MONOFILAMENT ASSESSMENT OF NEUROPATHY IN A COMMUNITY DIABETES CLINIC

P Rheeder, J T van Wyk, J W E Hokken, H M Hueting

Objective. To compare the detection of diabetic neuropathy using monofilament, cotton wool, pinprick, vibration sense and symptom evaluation.

Setting. The diabetes clinic of a community hospital.

Methods. Two examiners evaluated 89 women with diabetes mellitus (DM) using a 10 g monofilament, cotton wool, pinprick and a 128 Hz tuning fork after completion of a University of Texas subjective peripheral neuropathy verbal questionnaire.

Results. Vibration sense was abnormal in either foot in 8% of subjects. Neuropathy as defined by monofilament, cotton wool and pinprick was present in 26%, 3% and 6% of patients respectively. The respective kappa values (κ) for the comparison between monofilament neuropathy and cotton wool neuropathy, pinprick neuropathy and symptom-defined neuropathy were 0.18, 0.21 and 0.06. The κ-value comparing monofilament and tuning fork-defined neuropathy was 0.24. There was fair agreement between 10 versus 3 sites (κ = 0.60).

Conclusion. More abnormalities were detected using the monofilament compared with cotton wool or pinprick. There was poor concordance between symptoms and clinically detected neuropathy. The ideal number of sites that need to be evaluated is still contentious.

S Afr Med J 2002: **92:** 715-719.

Diabetic foot complications are the commonest cause of non-traumatic lower extremity amputations in the industrialised world. The risk of lower extremity amputation is 15 - 46 times higher in patients with diabetes mellitus (DM) than in persons who do not have DM.[1,2] Furthermore, diabetic foot complications are the most frequent reason for hospitalisation in patients with DM, accounting for up to 25% of all diabetic admissions in the USA and Great Britain.[3] A non-healing foot ulcer precedes approximately 85% of all amputations. Diabetic foot ulcers and lower extremity amputations are serious and expensive complications that occur in as many as 15% of people with DM during their lifetime.[4] The incidence of diabetes-related lower extremity amputation in South Africa is unknown. Relatively simple inexpensive interventions may decrease the amputation rate by up to 85%.[5] The neuropathic component in the aetiological pathway (less than 15% of ulcers are purely ischaemic)[6,7] is so important that the emphasis in the foot examination is on neurological testing.

Various studies have identified the monofilament as a valid and sensitive instrument to predict foot ulceration and/or amputation by detecting neuropathy.[8-11] However, the method employed and the number of sites tested varies in different studies and guidelines. The International Working Group on the Diabetic Foot[12] advises that 3 sites be tested, in comparison with the 10 sites used by Armstrong and Lavery[8] (Fig. 1). Holewski *et al.*[13] used the dorsal surface of the foot between the first and second toes and the base of the third and fifth metatarsals. Olmos *et al.*[14] tested three sites, the Hansen's Disease Center[15] recommends testing 10 sites and Kumar *et al.*[16] tested only one site. The monofilament is not widely available in all settings in South Africa. Many clinics use cotton wool, pinprick and vibration sense to detect neuropathy. The aim of our study was to determine the prevalence of and agreement between monofilament, cotton wool, pinprick, vibration sense and symptom-defined neuropathy in a group of South African DM subjects.

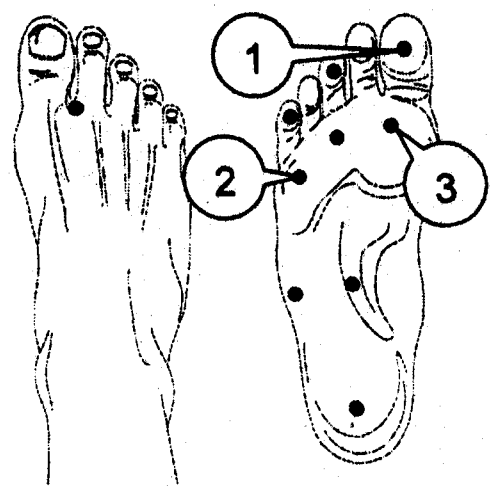

Fig. 1. Possible monofilament testing sites (10 sites (dots) of Armstrong and Lavery[8] and 3 sites (call outs) of the International Working Group on the Diabetic Foot[12]).

METHODS

This cross-sectional study was done at Mamelodi Hospital, a community hospital in the Mamelodi suburb of Pretoria, South Africa. For most patients with DM this hospital serves as their source of primary care. Female patients in the waiting room of

Clinical Epidemiology Unit, University of Pretoria
P Rheeder, MB ChB, FCP(SA), MMed, MSc
J T van Wyk, MB ChB
J W E Hokken, medical student
H M Hueting, medical student

the Mamelodi Hospital diabetes outpatient clinic, aged between 30 and 70 years and with type 2 DM, were invited to participate. Female subjects were chosen because they represent approximately three-quarters of the diabetes clinic and in our experience they are also more likely to keep research-related appointment visits than the men. A total of 134 women were invited and 112 (83.6%) wished to participate. Of these, 93 patients (69.4%) subsequently came to the clinic for evaluation. Patients were compensated for their transportation costs. Approval was obtained from the Ethics and Protocol Committee of the Pretoria Academic Hospital. Informed consent was obtained from every participant.

Two medical students evaluated the feet during their research elective. Before the project they completed a 3-week period of orientation and training. During this period the questionnaire and examination were standardised. All patients visited the clinic twice. Approximately six patients a day were examined, on three days of the week.

The evaluation included a standardised questionnaire, basic clinical measurements and neurovascular evaluation of the patients' feet. Neurological symptoms were evaluated using the University of Texas subjective peripheral neuropathy verbal questionnaire.[9] This consists of four questions: (*i*) do your feet ever feel numb?; (*ii*) do your feet ever tingle, as if electricity were travelling into your foot?; (*iii*) do your feet ever feel as if insects were crawling on them?; and (*iv*) do your feet ever burn? A positive answer to any of the four questions was regarded as a positive response for neuropathy. An interpreter was used when a patient was not able to understand or answer the questions in English.

Weight was determined to the nearest 0.1 kg standing barefoot in light clothing on a calibrated electronic scale (Tanita, Tokyo). Height was determined to the nearest 0.1 cm using a measuring stick attached to the wall. Body mass index (BMI) was calculated as mass/height in m^2. Waist-hip ratio was determined by measuring the waist at the smallest diameter below the xiphisternum and the umbilicus (at the end of a mild expiration), and the hips at the level of maximal protrusion of the gluteus maximus muscles posteriorly and the symphysis pubis anteriorly. Two measurements were taken and if there was more than 2 cm difference a third was taken. The mean of the two measurements or the closest two in the case of three measurements were used to calculate the waist-hip ratio. Measurements were done to the nearest 0.1 cm. Blood pressure was measured in the sitting position after at least 5 minutes' rest, with the right arm resting on a table, using a mercury baumanometer. Two measurements were taken with at least 1 minute between measurements. If there was a difference of more than 5 mmHg between readings a third reading was taken and the mean of the two closest measurements was used to determine the mean blood pressure. Mid-arm circumference was measured, and a large cuff (18 cm rubber bladder) was used for an arm circumference 33 cm or greater. The dorsalis pedis and tibialis posterior arteries were palpated in both feet.

Neurological evaluation

Vibration sense was tested using a 128 Hz tuning fork. The forehead was used as a reference of normal vibratory sense. This was evaluated by asking the subjects what they felt, a response indicating vibration was acceptable. The first metatarsal head was tested initially; if vibration sense was not present the test proceeded to the medial malleolus, and if still not present the tuberositas tibia was tested. Vibration sense was graded as present or absent.

Proprioception was tested by placing the examiner's fingers on the lateral aspects of the big toe and moving it plantarly and dorsally. The patients were asked to close their eyes and tell the examiner the position of the big toe (up or down). Sensation was evaluated using a 5.07/10 g monofilament (Sensory Testing Systems, Dallas) cotton wool and pinprick (using a wooden toothprick) at 10 specified sites. The forehead was used as a reference for normal sensory perception. Before evaluation, the testing was demonstrated on patients' hands so that they were familiar with the procedure. Subjects were instructed to close their eyes and to indicate when and in which foot they felt the monofilament. Where callus was present at a particular site, the closest area without callus was used. The order in which the sites were tested was random. The cotton wool and pinprick assessments were performed in the same way. A second examiner undertook the cotton wool and pinprick evaluations (blinded to the monofilament results. The testing instrument was applied once to each site, and absence of sensation at four or more sites was regarded as indicating neuropathy.[8,9]

Data analysis

Descriptive statistics included means and standard deviations for parametric data and medians with 25th and 75th quartiles for non-parametric data. Concordance was evaluated using the Kappa statistic. Kappa (κ) is a measure of agreement between two observers that takes into account the agreement expected by chance, in the formula: Agreement between observers (%) – agreement expected by chance (%) 100 – agreement expected by chance (%).

It has a maximum of 1.00 when agreement is perfect, a value of zero indicates agreement no better than chance, and negative values show less than chance agreement.[17] Continuous data between groups were compared using Student's *t*-tests or Mann-Whitney *U*-tests depending on the distribution of the data.

RESULTS

One patient was excluded from the analysis as she failed to understand the instructions regarding the foot examination and 3 subjects had their data recorded at a later date. Both examiners examined 21 patients and the κ-value for monofilament-defined neuropathy was 0.71 (good strength of

agreement).[17] Table I shows the basic characteristics of the study population. The mean age was 58.1 years, and the mean BMI 31.8 kg/m², with a mean body fat percentage of 42.1%. The results of the foot examination are given in Table II. In 11% of the subjects both tibialis posterior and dorsalis pedis arteries were not palpable in either foot. Vibration sense tested on the first metatarsal head was abnormal in 8% of all subjects. These were all at the level of the first metatarsal head; tested on the medial malleolus and tuberositas tibiae no abnormalities were found. Proprioception was normal in all the subjects. Regarding neuropathy, more abnormalities were detected with the monofilament (26%) compared with the pinprick (3%) and the cotton wool (6%). Most of the patients (75%) reported 'yes' to at least one of the neuropathy symptom questions.

Table I. Characteristics of the study population

	N	Mean (SD)	Median (25th and 75th percentile)
Age (yrs)	89	58.09 (8.31)	
Education (yrs)	89		6.00 (3.00, 8.00)
BMI (m/kg²)	88	31.75 (5.15)	
Waist-hip ratio	89	0.86 (0.07)	
Systolic BP (mmHg)	89	149.38 (25.47)	
Diastolic BP (mmHg)	89	88.75 (10.95)	
S-HbA1c (%)	81	9.81 (2.27)	
F-S LDL (mmol/l)	82	3.19 (1.20)	
F-S HDL (mmol/l)	82	1.37 (0.39)	
F-S TG (mmol/l)	82		1.19 (0.79, 1.87)
F-S cholesterol (mmol/l)	82	5.32 (1.54)	
F-S Lp (a) (mg/dl)	81		45.10 (25.20, 89.70)
S-creatinine (mmol/l)	82	76.78 (36.41)	
Albumin/creatinine ratio (mg/mmol)	80		1.15 (0.68, 4.18)
	N	*N* (%)	
Ethnic group	89		
Sotho/Pedi		40 (44.9)	
Zulu		18 (20.2)	
Other		31 (34.8)	
Postmenopausal	89	68 (76.4)	
Duration of DM	89		
≤ 5 years		42 (47.2)	
> 5 years		47 (52.8)	
DM treatment	88		
Diet		2 (2.3)	
Oral agents		66 (75.3)	
Insulin		20 (22.7)	
Hypertensive	89	70 (78.9)	
Alcohol users*	89	5 (5.6)	

* Answering 'yes' to 'Do you use alcohol?'.
SD = standard deviation; BMI = body mass index; BP = blood pressure; S-HbA_{1c} =haemoglobin A_{1c}; F-S-LD~L = fasting serum low-density lipoprotein; F-S HDL= fasting serum high-density lipoprotein; F-S TG = fasting serum triglyceride; F-S cholesterol = fasting serum cholesterol; F-S Lp(a) = fasting serum lipoprotein (a); S-creatinine = serum creatinine.

Table II. Abnormalities found on foot examination

Abnormality	*N*	Proportion (%)
Dorsalis pedis and tibialis posterior absent	89	10 (11.2)
Vibration sense abnormal*	89	7 (7.9)
Neuropathy†		
Monofilament	89	23 (25.8)
Pinprick	89	3 (3.3)
Cotton wool	89	5 (5.6)
Neuropathy according to questionnaire‡	89	67 (75.3)

* At first metatarsal head of either foot.
† Neuropathy defined as sensation absent at four or more sites either left and/or right.
‡ University of Texas Neuropathy Questionnaire.

Table III shows the comparison for neuropathy defined according to monofilament, pinprick cotton wool and the neurological questionnaire. The κ-values for the pinprick, cotton wool, the neurological questionnaire and vibration sense are 0.18, 0.21, 0.06 and 0.24 respectively. The same table shows the concordance between testing for neuropathy with a monofilament according to Armstrong *et al.*[9] and Lavery *et al.*[10] using 10 sites, and the method recommended by the International Working Group on the Diabetic Foot[12] using only 3 sites, under the hallux, metatarsal 1 and metatarsal 5. The κ-value is 0.60, which is considered moderate.[17]

We did not find any differences between the neuropathy group (monofilament-defined) and the non-neuropathy group as far as age, duration of diabetes, lipid values or haemoglobin A_{1c} (HbA_{1c}) were concerned ($P > 0.05$). The only other long-term complication measured in this study was nephropathy (urinary albumin creatinine ratio). The median ratio was 1.95 in the neuropathy group ($N = 20$) and 1.15 in the non-neuropathy group ($N = 60$, $P = 0.69$).

Discussion

In this sample of 89 women from a diabetic clinic with a study population of approximately 800 (men and women), 11% of patients had both foot pulses absent on palpation. Vibration sense was absent in at least one foot in 8% and monofilament-defined neuropathy was present in 26%. Cotton wool and the pinprick examination detected neuropathy far less frequently and the neuropathy symptom questionnaire showed poor concordance with monofilament-defined neuropathy. The Texas questionnaire appears to be overly sensitive in this

Table III. Concordance between different measures of neuropathy

			Agreement (%)	Expected (%)	Kappa value	Standard error
	Pinprick*					
Monofilament*	No	Yes	77.5	72.5	0.18	006
No	66	0				
Yes	20	3				
	Cotton wool					*
Monofilament*	No	Yes	77.5	71.4	0.21	0.07
No	65	1				
Yes	19	4				
	Questionnaire†					
Monofilament*	No	Yes	41.6	37.8	0.06	0.06
No	18	48				
Yes	4	19				
	Vibration sense‡					
Monofilament*	No	Yes	77.5	70.4	0.24	0.08
No	64	18				
Yes	2	5				
	Monofilament ≥ 2/3 sites absent					
Monofilament ≥ 4/10 sites absent	No	Yes	86.3	66.0	0.60	0.10
No	64	2				
Yes	10	13				

* Four or more sites absent either left or right.
† At least one neuropathy question affirmative.
‡ Vibration sense absent at the first metatarsal.

population, with 75% of subjects answering 'yes' to at least one of the questions.

Even though the subject selection was not completely random it is felt that the subjects were fairly representative of women seen at the clinic. Another possible limitation is that medical students performed the examinations. However, after a 3-week training period they performed these examinations up to standard. Both examiners (JWEH, HMH) evaluated the first 21 patients. They were blinded regarding each other's evaluation. The findings of the pinprick and cotton wool exam may have influenced the monofilament exam. Of the 21 patients, however, only 4 had cotton wool-defined neuropathy and 2 had pinprick-defined neuropathy.

There is currently an emphasis on prevention of lower extremity amputation in subjects with DM. A number of studies have recently been done with the aim of optimising the peripheral neurological screening exam.

Many of these studies did not use the monofilament as an explicit part of the screening evaluation. In those that do, there was no standard way of using the monofilament. There has been an attempt by the International Working Group on the Diabetic Foot[12] to standardise the monofilament screening (subsequently endorsed by the International Diabetes Federation). For details on the practical screening of the diabetic foot see **http://www.diabetic-foot-consensus.com** and **htt://ndep.nih.gov/materials/pubs/feet/feet.htm** as well as Fig. 2. Monofilaments can be ordered from the USA (**http://www.bphc.hrsa.gov/leap/**) or the Netherlands (**verkoop@wpbpododepot.nl**).

Pham *et al.*[11] evaluated predictors of ulceration prospectively in a group of subjects with diabetes. They identified the neuropathy disability score (a clinical examination) combined with a 10 g monofilament test as having the best sensitivity, and foot pressure measurement combined with the neuropathy disability score as having the best specificity for prediction of ulceration. Meijer *et al.*[18] devised a hierarchical scoring system based on the neuropathy disability score. Their resultant 8-item Diabetic Neuropathy Examination (DNE) at a cut-off level of 3 - 4 had a sensitivity and specificity of 0.96 and 0.57 for abnormal monofilament scores respectively. Franse *et al.*[19] have shown that although there is a significant association between symptoms of pain, sensory alteration and 'numbness of the feet' in particular, and a clinical neurological examination, the prediction of polyneuropathy from neuropathic symptoms was unsatisfactory.

In general, simple clinical measures such as ankle reflexes,

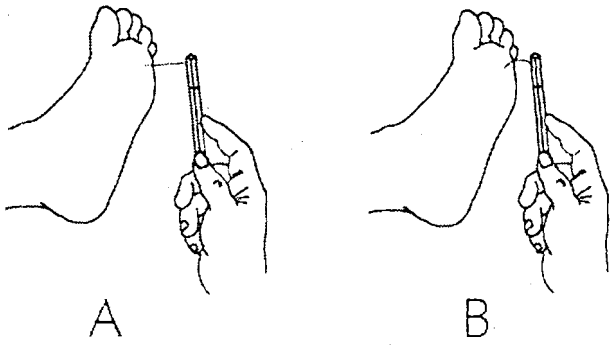

Fig. 2. Correct way of applying the 1.5-second buckling force of the monofilament.

vibration sense (as assessed by a 128 Hz tuning fork) and monofilament testing are recommended as basic screening tools for amputation prevention. Neuropathy detected by monofilament has been shown to predict ulceration and also has less inter-person and test-retest variability. Inter- and intra-rater agreement κ-values are 0.72 and 0.83.[20] Testing of the plantar surface of the toes and metatarsal heads provides most of the discriminatory ability; the dorsum and the heel provide little additional information according to some.[13] The proposed cut-offs for defining an insensate foot range from 1 to 3 out of 6 sites, providing a sensitivity of 0.84 - 1.00 and specificity of 0.77 - 1.00 to predict a current or future ulcer.[4]

The International Working Group on the Diabetic Foot[12] has proposed guidelines based on expert opinion. They advise monofilament testing at 3 sites, using three tests at each site with one sham. Two out of three abnormal tests at a particular site will then be regarded as abnormal. Others such as Armstrong *et al.*[8,9] and Lavery *et al.*[10] have validated their system using 10 sites and using a single 'yes' response as an indicator of sensation present.

Our study using only the single 'yes' response for sensation if present tested at 3 sites instead of 10 would have missed 10 of 23 subjects with neuropathy (as defined by 4 or more abnormal sites). In our patient population we find the use of 3 tests per site including one sham cumbersome and difficult for the patients to understand (this may reflect difficulties in communication because of language barriers).

McGill and co-workers[21] investigated the effect of testing at different sites and found that at least one abnormal test at the plantar aspect of the first metatarsal or the plantar aspect of the fifth metatarsal had the best combined sensitivity (80%) and specificity (86%). In practice they then advise testing these two sites only.

The use of the monofilament, even though simple in and of itself, can be complicated by a number of factors. Not all 10 monofilaments are the same with regard to buckling force and a single monofilament should not be used on more than 10 patients on a given day, after which adequate time should be given for filament recovery.[22]

Our study is small and represents approximately 15% of the diabetic women seen at this clinic. Neuropathy was also not validated by quantitative testing. The monofilament has, however, been validated in other studies as a screening tool for neuropathy and the high-risk foot. In our study the proportion of subjects deemed at risk according to screening guidelines varies depending on the examination technique used. Monofilament testing identifies a larger proportion of such patients than does cotton wool or pinprick examination, but the optimal sites to be tested are still unclear.

This study was part of the larger Mamelodi Diabetes Foot Study, which was funded by the Hendrik Verwoerd Research Trust.

References

1. Armstrong DG, Lavery LA, Quebedeaux TL, Walker SC. Surgical morbidity and the risk of amputation due to infected puncture wounds in diabetic versus nondiabetic adults. *South Med J* 1997; **90:** 384-389.
2. Lavery LA, Ashry HR, van Houtum W, Pugh JA, Harkless LB, Basu S. Variation in the incidence and proportion of diabetes-related amputations in minorities. *Diabetes Care* 1996; **19:** 48-52.
3. Pecoraro RE, Reiber GE, Burgess EM. Pathways to diabetic limb amputation. Basis for prevention. *Diabetes Care* 1990; **13:** 513-521.
4. Mayfield JA, Reiber GE, Sanders LJ, Janisse D, Pogach LM. Preventive foot care in people with diabetes. *Diabetes Care* 1998; **21:** 2161-2177.
5. Litzelman DK, Slemenda CW, Langefeld CD, *et al.* Reduction of lower extremity clinical abnormalities in patients with non-insulin-dependent diabetes mellitus. A randomized, controlled trial. *Ann Intern Med* 1993; **119:** 36-41.
6. Chantelau E, Breuer U, Leisch AC, Tanudjaja T, Reuter M. Outpatient treatment of unilateral diabetic foot ulcers with 'half shoes'. *Diabet Med* 1993; **10:** 267-270.
7. Ritz G, Kushner D, Friedman S. A successful technique for the treatment of diabetic neurotrophic ulcers. *J Am Podiatr Med Assoc* 1992; **82:** 479-481.
8. Armstrong DG, Lavery LA. Diabetic foot ulcers: prevention, diagnosis and classification. *Am Fam Physician* 1998; **57:** 1325-1328.
9. Armstrong DG, Lavery LA, Vela SA, Quebedeaux TL, Fleischli JG. Choosing a practical screening instrument to identify patients at risk for diabetic foot ulceration. *Arch Intern Med* 1998; **158:** 289-292.
10. Lavery LA, Armstrong DG, Vela SA, Quebedeaux TL, Fleischli JG. Practical criteria for screening patients at high risk for diabetic foot ulceration. *Arch Intern Med* 1998; **158:** 157-162.
11. Pham H, Armstrong DG, Harvey C, Harkless LB, Giurini JM, Veves A. Screening techniques to identify people at high risk for diabetic foot ulceration: a prospective multicenter trial. *Diabetes Care* 2000; **23:** 606-611.
12. International Working Group on the Diabetic Foot. *International Concensus on the Diabetic Foot.* 1999.
13. Holewski JJ, Stress RM, Graf PM, Grunfeld C. Aesthesiometry: quantification of cutaneous pressure sensation in diabetic peripheral neuropathy. *J Rehabil Res Dev* 1988; **25:** 1-10.
14. Olmos PR, Cataland S, O'Dorisio TM, Casey CA, Smead WL, Simon SR. The Semmes-Weinstein monofilament as a potential predictor of foot ulceration in patients with non-insulin-dependent diabetes. *Am J Med Sci* 1995; **309:** 76-82.
15. Gillis W. Long Hansen's Disease Center. *Care of the Foot in Diabetes: The Carville Approach.* US Government Printing Office, 1994.
16. Kumar S, Fernando DJ, Veves A, Knowles EA, Young MJ, Boulton AJ. Semmes-Weinstein monofilaments: a simple, effective and inexpensive screening device for identifying diabetic patients at risk of foot ulceration. *Diabetes Res Clin Pract* 1991; **13:** 63-67.
17. Altman DG. Some common problems in medical research. In: *Practical Statistics for Medical Research.* Londong: Chapman and Hall, 1994: 403-409.
18. Meijer JW, van Sonderen E, Blaauwiekel EE, *et al.* Diabetic neuropathy examination: a hierarchical scoring system to diagnose distal polyneuropathy in diabetes. *Diabetes Care* 2000; **23:** 750-753.
19. Franse LV, Valk GD, Dekker JH, Heine RJ, van Eijk JT. 'Numbness of the feet' is a poor indicator for polyneuropathy in Type 2 diabetic patients. *Diabet Med* 2000; **17:** 105-110.
20. Maser RE, Nielsen VK, Bass EB, *et al.* Measuring diabetic neuropathy, assessment and comparison of clinical examination and quantitative sensory testing. *Diabetes Care* 1989; **12:** 270-275.
21. McGill M, Molyneux L, Spencer R, Heng LF, Yue DK. Possible sources of discrepancies in the use of the Semmes-Weinstein monofilament. Impact on prevalence of insensate foot and workload requirements. *Diabetes Care* 1999; **22:** 598-602.
22. Booth J, Young MJ. Differences in the performance of commercially available 10-g monofilaments. *Diabetes Care* 2000; **23:** 984-988.

Accepted 24 April 2002.