Veterans Administration

Journal of Rehabilitation Research and Development Vol. 25 No. 2
Pages 1–10

Aesthesiometry: Quantification of cutaneous pressure sensation in diabetic peripheral neuropathy

JOHN J. HOLEWSKI, D.P.M., RICHARD M. STESS, D.P.M., PETER M. GRAF, D.P.M., and CARL GRUNFELD, M.D., Ph.D.

Rehabilitation Research and Development Department and Metabolism Section, Veterans Administration Medical Center, San Francisco, California, 94121; and, Department of Medicine, University of California, San Francisco, California 94121

Abstract—The Semmes-Weinstein pressure aesthesiometer, which measures cutaneous pressure sensation, was used for quantifying sensory loss in diabetic peripheral neuropathy. Eighty subjects comprising four groups were tested: nondiabetic controls (Group C); nonneuropathic, diabetic controls (Group DC); diabetic subjects with neuropathy and without a history of pedal ulcerations (Group DN); and, diabetic subjects with a history of or active pedal ulceration (Group DU). Cutaneous pressure sensation of 10 dorsal and plantar sites on the foot were tested, using a method of interval comparison modeled after the two-alternative forced choice algorithm. The sensitivity threshold level was defined as the lightest probe in which the subject accurately chose the correct interval in at least 2 out of 3 trials. The mean sensitivity threshold level for Group DC was not significantly increased ($p > .05$) compared to Group C. In contrast, patients with neuropathy (Group DN or DU) showed a significantly higher mean sensitivity threshold ($p < .001$) than either Group C or DC. In addition, this technique demonstrated that patients in Group DU had a mean sensitivity threshold that was statistically higher ($p < .001$) than Group DN, although both groups of patients had symptomatic neuropathy. This study provides a direct demonstration that decreased sensation of pressure occurs in the feet of diabetic patients with a history of ulceration. The best discrimination between groups is obtained by requiring that three of the six plantar forefoot sites have a sensitivity threshold level of greater than 5.07 log (0.1 mg) force as the risk discriminator level. Semmes-Weinstein aesthesiometry should now be tested in a prospective study to demonstrate its effectiveness in determining those patients at great risk of developing foot ulcers.

J. J. Holewski, R. M. Stess and P. M. Graf are with the Rehabilitation Research and Development Department, Veterans Administration, San Francisco, CA, and the Department of Medicine, University of California, San Francisco, CA.

C. Grunfeld is with the Department of Medicine, University of California, San Francisco, CA.

Address all correspondence and reprint requests to: John J. Holewski, D.P.M., Rehabilitation Research and Development Department (151-P), Veterans Administration Medical Center, 4150 Clement Street, San Francisco, CA 94121.

INTRODUCTION

Neurotrophic foot ulcerations lead to morbidity and mortality in diabetic patients (7,14,15). Boulton *et al.* have addressed the critical need for screening tests for diabetic neuropathy (5). An effective and simple screening test evaluating the extent of sensory damage caused by neuropathy is needed to identify those patients at risk for neurotrophic ulceration. A quantifiable way of measuring cutaneous sensation could be useful in following the natural history of diabetic neuropathy, and possibly may be used to stratify patients into risk groups for neurotrophic ulceration.

The standard neurological examination does not provide a quantifiable measure of sensation for the lower extremity and is strongly dependent on the examiner's technique and patient subjectivity.

Currently, many methods are available to quantify sensory thresholds and their deficit in diabetic neuropathy including: vibratory (5,18); touch-

Journal of Rehabilitation Research and Development Vol. 25 No. 2 Spring 1988

Table 1.
Subject Characteristics.

	Group C (20)	Group DC (20)	Group DN (20)	Group DU (20)
Mean age (yrs)*	63 ± 2	60 ± 2	63 ± 1	63 ± 2
Age range (yrs)	47–76	41–75	44–74	50–73
Diabetes duration mean (yrs)*	0	9 ± 1	13 ± 3	18 ± 2
Diabetes duration range (yrs)	0	1–23	3–40	5–39
Diabetic peripheral Neuropathy (percent)	0	0	100	100
Active ulceration or previous history (percent)	0	0	0	100

*Data given as mean ± SEM

pressure (4,8,12); thermal sensation (1,11); and an elaborate computer-driven system combining all three (10). Unfortunately, even with sophisticated techniques available, their widespread use and the feasibility of their being included in a screening exam are not practical. A quantifiable technique that can be readily used in the clinic and at the bedside, which could provide early recognition of patients with lower extremity sensory loss, is needed.

The evaluation of touch-pressure sensation (aethesiometry) is the only technique that uses simple compact instrumentation (inexpensive nylon monofilament probes) and has the advantage of being incorporated easily into a routine screening examination. The Semmes-Weinstein pressure aesthesiometer has been used in following the rehabilitation of nerve injuries of the hand (3,20) and in mapping sensitivity diminutions and losses of patients with Hansen's disease (4). This method has also demonstrated sensory deficits in the hands of diabetic patients with a history of neuropathy (8,12). Preliminary data indicate that Semmes-Weinstein aesthesiometry can be used effectively to measure cutaneous pressure sensation in the foot of patients with Hansen's disease and diabetes mellitus (4).

Sekuler *et al.* have described a two-alternative forced choice (2-AFC) algorithm as an objective procedure for evaluating response to light touch, reducing subjectivity in obtaining data (16). In this study, we have utilized a method of interval comparison, modeled after the 2-AFC algorithm, to test whether Semmes-Weinstein pressure aesthesiometry is sensitive enough and practical for quantification of sensory loss in peripheral neuropathy in diabetic patients.

SUBJECTS AND METHODS

Subjects

The protocol and consent form were approved by the Human Studies Committee of the University of California Medical School at San Francisco. A brief history providing the duration of diabetes, medications taken, and previous history of ulcerations was obtained. Subjects consisted of staff and patients at the San Francisco Veterans Administration Medical Center Outpatient Clinic. Eighty subjects consisting of four different groups were tested (**Table 1**). The subjects ranged from 49 to 75 years of age and all had good peripheral circulation with palpable pedal pulses. Patients who had other causes of peripheral neuropathy were excluded, including: patients with a history of heavy alcohol abuse; nerve entrapment; vitamin deficiencies; and, drug or chemically-induced neuropathy. We also excluded patients with excess callous formation on the plantar surface, if we were unable to test under the corresponding metatarsal head regions beside the callous tissue.

Group C (nondiabetic controls) consisted of 20 subjects with no history of diabetes mellitus.

Group DC (non-neuropathic, diabetic controls) consisted of 20 subjects with Type 1 or Type 2 diabetes mellitus of greater than 1-year duration and no history of pedal ulcerations or clinical symptoms of neuropathy. (Clinical symptoms of neuropathy include: numbness, burning, or any tingling or painful sensations in the feet or legs.)

Group DN (diabetic subjects with neuropathy and without a history of pedal ulceration) consisted of 20 subjects with Type 1 or Type 2 diabetes mellitus with clinical symptoms of neuropathy for greater than 1 year and absent ankle jerk reflexes.

Group DU (diabetic subjects with a history of or active ulceration) consisted of 20 subjects who had a recent or previous history of pedal ulceration.

All groups were matched in respect to age. Group DU had a significantly ($p < .01$) longer duration of

diabetes since diagnosis than Group DC. There was no significance ($p > .05$) between the mean duration in Groups DC and DN or Groups DN and DU.

Technique of aesthesiometry

Subjects were tested in the supine position in a quiet, distraction-free environment. A curtain was placed so that the subjects were unable to observe their feet or probes during testing. Ten sites (**Table 2**) were mapped out on each subject's foot with an ink marker to assure that the stimulus was applied at the same sites consistently. These sites included areas prone to pressure ulceration and are representative of various peripheral nerves and dermatomes of the foot.

The Semmes-Weinstein aesthesiometer set (**Figure 1**) used for testing consisted of a precisely calibrated series of nylon monofilaments of equal length (35 mm) and varying diameters set into individual Lucite rods (Research Designs, Inc., 7320 Ashcroft, Suite 103, Houston, TX). The common log of the force exerted by these filaments yields an approximate linear function, providing an interval scale for the computation of threshold, and has been represented by Semmes *et al.* in units of log (0.1 mg) force (17). This value represents the common logarithm of 10 times the force in milligrams required to bow the monofilament (13). Six different filaments were used, calibrated to represent 3.22, 3.61, 4.31, 5.07, 6.10 and 6.45 log (0.1 mg) force. These filaments were applied to each site by the previously described methods (3,4,8,12,13,20) exerting a consistent force at the surface of the skin when the filament buckles (**Figure 2a and 2b**).

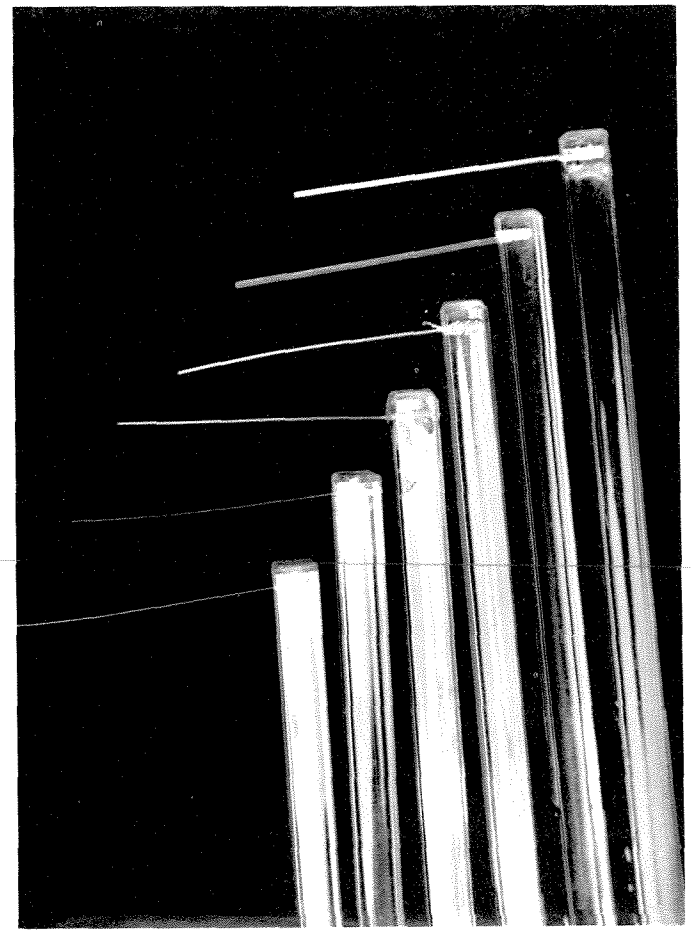

Figure 1.
Semmes-Weinstein aesthesiometer set with individual nylon monofilament probes from left to right are calibrated to represent 3.22; 3.61; 4.31; 5.07; 6.10 and 6.45 log (0.1 mg) force.

Table 2.
Sites tested.

Site No.	Location	Nerve innervation
1	Plantar—first metatarsal head	medial plantar
2	Plantar—second metatarsal head	medial plantar
3	Plantar—third metatarsal head	medial plantar
4	Plantar—fourth metatarsal head	lateral plantar
5	Plantar—fifth metatarsal head	lateral plantar
6	Plantar—hallux	medial plantar
7	Plantar—heel	medial plantar
8	Dorsal—between base of hallux and second digit	anterior tibial
9	Dorsal—base of third digit	intermediate dorsal
10	Dorsal—base of fifth metatarsal	sural

The interval comparison method was performed as follows. Based on a random-number data sheet, the filament was applied to each site during only one of two time intervals, with the count of either "one" or "two." The subject was then asked whether they felt any sensation after the first or second interval. Care was taken to be consistent, with no change in voice inflections to provide any additional clues about when the stimulus was applied. This method provides one interval of background with no stimulus and another interval of stimulus. Subjects were encouraged to select the

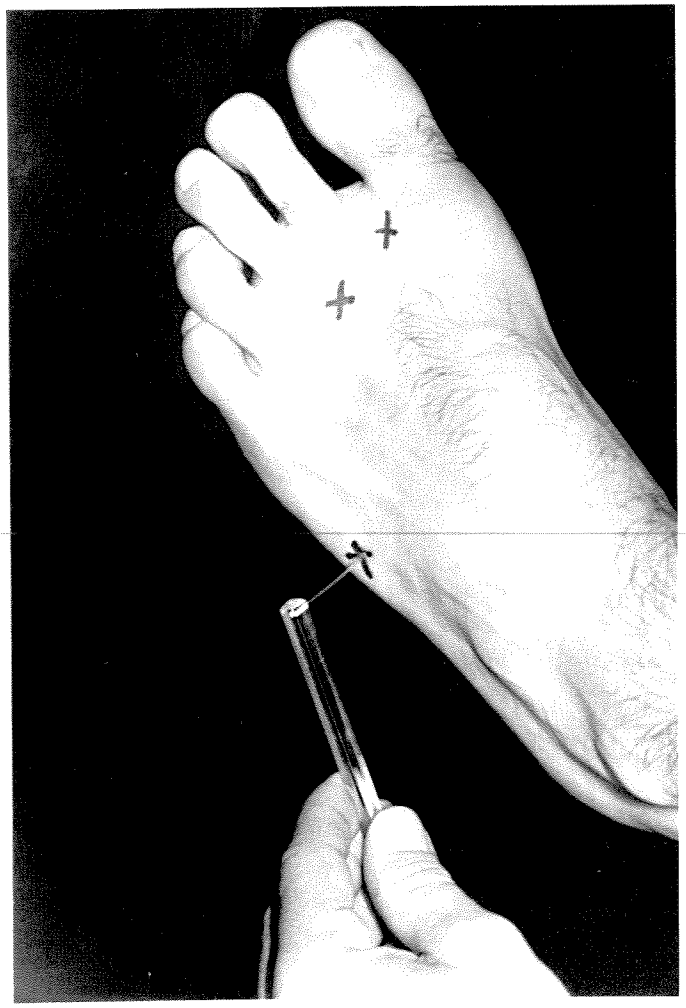

Figure 2a.
Application of an aesthesiometer probe to a site on the foot.

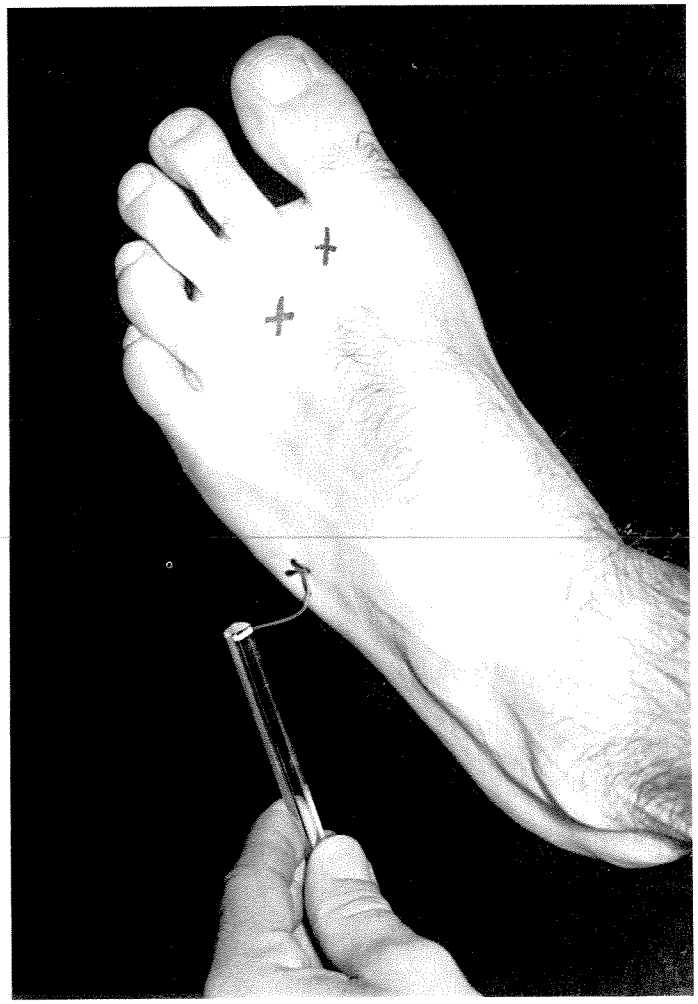

Figure 2b.
Demonstration of pressure exerted using an aesthesiometer probe; notice the bowing of the filament.

interval in which they felt the stimulus, but were allowed to report that they could not determine in which interval the stimulus was applied. One of the following three options was obtained after the subject's response: 1) the subject selected the correct count interval for the stimulus; 2) the wrong count interval was selected; or, 3) the subject was unable to select a count interval (could not feel the probe). Ordinarily in a 2-AFC method, the subjects are forced to choose an interval and the percentage correct would determine if the stimulus was perceived, usually requiring 10 to 25 trials (16).

The first 10 control patients were tested in triplicate to determine reproducibility of the interval comparison method and the appropriate number of trials that would be required to determine a sensitivity threshold. Patients were tested with all 6 probes on both feet at 10 sites; in both the descending (strongest to lightest) and ascending (lightest to strongest) direction for a total of 720 trials per patient (or 240 triplicate repetition sets per patient). The probes were used in series, not by repeating each probe multiple times.

These subjects selected the wrong interval only in 0.7 percent of all trials; i.e., 99.3 percent of all trials were either correct or the subject could not feel the probe. In 89 percent of all triplicate repetition sets, the three repetitions were concordant; either the correct interval was selected or the stimulus was not felt. The remaining 11 percent of the repetition sets were equally distributed, containing either two trials with the correct interval selected or two trials where

the subject was unable to select an interval. There were no triplicate repetition sets that included all three possible patient responses (i.e., correct, wrong, not felt).

A Sensitivity Threshold Level (STL) was determined, therefore, by selecting the smallest filament with at least two correct interval responses in a triplicate repetition set. No significant difference ($p > .05$) was noted between ascending and descending trials. Thus, for the purpose of this study, only descending threshold values were analyzed.

Statistical analysis

Results are given as mean ± SEM. Student's two-tailed t-test for paired and unpaired data was used when applicable. Analysis of variance (ANOVA) was used to determine if the heterogeneity among the means of the four-subject groups is statistically significant.

RESULTS

STL for control subjects

A mean STL (lightest probe felt) was determined for each site in the control group and is represented in **Table 3.** The sites can be grouped by their anatomical locations, which also separates them into three regions of decreasing sensitivity: dorsal (sites 8–10); plantar (sites 1–6); and, heel (site 7). No significant difference ($p > .05$) was noted between the sites within a region, but a significant difference ($p < .01$) was noted between the sites from different regions.

Table 3.
Mean sensitivity threshold levels for Group C, according to site.

Site	Sensitivity Threshold Level (mean ± SEM)
1	4.40 ± .07
2	4.56 ± .08
3	4.58 ± .07
4	4.58 ± .07
5	4.49 ± .07
6	4.28 ± .09
7	5.12 ± .13
8	3.87 ± .07
9	3.81 ± .07
10	3.73 ± .06

STL for diabetic subjects

Results for the STL for all 10 sites in each of the 3 diabetic subject groups and the control group are represented by a frequency distribution in **Figure 3.** The diabetic subjects followed a pattern similar to that of the control group, indicating three distinct STL frequency-distribution patterns separating the 10 sites into the same 3 distinct regions: the plantar forefoot sites (sites 1–6); heel (site 7); and, dorsum of the foot (sites 8–10). These sites were pooled and a mean STL was determined for each region in all four subject groups (**Figure 4**). An absolute mean STL could not be determined for Group DU for any sites, since many patients could not feel even the highest-force probe tested: 6.45 log (0.1 mg) force. Therefore, a minimal mean was calculated for Group DU using 6.45 log (0.1 mg) force for patients testing greater than this level. There was no significant difference ($p > .05$) between the means of Group C and DC at any region. In contrast, patients with neuropathy (Group DN or DU) showed a significantly higher mean STL ($p < .001$) than Group C or DC—except when comparing Group DN to C or DC in the heel region ($p < .05$). In addition, Group DU had a mean STL that was statistically higher ($p < .001$) than Group DN, although both groups of patients had symptomatic neuropathy.

Risk discriminator level

We therefore sought to determine how to use these STLs to best discriminate between diabetic patients with foot ulcers and control patients, in the hope that we could develop a technique that could eventually be tested in prospective studies to determine patients at risk. We found that a STL above 5.07 log (0.1 mg) force occurs with great frequency in diabetic subjects with ulcerations but rarely occurs in controls or in diabetic subjects without ulcerations (**Figure 3**).

The heel provided the poorest discrimination between Groups C and DU, since in 32 percent of the trials, controls were unable to feel the 5.07 log (0.1 mg) force probe.

The dorsal sites (sites 8–10) were the most specific, but least sensitive, as 45 ± 5 (mean calculated by averaging all sites within the region ± SEM) percent of the time subjects with ulcerations were also able to feel this probe level. The plantar sites (sites 1–6) at the 5.07 log (0.1 mg) force STL best discriminated between Group C and Group

Journal of Rehabilitation Research and Development Vol. 25 No. 2 Spring 1988

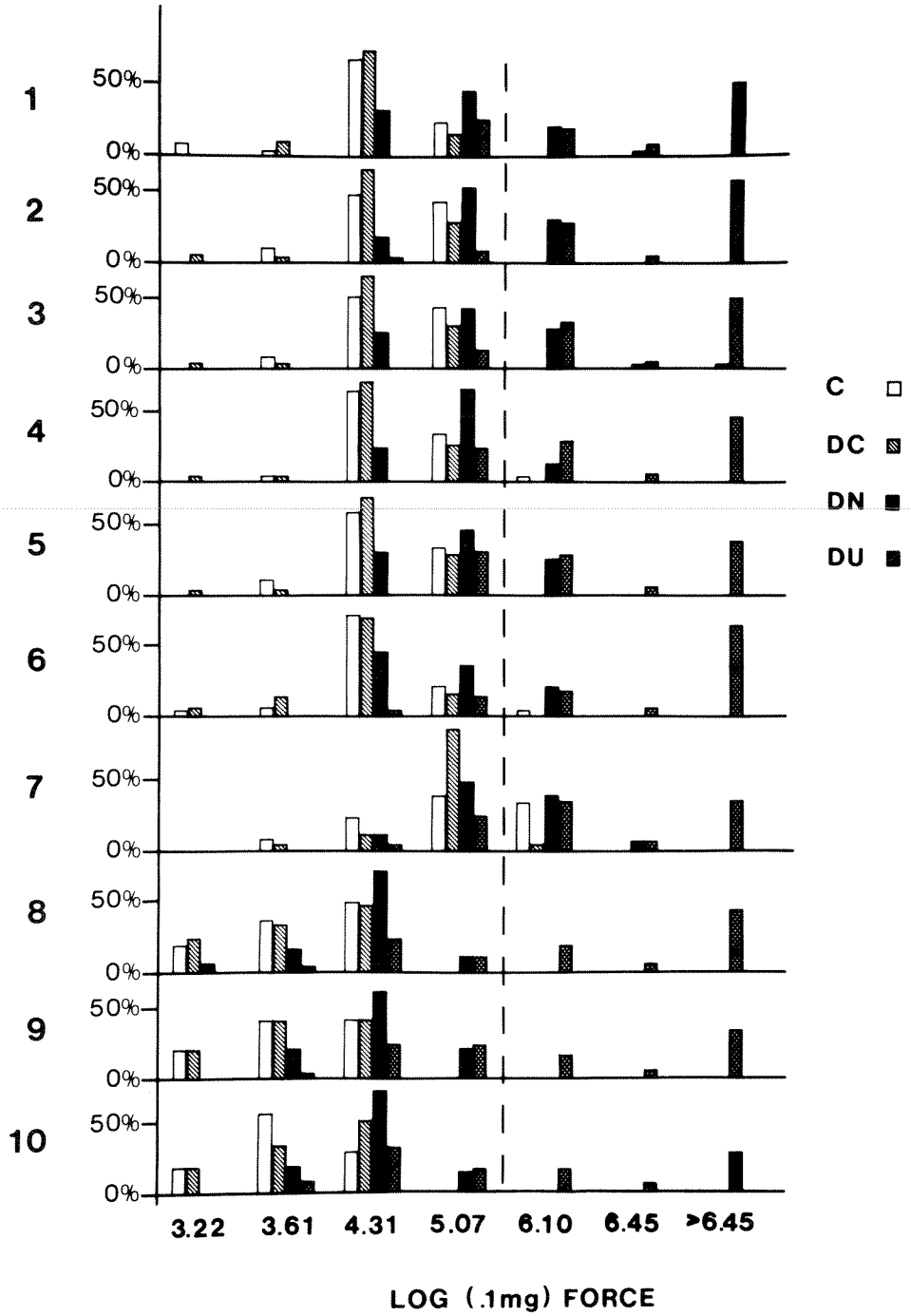

Figure 3.
Frequency distribution for sensitivity thresholds for each of the four groups at each site. The dashed line represents a sensitivity threshold level occurring with great frequency in diabetic subjects with ulcerations, but rarely occurring in control subjects.

DU. Diabetic patients with foot ulcers had a STL less than or equal to 5.07 log (0.1 mg) force only 20 ± 3 (x ± SEM) percent of the time and the control patients had a STL at or below the 5.07 probe 99 ± 0.3 (x ± SEM) percent of the time in the plantar forefoot sites. If a lighter discriminator level was used for the dorsal sites (4.31 log [0.1 mg] force), patients with ulcerations would still feel the probe in 29 ± 4 (x ± SEM) percent of the trials.

In order to improve discrimination between

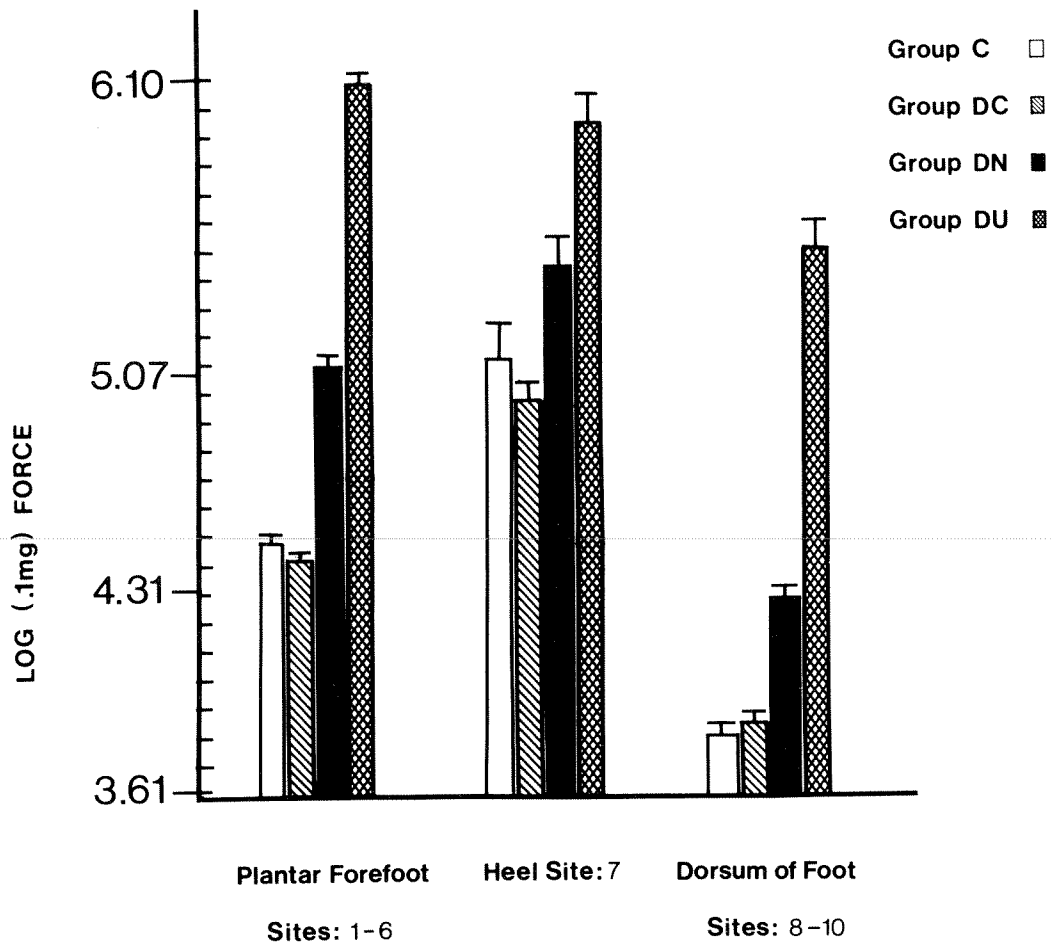

Figure 4.
The mean sensitivity thresholds for each of the three regions for all four of the subject groups. The error bars represent the SEM. The observed heterogeneity among the means is statistically significant ($P < .001$) by analysis of variance (ANOVA).

Groups C and DU, we analyzed data to discover at what fraction of the six plantar forefoot sites an individual subject had a STL greater than 5.07 log (0.1 mg) force and determined sensitivity, specificity, and accuracy (**Table 4**). A general trend is noted: as the number of plantar forefoot sites with a STL greater than 5.07 log (0.1 mg) force increases from one out of six to six out of six sites, sensitivity is decreased and specificity increased.

Because it is more important to assess patients at risk, an ideal discriminator would maximize sensitivity but still have high specificity, yielding excellent accuracy. By requiring that three of the six plantar forefoot sites have a STL greater than 5.07 log (0.1 mg) force, a risk discriminator level yielding 100 percent sensitivity, 100 percent specificity, and 100 percent accuracy in this patient population is obtained.

The same accuracy was not obtained by collectively using the dorsal sites with a lighter discriminator level (4.31 log [0.1 mg] force). At best, 80 percent sensitivity, 100 percent specificity, and 90 percent accuracy was achieved, by requiring that two of the three dorsal sites have a STL greater than 4.31 log (0.1 mg) force.

DISCUSSION

This study suggests that Semmes-Weinstein aesthesiometry of the foot may be an effective, practical method for quantifying the extent of sensory loss in peripheral neuropathy in the lower extremity of diabetic patients. Our experience with this method has shown it to be both reliable and sensitive.

Journal of Rehabilitation Research and Development Vol. 25 No. 2 Spring 1988

Table 4.
Sensitivity, specificity, and accuracy of testing all six plantar forefoot sites for a sensitivity threshold level greater than 5.07 log (.1 mg) force for group C versus group DU.

Number of plantar sites	Number of Patients with a Sensitivity threshold >5.07 log (.1 mg) force*				
At least:	Group C	Group DU	Sensitivity	Specificity	Accuracy
6 of 6	0	12	60	100	80
5 of 6	0	14	70	100	85
4 of 6	0	18	90	100	95
3 of 6	0	20	100	100	100
2 of 6	1	20	100	95	98
1 of 6	1	20	100	95	98
0 of 6	19	0	—	—	—

*Values were determined by using the least sensitive foot in patients that were not symmetrical.

We found that sites on the foot can be grouped into three regions of decreasing sensitivity: dorsal, plantar, and heel. These differences demonstrate the importance of using consistent sites (dorsal versus plantar) when sequentially following a patient. Multiple sites were better at discriminating between subject groups than monitoring one single site. The plantar forefoot sites, collectively, were the most accurate in discriminating between Group C and DU, therefore we recommend testing only sites 1–6. Of note is the fact that these sites beneath the metatarsal heads are also more prone to ulceration, due to local pressure factors and to the mechanics of neurotrophic ulcer formation.

We have created an interval comparison method of testing (modeled after the 2-AFC algorithm) and have provided more stringent guidelines on how the test should be performed. Previous studies utilizing aesthesiometry (3,4,8,12,20) evaluate sensory thresholds without using a 2-AFC algorithm. The 2-AFC algorithm has been shown to produce more reliable data than previous "yes/no" or "touch/no-touch" options provide (16). The 2-AFC method forces the subject to choose when the stimulus was applied during one of two possible intervals, eliminating the need for the subject to decide when a stimulus was sufficiently above the background level to justify a response. With the 2-AFC method, the subject is asked to identify the interval in which the stimulus occurred, not whether or not it occurred.

The original 2-AFC algorithm provides a method of obtaining thresholds free of response bias, but it requires many trials that greatly lengthen the examination time. The method of interval comparison employed in our study is modeled after the 2-AFC algorithm with one modification. Since patients will not be able to feel all the probes, we believe a response should not be forced when patients are certain there was no difference between intervals. This modification greatly shortens the number of trials required to determine if a stimulus was perceived.

Our data, as well as findings of Birke *et al.* (4) demonstrate a direct correlation between ulcer formation and decreased pressure sensation. Striking sensitivity, specificity, and accuracy were demonstrated on this subject population, although increasing the population size may decrease these figures. The high specificity possible in this method may be due in part to the evaluation of cutaneous pressure sensation. Repetitive pressure, or localized areas of high pressure loading (2,6,9,19), play an important role in the mechanism of ulcer formation. Testing touch-pressure sensation may directly assess a patient's ability to sense abnormal pressure, and may thereby evaluate one's ability to avoid ulceration. This does not prove that decreased sensation causes ulceration; only that it is present in all patients with neurotrophic ulcers.

In the prevention of neurotrophic ulceration, we

are concerned not merely with early detection of neuropathy, as possibly demonstrated in evaluating temperature sensation, but also in being able to determine when a sufficient level of sensation loss has occurred, so that it may predispose patients to neurotrophic ulceration. Cutaneous pressure sensation evaluation may provide a method of quantifying near this end-stage sensory loss. Comparative studies evaluating all sensory modalities and their abilities to discriminate which patients are prone to ulceration from a group of patients with symptomatic neuropathy, are needed.

In addition, other factors are relevant for ulcer formation including: structural deformity, changes in proprioception, and biochemical changes. This study does not explore which factors are the best discriminates or whether multiple factors in common are the best discriminates. We have shown that cutaneous pressure sensation does correlate with ulcer formation. This data suggests that further prospective studies are indicated to establish the relative role of cutaneous pressure sensation in ulcer formation.

Our intention was to develop a screening technique that can discriminate between Groups C and DU in order to detect patients who are "at risk" for neurotrophic ulcer formation. This can be done in a 1-minute screening exam, if three of the six plantar sites have a STL greater than 5.07 log (0.1 mg) force (the patient can not accurately identify the correct interval the 5.07 log (0.1 mg) force filament was applied in at least 3 sites in one foot). This risk discriminator level must be tested prospectively in order to determine its ability to predict accurately the risk of development of neurotrophic ulcers. However, using these criteria, we can predict that 6 out of 20 of the group DN patients are currently "at risk" for development of foot ulceration; although these patients had no previous history of ulcer at the time of the study, they did have symptomatic neuropathy. In contrast, none of the 20 subjects from Group DC (who do not have symptoms of neuropathy) would be classified as "at risk" for development of foot ulcers at this time.

Aesthesiometry can determine a patient's STLs for individual sites on the foot, in addition to a brief screening evaluation. By using progressively-sized diameter filaments (in addition to the 5.07 log [0.1 mg] force filament used in the brief screening exam), a baseline STL can be obtained and the value can be compared with future readings to evaluate changes. This quantification may allow monitoring the progression of a patient's neuropathy, in addition to merely detecting patients with insensate feet. Early recognition of decreased sensitivity is important to enable one to intervene with appropriate treatment or preventative modalities prior to neurotrophic ulcer formation.

Having documented the ability of Semmes-Weinstein aesthesiometry to discriminate patients with and without neurotrophic ulceration, it is now appropriate to prospectively test its usefulness in assessing the risk and natural history of foot ulceration in a prospective study. Such a long-term study has begun.

ACKNOWLEDGMENTS

We wish to thank the Veterans Administration Rehabilitation Research and Development Service for support of this project, and Bernadette Paolini for her graphic art work and editorial assistance.

REFERENCES

1. **Arezzo JC, Schaumburg HH, Laudadio C**: Thermal sensitivity tester: Device for quantitative assessment of thermal sense in diabetic neuropathy. *Diabetes* 5:590-592, 1986.
2. **Barrett JP, Mooney V**: Neuropathy and diabetic pressure lesions. *Orthop Clin N Am* 4:43-47, 1973.
3. **Bell JA**: Light touch-deep pressure testing using Semmes-Weinstein monofilaments. In: *Rehabilitation of the Hand*, Hunter JM, Schneider LH, Mackin EJ, Callahan AD (Eds.). St. Louis: The CV Mosby Co., 399-406, 1984.
4. **Birke JA, Sims DS**: Plantar sensory threshold in the Hansen's disease ulcerative foot. In: *Proceedings of the International Conference on Biomechanics and Clinical Kinesiology of Hand and Foot*, IJT, Madras, India, 137-138, 1985.
5. **Boulton AJ, Hardisty CA, Betts RP, Franks CI, Worth RC, Ward JD, Duckworth T**: Dynamic foot pressure and other studies as diagnostic and management aids in diabetic neuropathy. *Diabetes Care* 6:26-33, 1983.
6. **Brand PW**: The diabetic foot. In: *Diabetes mellitus*. Ellenberg M, Rifkin H (Eds.). New York: Medical Examination Publishing Co. Inc., 829-849, 1983.
7. **The Carter Center of Emory University**: Closing the gap: The problem of diabetes mellitus in the United States. *Diabetes Care* 8:391-406, 1985.
8. **Chochinov RH, Ullyot GLE, Moorhouse JA**: Sensory perception thresholds in patients with juvenile diabetes and their close relatives. *N Engl J Med* 286:1233-1237, 1972.
9. **Ctercteko GC, Dhanendran M, Hutton WC, Le Quesne LP**: Vertical forces acting on the feet of diabetic patients with neuropathic ulceration. *Br J Surg* 69:608-614, 1981.

10. **Dyck PJ, Karnes J, Bushek W, Spring E, O'Brien PC**: Computer assisted sensory examination to detect and quantitate sensory deficit in diabetic neuropathy. *Neurobehav Toxicol Teratol* 5:697-704, 1983
11. **Guy RJ, Clark CA, Malcolm PN, Watkins PJ**: Evaluation of thermal and vibration sensation in diabetic neuropathy. *Diabetologia* 28:131-137, 1985.
12. **Heinrichs RW, Moorhouse JA**: Touch-perception thresholds in blind diabetic subjects in relation to the reading of Braille type. *N Engl J Med* 280:72-75, 1969.
13. **Levin S, Pearsall G, Ruderman RJ**: Von Frey's method of measuring pressure sensibility in the hand: An engineering analysis of the Weinstein-Semmes pressure aesthesiometer. *J Hand Surg* 3:211-216, 1978.
14. **Lippman HI**: Must loss of a limb be a consequence of diabetes mellitus? *Diabetes Care* 2:432-436, 1979.
15. **Most RS, Sinnock P**: The epidemiology of lower extremity amputations in diabetic individuals. *Diabetes Care* 6:87-91, 1983.
16. **Sekuler R, Nash D, Armstrong R**: Sensitive objective procedure for evaluating response to light touch. *Neurology* 23:1282-1291, 1973.
17. **Semmes J, Weinstein S, Ghent L, Teuber HL**: *Somatosensory Changes after Penetrating Brain Wounds in Man.* Cambridge, MA: Harvard University Press, 1960.
18. **Steiness I**: Vibratory perception in diabetics. *Acta Med Scand* 158:327-335, 1957.
19. **Stokes IA, Faris IB, Hutton WC**: The neuropathic ulcer and loads on the foot in diabetic patients. *Acta Orthop Scand* 46:839-847, 1975.
20. **Szabo RM, Gelberman RH, Dimick MP**: Sensibility testing in patients with carpal tunnel syndrome. *J Bone Joint Surg* 66-A:60-64, 1984.