Lepr Rev (1998) **69,** 367–375

A field trial of detection and treatment of nerve function impairment in leprosy—Report from national POD pilot project

J. JIANG*, J. M. WATSON**, G. C. ZHANG* & X. Y. WEI*

**Institute of Dermatology, Chinese Academy of Medical Sciences and Peking Union Medical College, 12 Jiangwangmiao Street, Nanjing, 210042, People's Republic of China*

***The Leprosy Mission International, 80 Windmill Road, Brentford, Middlesex TW8 0QH, UK*

Accepted for publication 1 September 1998

Summary As part of a collaborative project between the Ministry of Health of China (MOH) and The Leprosy Mission International (TLMI) on leprosy rehabilitation and prevention of disability (POD), a total of 1407 patients was monitored for possible nerve function impairment (NFI) through standardized clinical nerve function assessment between May 1995 and February 1998. Of these, 191 patients were found to have NFI and were put on a fixed regimen of prednisolone. In this study, 36·7% of NFI occurred before diagnosis of leprosy, 35·6% developed during MDT and 25·7% after their release from MDT. Overall, 7·5% (105 out of 1407) of all patients, or 55·9% of patients with NFI, suffered from silent neuropathy. Of the affected nerves, 62·6% had silent neuropathy. Sensory impairment responded to prednisolone satisfactorily, giving a recovery rate of 73·8%, 76·5% and 81·0% in ulnar, median and posterior tibial nerve, respectively. Sensibility in patients even with a NFI duration longer than 6 months made significant improvement ($p < 0·05$). Motor function improvement was less satisfactory, especially in ulnar and c. popliteal nerve. The possible reasons are analysed. Our findings with regard to sensibility changes confirm that once it becomes clinically detectable, NFI is no longer at the 'early' stage. More sensitive tests are necessary to detect real 'early' sensory impairment in the field. Our study also indicates that with well-trained field staff and proper equipment for nerve function assessment, early detection and treatment of NFI can be practical and effective.

Introduction

Leprosy is an infectious disease which causes deformity and disability, due to damage to peripheral nerves. It has been increasingly recognized that prevention of disability (POD)

Correspondence to: J. Jiang

0305-7518/98/069367+09 $1.00

activities are an integral part of leprosy control services. The most important aspect of POD is early detection and adequate treatment of neural impairment. Corticosteroids are fairly well known to be effective in the treatment of leprosy reactions and recent nerve function impairment (NFI) in leprosy.[1–3]

The introduction of treatment in the field of recent NFI using a standardized corticosteroid regimen has been encouraged in China, particularly since 1991 when the collaborative pilot project on POD and rehabilitation between MOH and TLMI was undertaken.[4,5] As part of the project activities, a pilot study was established to detect NFI through standardized clinical examination and to treat NFI patients with prednisolone. The pilot project involved 14 provinces with different leprosy prevalence from 1995 to 1998. The objectives of this study were:

1 To determine the progress of sensory and motor function recovery with prednisolone therapy.
2 To analyse results with respect to duration of impairment, the relationship of NFI to MDT, the proportion of silent neuritis and the feasibility and effectiveness of leprosy field staff in dealing with NFI.

Materials and methods

CASE SELECTION

Patients in the pilot areas on MDT treatment or released from MDT during the past year were considered to be at risk of neuritis and were monitored for possible neuritis. All newly detected cases during the study period were included. The total number of cases monitored and followed up was 1407.

DEFINITION OF NERVE FUNCTION IMPAIRMENT (NFI)

NFI refers to a clinically detectable impairment of motor, sensory or autonomic nerve function and may occur in an obvious way or silently. Patients were considered to have neurological impairment when the scores in the deterioration of voluntary muscle test (VMT) and/or the touch sensitivity test (TST) occurring in the same nerve trunk distribution area were one or more points and two or more points higher, respectively, compared with the previous result. If previous VMT and TST results were not available, a patient was considered to have motor impairment when his VMT score was one or more points above the normal score; and sensory impairment, when his TST score was 2 or more points above the normal score. When it had existed for 6 months or less, NFI was considered to be 'recent'. Where patients had NFI for more than 6 months (7–12 months), especially in newly diagnosed cases, they were also put on prednisolone. Silent neuropathy was defined as NFI without skin manifestation (of RR, ENL), without complaints of nerve pain and without awareness of nerve tenderness.

NERVE FUNCTION ASSESSMENT

TST

Touch sensibility was tested by a light touch of the tip of a ballpoint pen. In one province

Table 1. Muscle strength scoring in this study

Muscle strength finding	Score
S – Full ROM*, full resistance	0
R – Full ROM, reduced resistance	1
M – Reduced ROM, some joint movement	3
P – Paralysis	5

Muscle testing in this study for each nerve: Facial, lid gap on light eye closure (nm); Ulnar, abduction of little finger; Median, abduction of thumb; Radial, extension of wrist; Popliteal, dorsiflexion of foot.

*ROM = range of movement.

(Sichuan) we tried the nylon monofilament in the field and also provided extra National Centre training and supervision. Pressures of 4 g and 10 g, respectively, were taken as the protective thresholds for hand and foot separately. On the hands, 10 standard points were tested: four on the ulnar part of the palm and six on the median part. On the feet, 10 points on the sole were tested, including the pulp of each of the five toes, the first, third and fifth metatarsal head, the base of the fifth metatarsal and the heel. One insensitive spot was calculated as one point.

VMT

Muscle strength was graded as strong (S), resistance reduced (R), range of joint movement reduced (M) and paralysed (P). In the case of lagophthalmos, the lid gap was recorded. Muscle strength scoring system is presented in Table 1.

Nerve pain or tenderness

The nerves of ulnar, median, posterior tibial and c. popliteal were recorded in terms of pain (Pn) and/or tenderness (Td). Radial and facial nerves were not examined because they were difficult to access and less affected.

PREDNISOLONE REGIMEN

The standardized prednisolone treatment started with a daily dose of 40 mg in the morning. However, the initial dosage was adjusted for body weight and also for the severity of reaction/NFI. The dosage tapered down at the rate of 10 mg per month until the dosage was 20 mg, after which it was reduced by 5 mg per month, thus giving a course duration of 6 months. This tapering also depended on the progress of the individual patient. Patients with recent NFI who had no other concurrent severe disease, such as untreated tuberculosis, were given systemic steroid treatment.

MONITORING AND FOLLOW-UP ROUTINES

New patients were monitored once a month over a period of 6 months when the diagnosis of leprosy was established. Patients on MDT as well as those on the first year of surveillance

were assessed every 3 months. Once NFI was detected, the assessment of nerve function was repeated monthly during prednisolone treatment and every 3 months after finishing prednisolone therapy. Patients were taught to come back to the staff if there were any signs of nerve function deterioration. The treatment was given mainly on an outpatient basis. The nerve function assessment and NFI treatment were carried out by trained local leprosy staff and supervised by provincial, national and TLMI supervisors.

The data from the study were used to establish a database which was analysed using STATA 3·0 version, a computer software for the statistical analysis. The Student's *t*-test was applied on the differences between group means at the level of statistical significance of $p < 0{\cdot}05$.

Results

A total of 1407 leprosy patients (MB 1118, PB 289) was monitored and their nerve functions were regularly assessed during the study period. Out of 1407 patients, 191 patients (MB 159, PB 32) were found to have NFI, the overall incidence rate was 4·7 per 100 person years at risk. In MB and PB, the incidence rates were 4·9 and 3·9 per 100 person years at risk, respectively. The mean age of patients with NFI was 38·7 years (range: 11–75 years). The mean follow-up period after the completion of prednisolone treatment was 14·8 months (range: 1–23 months). Table 2 shows the basic information of patients with NFI in this study. More than one-third (36·7%) of NFI took place before the diagnosis of leprosy, 35·6% on MDT and 25·7% after release from treatment (RFT). Four hundred and thirty-two nerves were affected, including 124 ulnar nerve (sensory 107, motor 47), 74 median (sensory 68, motor 28), 179 posterior tibial, 27 c. popliteal, 21 facial and seven radial. The posterior tibial nerve was the most frequently involved, the facial and radial nerves the least. The percentage of silent neuropathy of the total affected nerves was 62·6% (Table 3). The total number of patients with silent neuropathy was 105, which was 55·9% of all NFI patients.

Figure 1 illustrates the effect of prednisolone on affected nerves. Sensory function improved in 73–81% of the nerves either partially or completely. The full recovery of sensibility in ulnar, median and p. tibial nerve is 62·6%, 55·9% and 57·4%, respectively. A high percentage of motor function improvement was found in facial and radial nerves but much less in ulnar and peroneal nerve.

Table 2. Basic data of patients with NFI in the study

	Sex		Type of leprosy		Relationship of MDT and NFI			
Age at diagnosis of NFI	M	F	MB	PB	Pre-MDT	On-MDT	RFT	?
≤14	2	0	2	0	1	0	1	
15–29	37	11	40	8	20	19	8	
30–39	38	14	46	6	18	23	11	
40–49	34	9	32	11	14	16	12	
50–59	28	5	27	6	11	8	12	
≥60	10	3	12	1	6	2	5	
Total	149	42	159	32	70	68	49	4

Table 3. Details of nerve involvement and percentage of silent neuropathy among affected nerves

Nerve	Total affected nerves	Silent neuropathy		Nerve pain	Nerve tenderness
		Nerves	%		
Facial[a]	21				
Ulnar	124	72	58·1%	12	40
Median	74	50	67·6%	7	17
Radial[a]	7				
C. popliteal	27	18	66·7%	2	7
P. tibial	179	113	63·1%	21	45
Total	432	253	62·6%	42	109

[a]Facial and radial nerves were not required to record pain/tenderness in this study.

Tables 4 and 5 set forth the details of response to prednisolone in different nerves associated with NFI duration. Using Student's *t*-test to analyse sensibility score before and after prednisolone therapy, significant improvements in all nerves, even in those with a NFI duration longer than 6 months, were obtained. Motor function recovery was much less encouraging. There were no significant differences ($p > 0{\cdot}05$) between the mean motor score at the diagnosis of NFI and at the end of follow-up in both ulnar and c. popliteal nerves. On the other hand, the median nerve with a short duration of NFI presented a significant change ($p < 0{\cdot}05$). We analysed facial nerve as a whole group because of the small number and obtained a highly significant outcome ($p < 0{\cdot}01$).

Common sense would suggest that NFI treated at an 'early' stage should respond better to

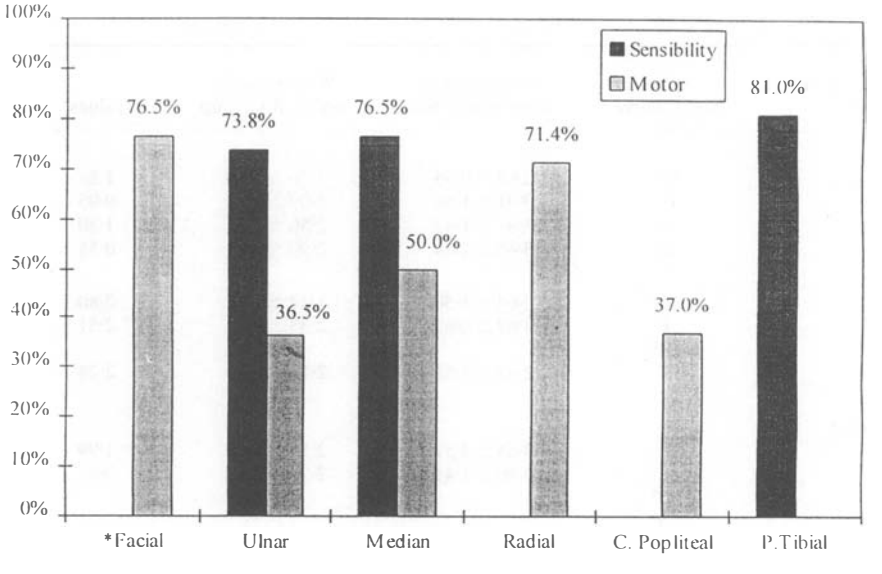

Figure 1. Percentage of nerve function improvement with prednisolone treatment in individual nerves. Two patients with bilateral facial nerves were excluded, because they were only on prednisolone for 1 and 2 months, respectively, when data were collected.

Table 4. Sensitivity changes with prednisolone treatment associated with NFI duration

Duration of NFI (months)	No. of nerves	Mean score at diagnosis of NFI	Mean score by end of follow up	*t*-values	*p*-values
Ulnar					
<1	25	2·80 ± 0·88	0·2 ± 0·5	12·84	<0·01
1–3	43	3·19 ± 0·93	1·58 ± 1·76	5·30	<0·01
4–6	18	2·50 ± 0·99	0·38 ± 0·70	7·42	<0·01
≥7	21	2·95 ± 1·02	1·47 ± 1·69	3·44	<0·05
Median					
<1	15	3·33 ± 1·63	0·27 ± 0·79	6·54	<0·01
1–3	25	3·88 ± 1·92	2·04 ± 2·41	2·99	<0·01
4–6	10	2·90 ± 1·97	1·00 ± 1·49	2·43	<0·05
≥7	18	2·94 ± 1·55	1·67 ± 1·78	2·28	<0·05
P. tibial					
<1	47	5·21 ± 2·91	0·38 ± 0·99	10·77	<0·01
1–3	61	5·36 ± 3·12	2·26 ± 3·06	5·54	<0·01
4–6	35	6·14 ± 2·95	1·58 ± 2·80	6·63	<0·01
≥7	36	7·17 ± 1·62	4·52 ± 3·91	3·76	<0·01

treatment than if treated at a 'late' stage. This is confirmed by Table 6, which reveals a significant difference in sensibility changes between the group with NFI duration less than 1 month and any other groups with longer duration, with the exception of t1–t3.

Table 7 presents the changes of nerve scores which were calculated by individual person instead of by individual nerve. Comparisons of nerve score changes by calculating the difference of scores at diagnosis of NFI from that at the completion of follow-up show highly

Table 5. Motor function changes with prednisolone treatment associated with NFI duration

Duration of NFI (months)	No. of nerves	Mean score at diagnosis of NFI	Mean score by end of follow up	*t*-values	*p*-values
Ulnar					
<1	17	2·88 ± 0·65	1·76 ± 1·86	1·86	>0·05
1–3	11	3·91 ± 1·64	3·09 ± 2·34	0·95	>0·05
4–6	9	3·67 ± 1·41	2·56 ± 2·13	1·30	>0·05
≥7	10	3·40 ± 1·84	2·90 ± 2·23	0·55	>0·05
Median					
<1	11	2·64 ± 1·50	1·27 ± 1·42	2·80	<0·05
1–3	6	4·67 ± 0·82	2·33 ± 2·34	2·31	<0·05
4–6	4[a]				
≥7	7	2·43 ± 1·52	2·14 ± 1·86	2·24	>0·05
C. popliteal					
<1	11	3·55 ± 1·57	2·18 ± 1·66	1·99	>0·05
1–3	8	3·50 ± 1·41	2·75 ± 2·19	0·81	>0·05
4–6	3[a]				
≥7	5[a]				
Facial					
≤6	17	2·59 ± 0·87	0·88 ± 1·17	4·84	<0·01

[a]Numbers are too small to make any meaningful statistical analysis.

Table 6. Comparison of mean differences in sensitivity associated with duration of NFI (the difference of score at diagnosis of NFI from that at the completion of follow-up)

Nerves by groups	No. nerves with NFI		Difference (mean ± SD)			
A B	A	B	A	B	*t* values	*p* values
Ulnar						
u1–u2	25	43	2·68 ± 0·9	1·79 ± 1·77	2·34	<0·05
u1–u3	25	18	2·68 ± 0·9	2·11 ± 0·94	2·01	=0·05
u1–u4	25	21	2·68 ± 0·9	1·48 ± 1·51	3·33	<0·01
u2–u3	43	18	1·79 ± 1·77	2·11 ± 0·94	0·72	>0·05
u2–u4	43	21	1·79 ± 1·77	1·48 ± 1·51	0·69	>0·05
u3–u4	18	21	2·11 ± 0·94	1·48 ± 1·51	1·52	>0·05
Median						
m1–m2	15	25	3·07 ± 1·39	1·84 ± 1·99	2·1	<0·05
m1–m3	15	10	3·07 ± 1·39	1·90 ± 1·30	2·1	<0·05
m1–m4	15	18	3·07 ± 1·39	1·28 ± 1·97	2·96	<0·01
m2–m3	25	10	1·84 ± 1·99	1·90 ± 1·30	0·09	>0·05
m2–m4	25	18	1·84 ± 1·99	1·28 ± 1·97	0·91	>0·05
m3–m4	10	18	1·90 ± 1·30	1·28 ± 1·97	0·89	>0·05
P. tibial						
t1–t2	47	61	4·83 ± 2·90	3·10 ± 3·52	2·73	<0·01
t1–t3	47	35	4·83 ± 2·90	4·51 ± 3·18	0·47	>0·05
t1–t4	47	36	4·83 ± 2·90	2·67 ± 2·75	3·44	<0·01
t2–t3	61	35	3·10 ± 3·52	4·51 ± 3·18	1·96	=0·05
t2–t4	61	36	3·10 ± 3·52	2·67 ± 2·75	0·63	>0·05
t3–t4	35	36	4·51 ± 3·18	2·67 ± 2·75	2·61	>0·05

u, ulnar u1, u2, u3, u4 indicate the duration of NFI <1 month, 1–3 months, 4–6 months, ≥7 months, respectively.
m, median m1, m2, m3, m4 as the same as ulnar nerve.
p. tibial t1, t2, t3, t4 as the same as ulnar nerve.

significant differences between matching groups of I–II and I–III, and significant difference between groups I–IV. There is no significant difference among each matching groups of II–III, II–IV and III–IV. In group I, extra intensive training was given annually by experts at national level, and the nylon monofilament instead of ballpoint was applied in the sensitivity test in the present study.

The months taken to reach a maximum improvement in each nerve are: ulnar 3·52 ± 1·90, median 3·54 ± 1·84, posterior tibial 5·37 ± 2·87 for sensation and ulnar 4·71 ± 2·78, median 4·31 ± 2·09, c. popliteal 4·40 ± 3·00, facial 4·92 ± 2·53 for motor.

Discussion

This study is part of a collaborative project between the MOH of China and TLMI on leprosy rehabilitation and POD, and is primarily concerned with the feasibility and effectiveness of treating NFI with a standardized regimen of prednisolone in the field. Nerve function assessment and NFI treatment were implemented by experienced leprosy control staff who received intensive training in POD courses, which included the very important aspects of early detection and treatment of NFI. The results of this study are encouraging.

Table 7. Comparison of nerve score changes in individual person between groups (the difference of score at diagnosis of NFI from that at the completion of follow-up)

Comparison between groups	No. with NFI		Difference (mean ± SD)			
A B	A	B	A	B	*t* values	*p* values
I–II	97	36	7·08 ± 5·59	4·11 ± 4·17	2·90	<0·01
I–III	97	46	7·08 ± 5·59	4·33 ± 4·39	2·93	<0·01
I–IV	97	20	7·08 ± 5·59	3·90 ± 4·56	2·38	<0·05
II–III	36	46	4·11 ± 4·17	4·33 ± 4·39	0·23	>0·05
II–IV	36	20	4·11 ± 4·17	3·90 ± 4·56	0·17	>0·05
III–IV	46	20	4·33 ± 4·39	3·90 ± 4·56	0·36	>0·05

Group I Pilot areas in Sichuan province (Leprosy endemic areas, with a monofilament trial and intensive training from national centre).
II Pilot areas in Yunnan province (leprosy endemic areas).
III Pilot areas in Fujian, Guangxi, Hubei, Anhui and Shaanxi provinces (non-endemic areas anymore, but have not attained the goal of elimination).
IV Pilot areas in Shanghai, Jiangsu, Yangzhou, Shangdong (have already achieved the goal of elimination).

The occurrence of NFI varies in different studies.[7,8] In our study, the overall incidence rate of NFI in PB group was 3·9 per 100 person years at risk which compares well with that of Richardis', but in MB group, it was 4·9 per 100 person years at risk, which is lower than that of Richardis' 7·5%.[9] In this study, 36·7% of NFI occurred before the diagnosis of leprosy. That means the history of this group was dependent on the observations and recollection of patients. Others developed on-MDT (35·6%) and after release from MDT (25·7%). Quite a number of patients develop new NFI after their release from MDT and a nerve function assessment should be given at regular intervals during the first year after RFT. The frequency of silent neuropathy varies according to different studies.[5,10] Overall, 7·5% of all patients (105/1407), or 55·9% of NFI patients, suffered from silent neuropathy; and the percentage of silent neuropathy in NFI nerves was 62·6%. Some authors had even observed over 65% of patients with recent NFI who did not present complaints spontaneously.[9] In one study, 33% of patients were found with silent neuritis.[5] Without regular and proper ST/VMT assessment, the high percentage of 'silent neuropathy' will undoubtedly result in impairment and disabilities in many patients.

Sensory impairment responded to prednisolone satisfactorily, giving a recovery rate of 73·8%, 76·5% and 81·0% in ulnar, median and posterior tibial nerve, respectively. Where NFI had existed for a short period, the chances for recovery were better. In our study, nerve function may attain significant improvement in those patients with a duration of NFI (sensation) longer than 6 months, especially in posterior tibial nerve (Table 4). Thus, the duration of 6 months of NFI is not a strict demarcation line between giving or not giving conticosteroid therapy.

Motor function recovery varies in different nerves. Facial nerve presented a satisfactory result (76·5%) which is in line with another study.[3] The recovery rates of ulnar, median and c. popliteal nerve were low as shown in Table 5, in which there is no significant difference of motor scores at diagnosis of NFI and at completion of follow-up in ulnar and c. popliteal nerves. The possible reasons are:

1 VMT tests in this study only include four grades for practical reasons.

2 VMT tests seem more difficult than ST tests for field staff and may result in more mistakes.
3 We noted some persons affected by leprosy who only had motor function loss without sensation loss. This phenomenon showed that sensory impairment recovered in the past without recovery in motor impairment.

We can try to explain the variation of sensibility recovery associated with the duration of NFI. The changes in sensory scores are calculated by using the scores at diagnosis of NFI minus those at the completion of follow-up. The groups are divided by NFI duration (Table 6). We find that only the group with NFI duration less than 1 month had score changes significantly different from each of the other groups (NFI duration 1–3, 4–6, ≥7 months). Differences in score changes between the other groups are not significant. It is clear from available pathological evidence that extensive neuropathy is already present before the patients had any sign and/or symptom of NFI. Motor and sensory nerve conduction velocity measurements are able to pick up NFI before it becomes clinically evident.[11] Once it becomes clinically detectable, NFI is not at the 'early' stage. That there is no significant difference in score changes among those groups with NFI duration of 1–3, 3–6 and ≥7 months seems to prove the above point. Therefore, it is important to develop more sensitive equipment to detect the real 'early' sensitivity impairment in the field.

Our study also indicated that with well-trained field staff and proper equipment for nerve function assessment, NFI management is more effective.

Acknowledgements

We would like to thank all the staff who are involved in this project for spending a lot of time on visiting patients and performing detailed nerve function assessments. We are grateful to Dr P. D. Samson and Miss A. Piefer for their financial and technical support. Thanks are also due to Dr X. S. Chen and Mr C. B. Zhu for their substantial help in statistical analysis.

References

[1] Van Brakel WH, Khawas IB. Nerve function impairment in leprosy: an epidemiological and clinical study—Part 2: results of steroid treatment. *Lepr Rev*, 1996; **67:** 104–118.
[2] Croft RP, Richardus JH, Smith WCS. Field treatment of acute nerve function impairment in leprosy using a standardized corticosteroid regimen—first year's experience with 100 patients. *Lepr Rev*, 1997; **68:** 316–325.
[3] Kiran KU, Hogeweg M, Suneetha S. Treatment of recent facial nerve damage with lagophthalmos, using a semistandardized steroid regimen. *Lepr Rev*, 1991; **62:** 150–154.
[4] Smith WCS, Zhang GC. Prevention of impairment in leprosy; results from a collaborative project in China. *Int J Lepr*, 1995; **63:** 507–517.
[5] Jiang J, Wei XY, Zhang GC. Silent neuritis in leprosy—report from national rehabilitation project. *China Lepr J*, 1996; **12:** 159–162.
[6] Waston JM. Preventing disability in leprosy patients. TLMI 1986.
[7] Van Brakel WH, Khawas IB. Nerve damage in leprosy: an epidemiological and clinical study of 396 patients in west Nepal—part I. Definitions, methods and frequencies. *Lepr Rev*, 1994; **65:** 204–221.
[8] Richardus JH, Finlay KM, Croft RP, Smith WCS. 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.
[9] Becx-Blenmink M, Berhe D, Mannetje W'T. The management of nerve damage in the leprosy control services. *Lepr Rev*, 1990; **61:** 1–11.
[10] Bernink EHM, Voskens JEJ. Study on the detection of leprosy reactions and the effect of prednisolone on various nerves, Indonesia. *Lepr Rev*, 1997; **68:** 225–232.
[11] Brown RB, Kovindha A. Clinical assessment of early leprous neuropathy with electrophysiological correlation. Paper presented at the 14th International Leprosy Congress, Orlando, Florida, 1993 (Abstract No. 35).