (55.7)$ Surveillance $27 (38.6)$ Type of multibacillary leprosy (MB) leprosyBorderline tuberculoid (BT) $26 (37.1)$ Borderline borderline (BB) $3 (4.3)$ Borderline lepromatous (BL) $15 (21.4)$		50(714)
Age (years) $\leq 40$ $35 (50.0)$ $>40$ $35 (50.0)$ Mean (SD) $43 (15.75)$ Hometown (region) $(central)$ Central $36 (51.4)$ Northeast $26 (37.1)$ Others (North, South, and East) $3 (4.3)$ Family history of leprosy $Presence$ Presence $19 (27.1)$ Absence $51 (72.9)$ Occupation $45 (64.3)$ Officers/merchants $13 (18.6)$ Unemployed/students $12 (17.1)$ Disease activity $New case$ New case $4 (5.7)$ During treatment $39 (55.7)$ Surveillance $27 (38.6)$ Type of multibacillary leprosy (MB) leprosyBorderline tuberculoid (BT) $26 (37.1)$ Borderline tuberculoid (BT) $26 (37.1)$ Borderline lepromatous (BL) $3 (4.3)$		
		20 (20.0)
>4035 (50.0)Mean (SD)43 (15.75)Hometown (region)36 (51.4)Central36 (51.4)Northeast26 (37.1)Others (North, South, and East)3 (4.3)Family history of leprosy9Presence19 (27.1)Absence51 (72.9)Occupation51 (72.9)Occupation13 (18.6)Unemployed/students12 (17.1)Disease activity13 (18.6)Unemployed/students12 (17.1)Disease activity27 (38.6)Type of multibacillary leprosy (MB) leprosy26 (37.1)Borderline tuberculoid (BT)26 (37.1)Borderline borderline (BB)3 (4.3)Borderline lepromatous (BL)15 (21.4)		25 (50.0)
Mean (SD)43 (15.75)Hometown (region)36 (51.4)Central36 (51.4)Northeast26 (37.1)Others (North, South, and East)3 (4.3)Family history of leprosy9 (27.1)Absence51 (72.9)Occupation51 (72.9)Occupation13 (18.6)Unemployed/students12 (17.1)Disease activity12 (17.1)Disease activity27 (38.6)Type of multibacillary leprosy (MB) leprosy26 (37.1)Borderline tuberculoid (BT)26 (37.1)Borderline borderline (BB)3 (4.3)Borderline lepromatous (BL)15 (21.4)	<u> </u>	
Hometown (region) Central36 (51.4)Northeast26 (37.1)Others (North, South, and East)3 (4.3)Family history of leprosy Presence19 (27.1)Absence51 (72.9)Occupation51 (72.9)Occupation13 (18.6)Unemployed/students12 (17.1)Disease activity New case4 (5.7)During treatment39 (55.7)Surveillance27 (38.6)Type of multibacillary leprosy (MB) leprosy Borderline tuberculoid (BT)26 (37.1)Borderline borderline (BB)3 (4.3)Borderline lepromatous (BL)15 (21.4)		· /
Central36 (51.4)Northeast26 (37.1)Others (North, South, and East)3 (4.3)Family history of leprosy9Presence19 (27.1)Absence51 (72.9)Occupation51 (72.9)Occupation13 (18.6)Unemployed/students12 (17.1)Disease activity9 (55.7)Surveillance27 (38.6)Type of multibacillary leprosy (MB) leprosy80 (55.7)Borderline tuberculoid (BT)26 (37.1)Borderline borderline (BB)3 (4.3)Borderline lepromatous (BL)15 (21.4)	Mean (SD)	43 (15.75)
Northeast26 (37.1)Others (North, South, and East)3 (4.3)Family history of leprosy9Presence19 (27.1)Absence51 (72.9)Occupation45 (64.3)Officers/merchants13 (18.6)Unemployed/students12 (17.1)Disease activity9 (55.7)Surveillance27 (38.6)Type of multibacillary leprosy (MB) leprosy26 (37.1)Borderline tuberculoid (BT)26 (37.1)Borderline borderline (BB)3 (4.3)Borderline lepromatous (BL)15 (21.4)		
Others (North, South, and East)3 (4.3)Family history of leprosy Presence19 (27.1) AbsenceAbsence51 (72.9)Occupation Agriculturists/employees45 (64.3) Officers/merchantsOfficers/merchants13 (18.6) Unemployed/studentsUnemployed/students12 (17.1)Disease activity New case4 (5.7) 27 (38.6)Type of multibacillary leprosy (MB) leprosy Borderline tuberculoid (BT) Borderline borderline (BB) Borderline lepromatous (BL)26 (37.1) 3 (4.3)	Central	36 (51.4)
Family history of leprosy Presence19 (27.1) AbsenceAbsence51 (72.9)Occupation Agriculturists/employees45 (64.3) Officers/merchantsOfficers/merchants13 (18.6) Unemployed/studentsUnemployed/students12 (17.1)Disease activity New case4 (5.7) During treatmentDuring treatment39 (55.7) SurveillanceType of multibacillary leprosy (MB) leprosy Borderline tuberculoid (BT)26 (37.1) 3 (4.3) Borderline lepromatous (BL)		· · · · ·
Presence19 (27.1)Absence51 (72.9)Occupation45 (64.3)Agriculturists/employees45 (64.3)Officers/merchants13 (18.6)Unemployed/students12 (17.1)Disease activity12 (17.1)New case4 (5.7)During treatment39 (55.7)Surveillance27 (38.6)Type of multibacillary leprosy (MB) leprosy26 (37.1)Borderline tuberculoid (BT)26 (37.1)Borderline borderline (BB)3 (4.3)Borderline lepromatous (BL)15 (21.4)	Others (North, South, and East)	3 (4.3)
Absence51 (72.9)Occupation-Agriculturists/employees45 (64.3)Officers/merchants13 (18.6)Unemployed/students12 (17.1)Disease activity-New case4 (5.7)During treatment39 (55.7)Surveillance27 (38.6)Type of multibacillary leprosy (MB) leprosy-Borderline tuberculoid (BT)26 (37.1)Borderline borderline (BB)3 (4.3)Borderline lepromatous (BL)15 (21.4)	Family history of leprosy	
Occupation45 (64.3)Agriculturists/employees45 (64.3)Officers/merchants13 (18.6)Unemployed/students12 (17.1)Disease activity12 (17.1)New case4 (5.7)During treatment39 (55.7)Surveillance27 (38.6)Type of multibacillary leprosy (MB) leprosyBorderline tuberculoid (BT)Borderline borderline (BB)3 (4.3)Borderline lepromatous (BL)15 (21.4)	Presence	19 (27.1)
Agriculturists/employees45 (64.3)Officers/merchants13 (18.6)Unemployed/students12 (17.1)Disease activity12 (17.1)New case4 (5.7)During treatment39 (55.7)Surveillance27 (38.6)Type of multibacillary leprosy (MB) leprosyBorderline tuberculoid (BT)Borderline borderline (BB)3 (4.3)Borderline lepromatous (BL)15 (21.4)	Absence	51 (72.9)
Agriculturists/employees45 (64.3)Officers/merchants13 (18.6)Unemployed/students12 (17.1)Disease activity12 (17.1)New case4 (5.7)During treatment39 (55.7)Surveillance27 (38.6)Type of multibacillary leprosy (MB) leprosyBorderline tuberculoid (BT)Borderline borderline (BB)3 (4.3)Borderline lepromatous (BL)15 (21.4)	Occupation	
Officers/merchants13 (18.6)Unemployed/students12 (17.1)Disease activity12 (17.1)New case4 (5.7)During treatment39 (55.7)Surveillance27 (38.6)Type of multibacillary leprosy (MB) leprosyBorderline tuberculoid (BT)Borderline borderline (BB)3 (4.3)Borderline lepromatous (BL)15 (21.4)		45 (64 3)
Unemployed/students12 (17.1)Disease activity12 (17.1)New case4 (5.7)During treatment39 (55.7)Surveillance27 (38.6)Type of multibacillary leprosy (MB) leprosyBorderline tuberculoid (BT)Borderline borderline (BB)3 (4.3)Borderline lepromatous (BL)15 (21.4)	8	· · ·
Disease activity New case4 (5.7) 39 (55.7) 27 (38.6)During treatment Surveillance39 (55.7) 27 (38.6)Type of multibacillary leprosy (MB) leprosy Borderline tuberculoid (BT) Borderline borderline (BB) 3 (4.3) Borderline lepromatous (BL)26 (37.1) 3 (4.3)		· /
New case4 (5.7)During treatment39 (55.7)Surveillance27 (38.6)Type of multibacillary leprosy (MB) leprosyBorderline tuberculoid (BT)Borderline borderline (BB)3 (4.3)Borderline lepromatous (BL)15 (21.4)		12 (17.17)
During treatment39 (55.7)Surveillance27 (38.6)Type of multibacillary leprosy (MB) leprosy Borderline tuberculoid (BT)26 (37.1)Borderline borderline (BB)3 (4.3)Borderline lepromatous (BL)15 (21.4)		4 (5 7)
Surveillance27 (38.6)Type of multibacillary leprosy (MB) leprosy Borderline tuberculoid (BT)26 (37.1)Borderline borderline (BB)3 (4.3)Borderline lepromatous (BL)15 (21.4)		
Type of multibacillary leprosy (MB) leprosyBorderline tuberculoid (BT)26 (37.1)Borderline borderline (BB)3 (4.3)Borderline lepromatous (BL)15 (21.4)	e	
Borderline tuberculoid (BT)26 (37.1)Borderline borderline (BB)3 (4.3)Borderline lepromatous (BL)15 (21.4)		27 (38.6)
Borderline borderline (BB)3 (4.3)Borderline lepromatous (BL)15 (21.4)		
Borderline lepromatous (BL) 15 (21.4)		· /
Lepromatous (LL) 26 (37.1)	1	
	Lepromatous (LL)	26 (37.1)

 Table 2. Demographic data of the patients enrolled in the study (n = 70)

with adjusted OR of 69.66 (95% CI 7.98-608.07,  $p \le 0.001$ ).

Leprosy reaction was observed in 51 patients (72.9%), divided into type I (31.4%) and type II (41.4%) reaction. It significantly correlated with documented co-infection in each individual (p = 0.014). The most common co-infection in the present study group was upper respiratory tract infection (URI) (61.5%), followed by dental carries (23.1%), acute gastroenteritis (7.7%), and hepatitis B virus infection (HBV) (7.7%) respectively. However, peripheral nerve hypertrophy from physical examination was not considerably related with the occurrence of any leprosy reaction (p = 0.254).

#### Monofilament testing

The results of MFT between SWM and Thai conventional technique were not different for both ulnar and median nerve distribution (p = 1.000), as

shown in Table 4. In contrast to posterior tibial nerve distribution (p<0.001), we found statistical difference between the results of each method. However, after excluding test points at the heel area, the posterior tibial nerve sensation showed similar results for both techniques (p>0.05). MFT result, based on standard SWM technique, from two consecutive visits of each patient were mostly unchanged, as shown in Table 5, only one-fourth of cases had altered test results of which 14.4% showed progressive sensory impairment and 8.5% had improvement after the standard treatment of neuritis.

Twenty-eight patients (40%) who mentioned of numbness at either palms or soles significantly demonstrated impaired sensory function detected by SWM testing (p = 0.014). Furthermore, the median BI in cases with and without sensory impairment was 1.50 and 4.00 respectively with statistically significant difference (p = 0.002). On the other hand, BI did not show significantly associated with patients' complaint of numbness at either palms or soles (p = 0.151) or with abnormal MFT results (p = 0.296).

Regarding assessment of ulnar, median and posterior tibial nerve function, we found that patients with abnormal SWM result of the hands at ulnar distribution, significantly associated with ipsilateral ulnar nerve enlargement (p<0.05) and claw-hand deformities (p<0.001). In addition, enlargement of common peroneal nerve was observe considerably in the cases with the same side of foot deformity (p<0.05). Nevertheless, enlargement of posterior tibial nerve which mainly innervated sensory part of the foot did not correlate with abnormal monofilament test of the foot (p = 1.000). Owing to the absence of the case with median nerve enlargement in the present study, assessment of correlation between median nerve enlargement and other factors were not applicable.

#### Discussion

The present study investigated the results of Semmes-Weinstein MFT for detection of sensory function impairment on hands and feet in MB leprosy cases as compare to the Thai conventional technique used for MFT with more test points on palms and soles. The clinical course of neuritis occurring during the follow-up period is also described. From the demographic data, we found male predominance in our leprosy patients, in which corresponded with the results of many previous studies worldwide, including in Thailand, and some reported a greater MB disease tendency in males<sup>(2,3,12-15)</sup>. Although leprosy was

Characteristics	Low BI group	High BI group	Univariate analysis		Multivariate analysis	
	(n = 36), n (%)	(n = 34), n (%)	Crude odds ratio (95% CI)	<i>p</i> -value	Adjusted odds ratio (95% CI)	<i>p</i> -value
Type of lesion Hypopigmentation	9 (25.0)	1 (2.9)	1			
Annular lesion Ervthematous plaque/papule	11 (30.6) 16 (44.4)	2 (5.9) 31 (91.2)	1.64 (0.13-21.10) 17.44 (2.03-150.04)	0.706 0.009	0.29 (0.01-5.98) 3.49 (0.33-37.42)	0.421 0.302
Anhidrosis at the skin lesion						
Presence Absence	22 (61.1) 14 (38.9)	11 (32.4) 23 (67.6)	1 3.29 (1.23-8.78)	0.018	1 2.85 (0.48-16.92)	0.250
Hair loss at the skin lesion Presence Abence	15 (41.7) 21 (58 3)	13 (38.2)	1 1 15 (0 44-3 01)	077.0		
Sensory impairment at the skin lesion	( ( ( ) ) 17	(0.10) 17		0.1.0		
Presence Absence	27 (75.0) 9 (25.0)	18 (52.9) 16 (47.1)	1 2.67 (0.97-7.33)	0.057	0.43 (0.07-2.54)	0.351
Stocking-glove pattern of sensory impairment Presence Absence	13 (36.1) 23 (63.9)	15 (44.1) 19 (55.9)	1.40 (0.54-3.65) 1	0.495		
Number of skin lesion						
≤5	6 (16.7) 30 (83.3)	2 (5.9) 32 (94.1)	1 3.20 (0.60-17.10)	0.174		
Distribution of skin lesion Unilateral Bilateral	2 (5.6) 34 (94.4)	1 (2.9) 33 (97.1)	1 1.94 (0.17-22.45)	0.595		
Nerve enlargement Presence Absence	24 (66.7) 12 (33.3)	24 (70.6) 10 (29.4)	1.20 (0.44-3.30) 1	0.724		
Deformity Presence Absence	12 (33.3) 24 (66.7)	14 (41.2) 20 (58.8)	1.40 (0.53-3.70) 1	0.498		
Leprosy reaction Type I	17 (47.2)	5 (14.7)	1.57 (0.32-7.66)	0.578	2.67 (0.45-15.77	0.280
Type II Absence	3 (8.3) 16 (44 4)	26 (76.5) 3 (8 8)	46.22 (8.30-257.41) 1	<0.001	69.66 (7.98-608.07) 1	<0.001

J Med Assoc Thai Vol. 98 No. 11 2015

Nerve	Abnormal monofilament test, n (%)		<i>p</i> -value <sup>#</sup>	Accuracy of Thai techniqu	
	SWM (n = 140)	Thai (n = 140)		(% agreement)	
Lt ulnar	13 (9.3)	14 (10.0)	1.000	99.3	
Rt ulnar	14 (10.0)	14 (10.0)	1.000	100.0	
Lt median	5 (3.6)	6 (4.3)	1.000	97.9	
Rt median	6 (4.3)	7 (5.0)	1.000	99.3	
Lt PT	35 (25.0)	64 (45.7)	< 0.001	79.3	
Rt PT	35 (25.0)	62 (44.3)	< 0.001	80.7	
Lt PT (excluding heel)	35 (25.0)	39 (27.9)	0.289	94.3	
Rt PT (excluding heel)	35 (25.0)	36 (25.7)	1.000	95.0	

Table 4. Comparison of the results between monofilament methods (SWM & Thailand conventional technique)

SWM = Semmes-Weinstein monofilament; Lt = left; Rt = right; PT = posterior tibial nerve # McNemar's test

 Table 5. Monofilament tested results between two consecutive visits

Nerve	Total	Abnormal monofilament test, n (%)			
	(n)	Unchanged	Deteriorated	Improved	
Lt ulnar	70	69 (98.6)	-	1 (1.4)	
Rt ulnar	70	70 (100)	-	-	
Lt median	70	69 (98.6)	1 (1.4)	-	
Rt median	70	68 (97.1)	2 (2.9)	-	
Lt PT	70	63 (90.0)	3 (4.3)	4 (5.7)	
Rt PT	70	67 (95.7)	3 (4.3)	-	
Total	70	68 (97.1)	1 (1.4)	1 (1.4)	

Lt = left; Rt = right; PT = posterior tibial nerve

considered as one of genetic-associated diseases<sup>(16,17)</sup>, there is not yet well-understood mechanism and most of the literatures did not notably found the presence of family history in leprosy population including ours. The majority of cases in our study were employees or agriculturists, which reflects that low socioeconomic status may correlated with leprosy worldwide<sup>(2)</sup>. However, Moet et al reported no distinct association between leprosy and host career<sup>(17)</sup>.

Most of the cases in the current study presented with bilateral involvement of cutaneous lesions as erythematous plaques and papules of more than five lesions, which was classified as MB leprosy according to WHO classification criteria<sup>(8,10)</sup>. The presence of anhidrosis or hypohidrosis, suggesting sympathetic autonomic involvement, was remarkably observed in the low BI group. However, this association was not significant using multivariate analysis. However, there were no reports of association between BI and deterioration of sweat secretory function to date. Sensory impairment at cutaneous lesions and glovestocking sensory defect were observed equivalently in most of the cases in either low BI and high BI group in our study, these might be influenced by some confounding factors such as neuritis and leprosy reaction. In the present study, enlargement of peripheral nerve on palpation was not related with the occurrence of leprosy reaction, which presented the same trend reported in previous study with strict criteria for nerve hypertrophy<sup>(1)</sup>.

The incidence of type I and type II leprosy reaction in our MB leprosy population were 31.4% and 41.4% respectively, and all were treated with oral corticosteroid. This prevalence was slightly higher than previous reports<sup>(18-20)</sup>, which could be because the present study was conducted at Siriraj Hospital, a super tertiary care, and Raj Pracha Samasai Institute, the leprosy center of Thailand, where the cases may be more complicated than other general hospitals. In the present study, only erythema nodosum leprosum (ENL) or type II reaction was significantly correlated with high BI group from multiple logistic regression, which corresponded with the result of previous study mentioning that being LL classification, BI of 6, and HIV co-infection increased risk of ENL<sup>(20)</sup>.

In the present study, co-infection was observed to be correlated with leprosy reaction. The most common co-infection was URI, followed by dental carries. Previous studies revealed chronic oral infection, including dental carries, were the most frequent sources with explainable mechanism of higher C-reactive protein, interleukin-1, and interleukin-6 levels, which may play a role in pro-inflammatory phase<sup>(21-23)</sup>. This outcome may have obvious symptoms of URI that can be described by the patients themselves, but obscure unrecognized chronic oral infection may be overlooked by the investigators.

Regarding MFT, patients who mentioned of numbness were mostly related with abnormal test result. Additionally, silent neuritis or abnormal SWM test without patients' obvious signs or symptoms can be detected at any periods of the treatment. Early detection of sensory deficit was the key to prevent serious complication and should be provided in every hospital visit<sup>(1,3)</sup>. Although the MFT results between SWM and Thai conventional technique were different for posterior tibial nerve distribution, the results from these two techniques were not significantly different after excluding the heel area. The increased skin thickness at heels area for protective role in weight bearing points was considered as one confounding factor for the false negative results in MFT.

From the present study, abnormal MFT at ulnar nerve distribution was associated with ipsilateral ulnar nerve hypertrophy, but no such association was found for posterior tibial nerve. It had been explained that superficially located ulnar nerve could be easily palpated<sup>(13)</sup>. However, median nerve hypertrophy was not detected in this study; this may imply that median nerve is hard to access by palpation in general physical examination.

In conclusion, the present study revealed no significant difference between Semmes-Weinstein MFT and Thai conventional MFT technique for evaluation of sensory deficit in MB leprosy patients. Using SWM technique with lesser test points can minimize the time used to perform MFT in each patient; therefore, we encourage the application of this SWM technique to improve the medical care for leprosy patients in Thailand. Moreover, abnormal monofilament test or silent neuritis can be detected at any period of the disease course, so it is important for the physicians to early recognize this condition to prevent disabilities.

#### What is already known on this topic?

Monofilament testing is an inexpensive, easy-to-use, portable, and very useful tool to screen for sensory neuropathy in leprosy patients. Early detection and treatment of nerve function impairment is mandatory for prevention of disability in leprosy patients.

#### What this study adds?

Replacement of Thai conventional technique in monofilament testing by standard Semmes-Weinstein monofilament method could decrease the time spent to evaluate sensory function in each leprosy individual during the hospital visit, which would support the better service for leprosy patients in Thailand.

### Acknowledgment

We are grateful to all participants from Siriraj Hospital and Raj Pracha Samasai Institute, Dr. Chulaluk Komoltri for statistical advice, Ms. Pojana Thanyakittikul, registration nurse from Raj Pracha Samasai Institute, for her assistance with data gathering and monofilament testing.

This study was supported by Routine to Research Management (R2R) Fund, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand.

## Potential conflicts of interest

None.

#### References

- van Brakel WH, Nicholls PG, Das L, Barkataki P, Suneetha SK, Jadhav RS, et al. The INFIR Cohort Study: investigating prediction, detection and pathogenesis of neuropathy and reactions in leprosy. Methods and baseline results of a cohort of multibacillary leprosy patients in north India. Lepr Rev 2005; 76: 14-34.
- World Health Organization.WHO Expert Committee on Leprosy. World Health Organ Tech Rep Ser 2012; (968): 1-61.
- 3. van Brakel WH, Nicholls PG, Wilder-Smith EP, Das L, Barkataki P, Lockwood DN. Early diagnosis of neuropathy in leprosy--comparing diagnostic tests in a large prospective study (the INFIR cohort study). PLoS Negl Trop Dis 2008; 2: e212.
- Schreuder PA. The occurrence of reactions and impairments in leprosy: experience in the leprosy control program of three provinces in northeastern Thailand, 1987-1995 [correction of 1978-1995]. III. Neural and other impairments. Int J Lepr Other Mycobact Dis 1998; 66: 170-81.
- Richardus JH, Finlay KM, Croft RP, Smith WC. Nerve function impairment in leprosy at diagnosis and at completion of MDT: a retrospective cohort study of 786 patients in Bangladesh. Lepr Rev 1996; 67: 297-305.
- Croft RP, Nicholls PG, Steyerberg EW, Richardus JH, Cairns W, Smith S. A clinical prediction rule for nerve-function impairment in leprosy patients. Lancet 2000; 355: 1603-6.

- Van Brakel WH, Nicholls PG, Das L, Barkataki P, Maddali P, Lockwood DN, et al. The INFIR Cohort Study: assessment of sensory and motor neuropathy in leprosy at baseline. Lepr Rev 2005; 76: 277-95.
- Raj-Pracha-Samasai-Institute. Manual of diagnosis and treatment of leprosy. Bangkok: Karn-Sassana, Baan Batr; 2007.
- 9. Koelewijn LF, Meima A, Broekhuis SM, Richardus JH, Mitchell PD, Benbow C, et al. Sensory testing in leprosy: comparison of ballpoint pen and monofilaments. Lepr Rev 2003; 74: 42-52.
- World Health Organization. WHO Expert Committee on Leprosy. World Health Organ Tech Rep Ser 1998; 847: 1-43.
- Brandsma JW, Van Brakel WH. WHO disability grading: operational definitions. Lepr Rev 2003; 74: 366-73.
- Lienhardt C, Currie H, Wheeler JG. Inter-observer variability in the assessment of nerve function in leprosy patients in Ethiopia. Int J Lepr Other Mycobact Dis 1995; 63: 62-76.
- 13. Chen S, Wang Q, Chu T, Zheng M. Inter-observer reliability in assessment of sensation of skin lesion and enlargement of peripheral nerves in leprosy patients. Lepr Rev 2006; 77: 371-6.
- Schreuder PA. The occurrence of reactions and impairments in leprosy: experience in the leprosy control program of three provinces in northeastern Thailand, 1987-1995 [correction of 1978-1995].
   I. Overview of the study. Int J Lepr Other Mycobact Dis 1998; 66: 149-58.
- 15. Oliveira DT, Sherlock J, Melo EV, Rollemberg KC, Paixao TR, Abuawad YG, et al. Clinical variables associated with leprosy reactions and persistence of physical impairment. Rev Soc Bras Med Trop 2013; 46: 600-4.
- 16. Moet FJ, Pahan D, Schuring RP, Oskam L,

Richardus JH. Physical distance, genetic relationship, age, and leprosy classification are independent risk factors for leprosy in contacts of patients with leprosy. J Infect Dis 2006; 193: 346-53.

- 17. Moet FJ, Meima A, Oskam L, Richardus JH. Risk factors for the development of clinical leprosy among contacts, and their relevance for targeted interventions. Lepr Rev 2004; 75: 310-26.
- Becx-Bleumink M, Berhe D. Occurrence of reactions, their diagnosis and management in leprosy patients treated with multidrug therapy; experience in the leprosy control program of the All Africa Leprosy and Rehabilitation Training Center (ALERT) in Ethiopia. Int J Lepr Other Mycobact Dis 1992; 60: 173-84.
- Voorend CG, Post EB. A systematic review on the epidemiological data of erythema nodosum leprosum, a type 2 leprosy reaction. PLoS Negl Trop Dis 2013; 7: e2440.
- 20. Saunderson P, Gebre S, Byass P. ENL reactions in the multibacillary cases of the AMFES cohort in central Ethiopia: incidence and risk factors. Lepr Rev 2000; 71: 318-24.
- Motta AC, Pereira KJ, Tarquinio DC, Vieira MB, Miyake K, Foss NT. Leprosy reactions: coinfections as a possible risk factor. Clinics (Sao Paulo) 2012; 67: 1145-8.
- Motta AC, Furini RB, Simao JC, Vieira MB, Ferreira MA, Komesu MC, et al. Could leprosy reaction episodes be exacerbated by oral infections? Rev Soc Bras Med Trop 2011; 44: 633-5.
- Motta AC, Furini RB, Simao JC, Ferreira MA, Komesu MC, Foss NT. The recurrence of leprosy reactional episodes could be associated with oral chronic infections and expression of serum IL-1, TNF-alpha, IL-6, IFN-gamma and IL-10. Braz Dent J 2010; 21: 158-64.

## การศึกษาเปรียบเทียบผลการตรวจประเมินการรับความรู้สึกของเส้นประสาทในผู้ป่วยโรคแฮนเซนโดยการใช้ โมโนฟิลาเมนต์

สราญจิต วิมูลชาติ, เพ็ญวดี พัฒนปรีชากุล, อรจุฑา ชยางศุ, กมลพรรณ เลิศรุจิวณิช, พัชรี เอี่ยมธาราชัย, สุธีรพร เชาว์วัฒนาพานิช

ภูมิหลัง: โรคเรื้อนหรือโรคแฮนเซนเป็นโรคที่มีอาการแสดงทางผิวหนังและเส้นประสาทส่วนปลาย โดยผู้ป่วยโรคแฮนเซนมีโอกาส เกิดความพิการแทรกซ้อนจากการรับความรู้สึกของเส้นประสาทที่เสียไป โดยอาการเหล่านี้อาจเกิดขึ้นก่อน ระหว่าง หรือ หลังการ รักษาก็ได้ ดังนั้นการตรวจเพื่อประเมินการรับความรู้สึกของเส้นประสาทตั้งแต่ระยะแรกของการวินิจฉัย และในช่วงติดตามการรักษา เพื่อเฝ้าระวังอาการปลายประสาทอักเสบตั้งแต่ระยะแรก ๆ จึงถือเป็นมาตรการป้องกันความพิการที่มีประสิทธิภาพมากที่สุด

วัตถุประสงค์: เพื่อศึกษาเปรียบเทียบประสิทธิภาพของการตรวจประเมินการรับความรู้สึกของเส้นประสาทส่วนปลายในผู้ป่วยโรค แฮนเซนชนิดเชื้อมาก (multibacillary leprosy) โดยการใช้โมโนฟิลาเมนด์วิธีมาตรฐาน คือ Semmes-Weinstein monofilament (SWM) เปรียบเทียบกับวิธีที่ใช้อยู่ในประเทศไทยในขณะนี้ และศึกษาการดำเนินโรคของผู้ป่วยโรคแฮนเซนที่มีภาวะเส้นประสาท อักเสบระหว่างการรักษา

วัสดุและวิธีการ: การศึกษานี้รวบรวมผู้ป่วยโรคแเฮนเซนที่อยู่ระหว่างการติดตามการรักษาในคลินิกแฮนเซน หน่วยตรวจโรคผิวหนัง โรงพยาบาลศิริราช และคลินิกผิวหนังเนื้อชา สถาบันราชประชาสมาสัย กรมควบคุมโรค ผู้ป่วยได้รับการตรวจประเมินการรับความรู้สึก ของเส้นประสาทส่วยปลายด้วยโมโนฟิลาเมนต์ ทั้ง SWM และวิธีที่ใช้ในประเทศไทยปัจจุบัน รายละ 2 ครั้ง คือในครั้งแรกที่เข้าร่วม การศึกษาและครั้งถัดไปเมื่อมาตรวจติดตามการรักษา โดยทำการรวบรวมข้อมูลทั่วไป ประวัติโรคแฮนเซนในครอบครัว ประวัติอาการ ชา ชนิดของโรคแฮนเซนที่ผู้ป่วยเป็น ผลการตรวจร่างกาย ผลการตรวจทางห้องปฏิบัติการ ประวัติภาวะเห่อ ประวัติการเกิดภาวะ เส้นประสาทส่วนปลายอักเสบ และการรักษา

**ผลการศึกษา:** ผู้ป่วยโรคแฮนเซนชนิดเซื้อมากจำนวน 70 ราย ได้เข้าร่วมการศึกษานี้โดยมีผู้ป่วยเพศชาย 71.4% ผู้ป่วยทั้งหมด มีอายุเฉลี่ย 43±15.75 ปี โดยมีอายุอยู่ในช่วง 19-85 ปี จากการศึกษาผลการตรวจประเมินการรับความรู้สึกของเส้นประสาทulnar, median และ posterior tibial โดยไม่รวมตำแหน่งส้นเท้า ด้วยวิธี SWM และวิธีของไทยพบว่าไม่มีความแตกต่างกันทางสถิติ (p = 1.00) ผู้ป่วย 28 ราย (40%) ที่ให้ประวัติว่ามีอาการชาบริเวณฝ่ามือหรือฝ่าเท้าซึ่งสอดคล้องกับผลการตรวจพบความผิดปกติ ด้วยโมโนฟิลาเมนต์อย่างมีนัยสำคัญทางสถิติ (p = 0.014)

สรุป: จากการศึกษานี้ไม่พบความแตกต่างของผลการตรวจประเมินการรับความรู้สึกของเส้นประสาทส่วยปลายในผู้ป่วยโรคแฮนเซน ชนิดเชื้อมากระหว่างวิธี SWM และวิธีที่ใช้ในประเทศไทยปัจจุบัน ทั้งนี้เนื่องจากการตรวจด้วยวิธี SWM ที่ใช้จำนวนจุดในการประเมิน น้อยกว่าทำให้ใช้เวลาในการตรวจลดลง ดังนั้นจึงสามารถนำผลการศึกษานี้มาประยุกต์ใช้ เพื่อเพิ่มประสิทธิภาพในการให้บริการ และการติดตามการรักษาผู้ป่วยโรคแฮนเซนในประเทศไทยต่อไป