Motor Nerve Conduction Velocity in Diabetes Mellitus

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Disturbances in neurological function are among the most common of the complications of diabetes. The reported incidence of neurologic involvement varies from 25 to 90 per cent of adult diabetic patients.[1-6] The severity of the symptoms associated with diabetic neuropathy may vary from a degree so mild as to be unnoticed to a disorder so distressing that chronic invalidism results. The most common neurologic disturbance in diabetes is involvement of the peripheral nerves.

The early symptoms of peripheral nerve involvement are usually sensory. Evaluation is often difficult because of variation in the patients' interpretation of the symptoms, as well as the inherent subjectivity of sensory examination.

Therefore, a physical method for documentation and quantitation of peripheral nerve function could be of great aid in the study of diabetic neuropathy. The precise measurement of the conduction velocity of peripheral motor nerve fibers offers such a method. Even though many of the clinical disturbances in diabetic neuropathy are sensory, it could be postulated that altered excitability of the efferent fibers may occur without obvious weakness of muscles supplied by these motor fibers and that conduction velocity may reflect the general state of function of the peripheral nerve. Our studies utilizing measurement of nerve conduction velocity in 103 diabetic patients appear to confirm this hypothesis.

METHODS

Determinations of the conduction velocity of the peripheral motor fibers in the ulnar and peroneal nerves were made in 103 diabetic patients selected from the outpatient clinic or from hospitalized patients admitted to the division of Endocrinology and Metabolism of Ohio State University Hospital. Selection of diabetic patients was dependent chiefly on the individual patient's willingness and ability to take part in the study. Occasionally patients were included because they presented neurological findings which were felt to be of special interest.

Prior to the measurement of nerve conduction velocity, the clinic record of each patient was reviewed. Following this, a supplemental history was taken and a physical examination which included a special neurological examination was performed.

On the basis of these findings, an evaluation of the various degenerative complications of diabetes was made. Where necessary, these evaluations were substantiated by laboratory investigation. Subjects with either retinal microaneurysms, waxy exudates, or both were considered to have "diabetic retinopathy." Individuals having sustained diastolic blood pressure levels exceeding 90 mm. Hg in the supine position were classed as "hypertensive." Those who related a clear-cut history of angina pectoris or displayed electrocardiographic evidence of myocardial infarction were considered to have "arteriosclerotic heart disease." A diagnosis of "peripheral vascular disease" was made in subjects who presented a clear-cut history of intermittent claudication or showed definite signs of arterial insufficiency, such as, absent foot pulses or dependent rubor. The findings of edema unexplainable on the basis of congestive heart failure, proteinuria in excess of 20 mg. per cent, and elevation of the BUN above 20 mg. per cent were taken as presumptive evidence of diabetic "nephropathy."

For purposes of standardization, the neurological evaluations of the patients were made by the same individual. Physical findings such as the biceps, triceps, patellar and Achilles tendon reflexes and perception of light touch, painful stimuli and vibratory stimuli, were noted as either present or absent. Functional tests to evaluate motor function of the lower extremities were

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performed in all patients. They included walking on heels and toes, squatting and rising. Patients having any of these neurologic defects were considered to have "objective neuropathy." Symptoms such as numbness, paresthesias, hyperesthesias, and spontaneous pain sensations were recorded. Patients having symptoms only were grouped as "subjective neuropathy." Patients who showed decrements in blood pressure which exceeded 10 mm. Hg when rising from a supine position were classified within a "visceral neuropathy" group. All patients who met the criteria for inclusion in any of these groups were considered to have evidence for the diagnosis of clinical neuropathy. The findings and characteristics of these patients were then compared to those of the diabetic subjects who were not considered to have clinical neuropathy and to a group of nondiabetic patients.

Peroneal nerve conduction velocity was determined in one leg and in the ulnar nerve in the opposite arm. In selected individuals, repeated determinations were made. Normal values were established by measuring ulnar and peroneal nerve conduction velocity in a group of volunteers known to be free of neurological disease and of approximately the same age group as that of the diabetic patients.

Electromyographic studies, employing conventional technics, were done in a majority of patients selected at random.[7]

Percutaneous electrical stimulation of the peroneal and ulnar nerves was carried out in the following manner: The peroneal nerve was stimulated with bipolar electrodes at the knee and the ankle. The muscle action potential was picked up with 5 mm. cup-shaped surface electrodes on the skin over the extensor digitorum brevis. The reference electrode of similar construction was placed over the tendon of this muscle. A photograph of the oscilloscope screen showing the stimulation artifact and the amplified muscle action potential with an appropriate time base was taken. This was repeated three times at each stimulation point to rule out variation by patient movement. The distance between the artifact and the action potential was determined by inspection of the photograph. The distance on the skin between the points of stimulation was measured, and the conduction velocity was calculated in meters per second.

A similar procedure was carried out with the ulnar nerve, except that the stimulation was done at the elbow and at the wrist, and the pick-up electrode placed over the abductor digiti quinti.

The apparatus (figure 1) comprised a standard laboratory stimulator, a pre-amplifier, an oscilloscope with a polaroid camera, an audio amplifier and a loudspeaker, a

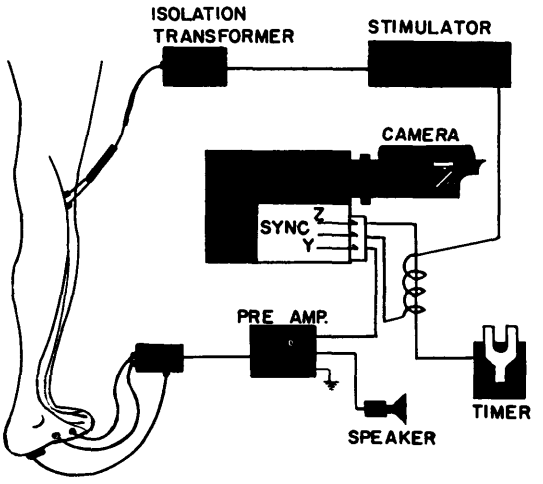

FIG. 1. Schematic diagram of apparatus used to measure nerve conduction velocity.

sturdily constructed set of stimulating electrodes, and electroencephalographic surface electrodes. The timing device was a tuning fork with a power supply, whose voltage applied to the "Z" axis of the oscilloscope, blanked out the sweep at one-millisecond intervals to provide the time base. Intramuscular temperature in the vicinity of the nerve was taken with a thermistor mounted in a twenty-five gauge hypodermic needle. Since reduced temperatures result in diminished conduction velocity, all results were corrected for temperature reduction (5 per cent/degree C.).

The procedure required only several minutes in a cooperative patient. Occasionally technical difficulties arose when the patient had edema of the foot and ankle. A description of this technic has been previously reported.[8]

RESULTS

A. Group Characteristics and Incidence of Neurologic Findings. The fifty-six women and forty-seven men studied had an average age of 51.9 years and an average duration of diabetes of 7.9 years (table 1). Two thirds had one or more degenerative complications of diabetes. The frequency of complications is similar to that reported in other series of diabetic studies.[2,3,5,9,10] As a group, the patients studied had a somewhat larger than usual insulin requirement; 51 per cent took insulin in an average daily dose of 44 U.

The frequency of the various symptoms and signs believed to be associated with diabetic neuropathy is depicted in figure 2. The incidence and variety of the neurological findings in the entire group and in patients with "diabetic neuropathy" are in general agreement with those reported in the literature.[1-8,5,9,10]

TABLE 1

Characteristics of the 103 diabetics studied

Age: Average—51.9 years, range—12 to 87 years
Duration of diabetes: Average—7.9 years, range—1 to 35 years
Sex: Female—54 per cent, Male—46 per cent

Associated complications	Per cent
Nephropathy	12
Retinopathy	23
Arteriosclerotic heart disease	28
Peripheral arteriosclerosis	28
Hypertensive cardiovascular disease	40
Therapy	
Diet only	7
Oral agents	
Chlorpropamide	29
Tolbutamide	7
Phenformin	4
Insulin (average dose 44 U.)	52

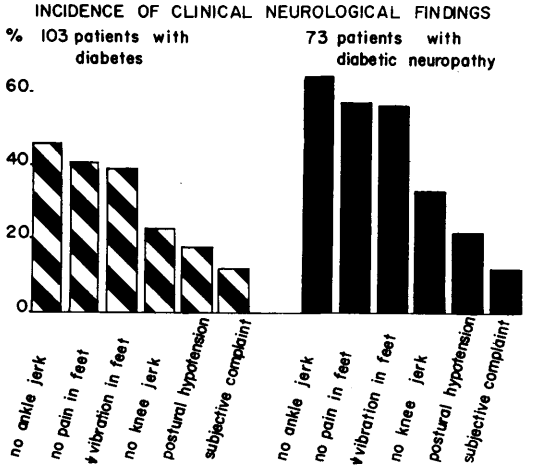

FIGURE 2

B. Nerve Conduction Velocity in Diabetics and Normals. Mean normal values for ulnar and peroneal nerve conduction velocity were 56.4 ± 6.2 and 49.3 ± 5.7 m./sec., respectively. These values compare favorably with those reported in the literature.[7,8] In diabetic patients the mean values for both ulnar and peroneal nerve conduction velocity were significantly below normal. Ulnar nerve conduction velocities averaged 48.6 m./sec. or 14 per cent less than that of the normal group. Peroneal velocity averaged 38.6 m./sec. or 22 per cent less than normal. When comparison was made between the group of diabetics with clinical neuropathy and nondiabetic normals, these differences became even greater. Figure 3 shows the distribution of ulnar nerve conduction velocities of diabetic patients with neuropathy and those of normals. The normal patients averaged 56.4 m./sec. and in 87 per cent of them the value exceeded 50 m./sec. In the diabetic neuropathy group, 77 per cent had a nerve

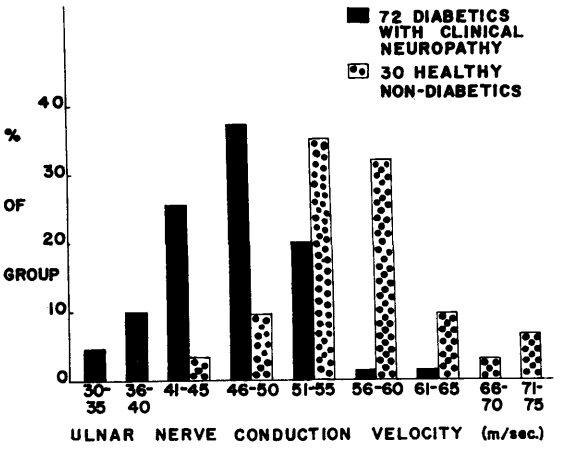

FIG. 3. Comparison of ulnar nerve conduction velocity in diabetic patients with neuropathy and normal patients.

conduction velocity of less than 50 m./sec.

An even greater difference between patients with neuropathy and normals was found when values of peroneal nerve conduction were studied. The seventy-three patients with neuropathy were found to have a mean of 36.5 m./sec. compared to 49.3 m./sec. Only 3 per cent of the normal group had values below 40 m./sec., but 77 per cent of the diabetic neuropathy group were below this level (figure 4).

When comparison of diabetics without clinical neuropathy and the normal group was made, values for both ulnar and peroneal nerve conduction were again lower (53.5 and 43.6 m./sec. respectively).

Statistical analysis of these data indicate significant differences for both ulnar and peroneal values in diabetic neuropathy patients compared to normal. In the group of diabetics without neuropathy, peroneal but not ulnar nerve conduction velocity was statistically different. These findings are listed in table 2.

C. Relationship of Nerve Conduction Velocity to Clinical Status. There was general agreement between the clinical findings interpreted as peripheral neuropathy and reduction of motor nerve conduction velocity. When values of two standard deviations below the mean of the normal group were regarded as reduced, peroneal conduction velocity was found to be reduced in 77 per cent of patients considered to have neuropathy and was within normal limits in 83 per cent of patients considered to be free of neuropathy (figure 5). In the ulnar nerve reduced values were found in only 35 per cent of patients with neuropathy and were also found in 10 per cent of patients without neuropathy.

The degree of reduction of velocity was found to be

TABLE 2

Statistical analysis of peroneal and ulnar conduction velocity

Nerve studied	Patient group	No. pts.	Mean velocity (m./sec.)	"p" compared to control
Peroneal	Diabetics with neuropathy	73	36.5±5.1	<.01
	Diabetics without neuropathy	30	43.6±6.0	<.01
	Nondiabetic controls	41	49.3±5.7	—
Ulnar	Diabetics with neuropathy	72	46.6±5.9	<.01
	Diabetics without neuropathy	30	53.5±6.2	>.05
	Nondiabetic controls	31	56.4±6.3	—

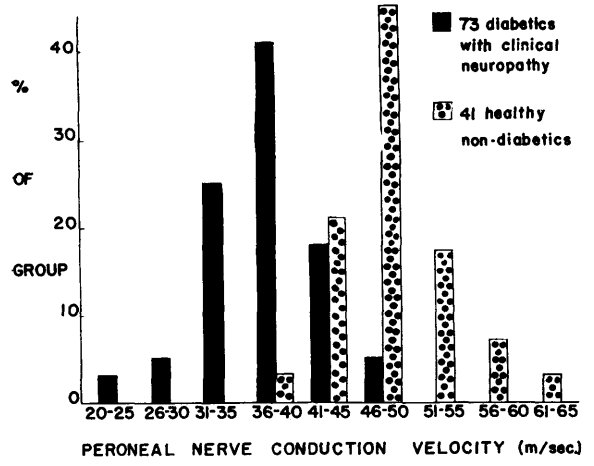

FIG. 4. Comparison of peroneal nerve conduction velocity in diabetic patients with peripheral neuropathy and normal patients.

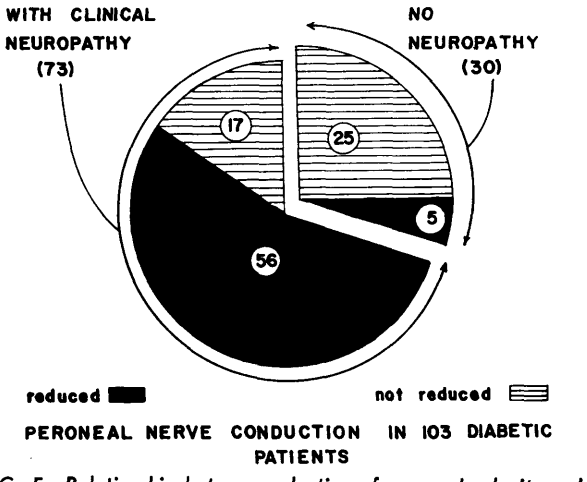

FIG. 5. Relationship between reduction of peroneal velocity and clinical neurological status (see text).

related to the severity of the neuropathy. For example the aggregate of patients having combinations of findings such as absence of patellar reflexes plus loss of pain and vibratory sense in the feet showed a mean peroneal conduction velocity of 31.5 m./sec. compared to one of 40.9 m./sec. found in diabetics free of these neurologic changes.

Most of the patients with no objective neurologic findings but with distressing "subjective neuropathy" (complaints of shooting pains, paresthesias, burning feet, and the like) had peroneal nerve conduction values below normal. These individuals averaged 35.5 m./sec., a value no different from that of patients with "objective neuropathy."

The ages and sex of the patients studied were also related to both the severity and incidence of neuropathy and the nerve conduction velocity. The frequency of clinical neuropathy increased with age. Only 45 per cent of the patients under forty years of age had neuropathy while all those over seventy were affected. Reductions in nerve conduction velocity roughly paralleled this trend. When the sexes were compared men were found to have a more severe clinical neuropathy as well as a greater reduction in both peroneal and ulnar conduction velocities.

D. Electromyographic Findings. Electromyographic studies were completed in seventy-eight patients. In twenty-six the findings were abnormal. Reduction in the number of motor unit action potentials was the most common abnormality. An increased proportion of polyphasic potentials was noted less often, and only in patients with severe neuropathies such as foot-drop were fibrillation potentials observed. All patients with abnormal electromyograms had clinical neuropathy and all but three had reduced peroneal conduction velocities (figure 6).

E. Relationship of Nerve Conduction to Complications Other Than Neuropathy. As noted above, degenerative complications of diabetes were present in exactly two thirds of the patients studied. Even though clinical neuropathy was present in twenty-seven of the thirty-six patients who were free of other complications, their mean peroneal conduction velocity was 40.6 m./sec., a value only 2 m./sec. higher than the average for all diabetics.

When neither neuropathy nor other complications existed, the mean value approached normal (44.1 m./sec.). On the other hand, the mean values for peroneal conduction were distinctly reduced when any of the several complications were present (table 3).

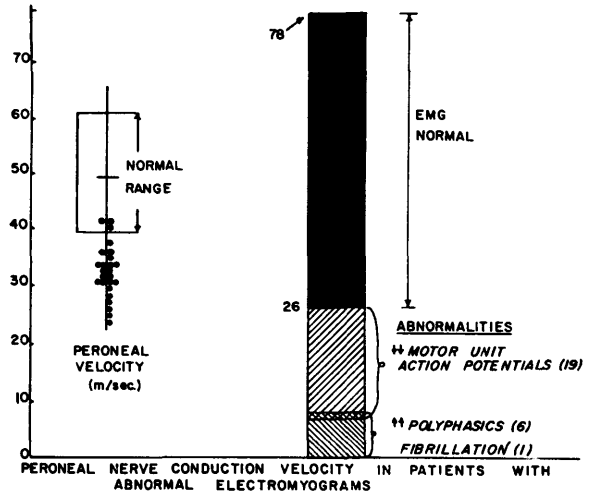

FIGURE 6

TABLE 3
Relationship of degenerative complications to peroneal nerve conduction velocity

Complication	Mean velocity m./sec.	Per cent reduction from normal
None	44.1	10
Neuropathy only	40.6	18
Hypertensive cardiovascular disease	38.5	22
Arteriosclerotic heart disease	37.9	23
Nephropathy	37.1	24
Peripheral arteriosclerosis	36.2	26
Retinopathy	34.9	29

DISCUSSION

The concept of measuring human motor nerve conduction velocity is not a new one. Helmholtz in 1852 measured the velocity of the median nerve and found about the same results as are found with the current apparatus.[8] Refinements in equipment have added precision and facility so that during the past two decades motor nerve stimulation with recording of the muscle action potential has been employed in the investigation of many disorders of the motor unit.[11-15] The application of this technic for the study of the peripheral nerves in patients with diabetes mellitus follows this trend. Mulder and co-workers are also engaged in this phase of investigation.[16]

The reduction of peroneal nerve conduction velocity in patients with neuropathy was anticipated and the degree of reduction in severely affected patients was similar to that observed in chronic peripheral neuropathies due to other causes.[8] The data obtained with respect to peroneal conduction velocity indicate that the degree of reduction is usually proportional to the severity of neurological involvement and that the measurement of motor function frequently reflects the state of neurological function of the lower extremity. The observation that diabetic patients without clinical manifestations of neuropathy may also have reduction of peroneal velocity suggests that in some instances dysfunction of the motor fibers of the peripheral nerve may occur in the absence of either sensory involvement severe enough to provoke symptoms or of motor involvement severe enough to permit the diagnosis of muscle weakness. Since clinical manifestations of neuropathy in the upper extremities were extremely uncommon, but reduction of ulnar velocity was noted often, similar states of subclinical neuropathy probably exist in the peripheral nerves of the arms of many diabetic patients with and without neuropathy of the lower limbs.

The finding that certain patients who exhibit abnormal neurologic signs may have normal conduction velocity values suggests that these individuals have only involvement of sensory fibers. It is also possible that clinical evaluation of symptoms may have been misleading and that some of these subjects may not have had neuropathy. On the other hand the demonstration of reduced conduction in the majority of patients who displayed subjective neuropathy suggests that motor fiber involvement frequently accompanies sensory fiber involvement.

Since abnormalities in the motor nerve conduction velocity were noted in 71 per cent and electromyographic abnormalities in 33 per cent of the patients' studies in our series, the former must be regarded as a more sensitive index of nerve involvement.

The precise relationship of degenerative complications other than neuropathy to nerve conduction velocity is not clear as most patients with one or more complications also had neuropathy. Nevertheless, both the severity of the neuropathy and reduction of velocity were greater in patients with complications. It is probable that peripheral neuritis is more severe in patients with clinical cardiac, renal and peripheral arterial diseases than in those without them.

SUMMARY

Motor nerve conduction measurements were made in 103 diabetic patients who averaged 51.9 years of age and had a mean duration of diabetes of 7.9 years. Seventy-three of these patients were found to have clinical evidence of peripheral neuropathy and a like number had other degenerative complications of diabetes. Values for ulnar nerve conduction velocity in patients with neuropathy averaged 46.6 ± 5.9 meters per second compared to 56.4 ± 6.3 m./sec. for normals. The mean values for peroneal velocity were 36.5 ± 5.1 m./sec. in dia-

betics and 49.3 ± 5.7 in normals. These differences were found to be statistically significant. The aggregate of diabetic patients without clinical evidence of neuropathy was also found to have a reduction in peroneal conduction velocity. The degree of reduction of velocity in clinically involved patients roughly paralleled the severity of the observed neurological deficit, and patients with subjective sensory findings alone had degrees of reduction similar to patients with objective findings. Some patients complaining of subjective sensory disturbances were found to have normal motor nerve conduction velocities indicating that quantitative technics measuring transmission of sensory nerve impulses would also contribute to knowledge of diabetic neuropathy. These findings permit the conclusions that determination of motor nerve conduction velocity provides an objective and quantitative evaluation of peripheral nerve function and, because conduction velocity is significantly reduced in most patients with diabetic neuropathy, it may be used as a guide to diagnosis and management.

SUMMARIO IN INTERLINGUA

Le Velocitate de Conduction del Nervos Motori in Diabete Mellite

Mesurationes del conduction de nervos motori esseva effectuate in 103 diabeticos de un etate medie de 51,9 annos, con un duration medie del diabete de 7,9 annos. Esseva trovate que septanta-tres de iste patientes habeva signos clinic de neuropathia peripheric; un simile numero habeva altere complicationes degenerative de diabete. Le valor medie del velocitate de conduction in le nervo ulnar esseva 46,6 ± 5,9 m/s (metros per secunda), a comparar con 56,4 ± 6,3 m/s in normales. Le valor medie del velocitate peronee esseva 36,5 ± 5,1 m/s in diabeticos e 49,3 ± 5,7 in normales. Esseva constatate que iste differentias es statisticamente significative. Esseva constatate in plus que le aggregato del patientes diabetic sin signos clinic de neuropathia habeva etiam un reducite velocitate de conduction peronee. Le grado de reduction del velocitate in clinicamente afficite patientes esseva grossiermente parallel al severitate del observate deficit neurologic, e patientes con constatationes sensori de typo subjective sol habeva grados de reduction simile a patientes in qui le constatationes esseva objective. Plure patientes qui se plangeva subjectivemente de disturbationes sensori revelava normal velocitates de conduction del nervos motori, lo que indica que technicas mesurante le transmission de impulsos de nervo sensori etiam contribuerea a nostre comprension del neuropathia diabetic. Le datos justifica le conclusion que le determination del velocitate de conduction del nervos motori provide un objective e quantitative evalutation del function del nervos peripheric, e—viste que le velocitate del conduction es significativemente reducite in le majoritate del patientes con neuropathia diabetic—illo pote esser usate como guida in le diagnose e tractamento de iste disordine.

ACKNOWLEDGMENT

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