Sensory nerve conduction in the upper limbs at various stages of diabetic neuropathy¹

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SUMMARY In 59 diabetic patients, sensory nerve potentials were recorded at various sites along the course of the median nerve. Pathological responses were characterized by reduced amplitude, desynchronization and decreased conduction velocity (CV). Four groups of patients with increasingly severe nerve dysfunction were distinguished. The presence and severity of clinical neuropathy in the upper limbs could be related to decreased maximal sensory nerve CV in the proximal segment of the limbs. When maximal sensory nerve CV was normal above the wrist, neuropathy usually remained latent. In severe cases where no sensory nerve potentials could be recorded, the cerebral evoked potentials nonetheless permitted a precise evaluation of the somatosensory conduction. In these cases, maximal sensory nerve CV was very low. In five patients with a so-called diabetic mononeuropathy, abnormal nerve potentials were recorded in the median nerve, although no clinical signs could be seen in the corresponding territory. It is proposed that the diabetic nature of a mononeuropathy can be assessed by the finding of latent abnormalities in seemingly normal nerve.

Previous electrophysiological studies of diabetic neuropathies have dealt mainly with voluntary electromyography and with the evaluation of motor nerve conduction velocities (CV). These were repeatedly shown to be reduced in patients both with and without clinical evidence of neuropathy (Lawrence and Locke, 1961; Mulder *et al.*, 1961; Gregersen, 1967; Lamontagne and Buchthal, 1970).

Sensory nerve potentials studies have been less frequently reported (Downie and Newell, 1961; Lamontagne and Buchthal, 1970; Noël *et al.*, 1971). They should, however, be particularly rewarding in evaluating a peripheral nerve dysfunction (Gilliat and Sears, 1958):

1. In sensory nerve potentials, an increase in temporal dispersion may be the earliest sign of impairment when conduction velocity along the fastest fibres is still within the normal range (Gilliat and Willison, 1962).

2. Sensory nerve fibres are often affected earlier than motor fibres (Gilliat and Sears, 1958; Buchthal and Rosenfalck, 1971). This is particularly true in diabetes mellitus where

sensory neuropathy is the most common clinical form of peripheral nerve involvement (Bischoff, 1963; Pirart, 1965; Eliasson, 1971).

The somatosensory cerebral evoked potentials (CEP) provide additional evidence for abnormal function in the central neurones, but they are also quite useful to assess peripheral nerve function. Apart from important changes in amplitude and waveform (Halliday and Wakefield, 1963; Giblin, 1964; Noël and Desmedt, 1972), the cerebral responses are significantly delayed in patients with lesions of the somatosensory pathway (Desmedt *et al.*, 1966; Desmedt, 1971). Moreover, a valuable estimation of the sensory CV in the peripheral nerve can be obtained by comparing the latencies of the cerebral potentials evoked by stimulation of the nerve at various sites (Desmedt *et al.*, 1966; Ball *et al.*, 1971; Desmedt *et al.*, 1973). This method is particularly useful in such pathological cases where the sensory nerve potential cannot be recorded (Desmedt and Noël, 1973).

In the present study, sensory nerve and cerebral evoked potentials were used to evaluate the sensory conduction in the distal and proximal median nerve of diabetic patients. The electro-

¹ This work was supported by a grant from the Fonds de la Recherche Scientifique Médicale to the Brain Research Unit.

physiological findings were compared with the clinical data.

METHODS

Fifty-nine diabetic patients with and without clinical evidence of neuropathy were investigated. Thirty-eight were male and 21 female. Age ranged from 18 to 68 years. The known duration of diabetes mellitus was a few months to 30 years. The patients were submitted to standard neurological examination with emphasis on sensory modalities in the four limbs. However, no examination methods other than those commonly used in neurological practice were used, so that minor defects such as those involving two-point discrimination and light touch might not have been detected (Heinrichs and Moorhouse, 1969; Chochinov *et al.*, 1972). Patients presenting clinical evidence of neuropathy in the upper limbs were included if: (1) the signs were not restricted to the median nerve, which could have resulted from a carpal tunnel syndrome; (2) there was no evidence of cervical rib or radiculopathy.

Arterial disease was looked for by oscillometry in the four limbs. None of the patients had any detectable circulatory defect in the upper limbs. Serological examination ruled out syphilis. Alcoholics were excluded.

A group of 55 normal subjects of comparable age and sex distribution was used as control.

The electrophysiological methods that were used have been described in detail (Debecker and Desmedt, 1964; Desmedt, 1971; Desmedt and Noël, 1973). The subjects were lying quietly on a couch in a sound-proofed air-conditioned electrically shielded room (24° C, 50% humidity). The temperature of the skin over the nerves was maintained at 34° C, so that the nerve temperature can be assumed to be 35–37° C. The stimulus was a square electrical pulse of 0.2 msec delivered to digits II and III through silver ring electrodes with the proximal cathode close to the metacarpophalangeal joint.

Sensory nerve potentials were recorded through fine uninsulated stainless steel needles, the active electrode being inserted close to the median nerve at several sites from the wrist to the supraclavicular notch, and the reference electrode being placed subcutaneously one cm therefrom at right angles to the nerve.

Somatosensory cerebral evoked potentials were recorded through fine subcutaneous needles, the active electrode being on the parietal focus for the hand in the contralateral hemisphere and the reference on the mid upper forehead.

The responses were fed into an oscilloscope triggered by each stimulation and 64–2,056 responses

were averaged with a digital computer Fabritek I062 with sweeps of 50 or 100 μ sec/address as necessary to define the potential. The interval between the stimulus artefact and the onset of the initial negative deflection was taken as the latency.

It was also possible to stimulate the median nerve trunk through the same electrodes as were used for recording sensory nerve potentials, thereby evoking larger cerebral responses.

RESULTS

Standard clinical examination revealed no sign of nerve impairment in 26 patients. In this group the mean age was 43 years (ranging from 25 to 68 years) and the known duration of diabetes ranged from one to 30 years (mean: eight years).

In 17 other patients, mild neurological signs were found in the lower limbs—namely, impaired vibration sensation at the ankle and reduced Achilles tendon reflexes. Feet paraesthesiae and muscular pain of cramping character were occasionally reported and were considered as evidence of a sensory polyneuropathy (Bruyn and Garland, 1971). In 11 other patients, a motor and sensory polyneuropathy involving the lower and upper limbs was found. Amyotrophy and muscle paresis were conspicuous features in six. One patient exhibited a pseudotabetic syndrome with ataxia of gait and painless ulcers of the soles. In these 28 patients with clinical evidence of neuropathy, age ranged from 18 to 68 (mean 53) years and the known duration of diabetes ranged from 1 to 38 (mean 12) years.

In the five remaining patients, the motor involvement affected a mononeuropathic pattern without evidence of traumatic or pressure neuropathy on clinical and radiographic examination. In three, the clinical examination of the lower limbs disclosed unequivocal but mild signs of sensory neuropathy. The ulnar (two patients), peroneal (two patients), or femoral (one patient) nerves were affected.

MAXIMAL SENSORY NERVE CONDUCTION VELOCITY (CV) Sensory nerve potentials could be recorded in nine of the 11 patients presenting a neuropathy involving the lower and upper limbs. The maximal sensory nerve CV ranged between 18 and 38 m/sec in the fingers-to-wrist segment and between 30 and 56 m/sec in the wrist-to-arm

FIG. 1. Maximal sensory CV in the distal (A, B, C, D) and proximal (E, F, G, H) segment of the median nerve. A, E: 55 normal subjects. B, F: 26 diabetic patients without clinical neuropathy. C, G: ■: five diabetic patients with mononeuropathy in the femoral, peroneal, or ulnar nerve. □: 17 diabetic patients with sensory polyneuropathy restricted to the lower limbs. D, H: nine diabetic patients with polyneuropathy in both upper and lower limbs. In two patients, the CV could not be evaluated proximally to the wrist.

segment (Fig. 1, D, H). These results were in striking contrast with the values found in normal subjects in which the maximal sensory nerve CV ranged from 48 to 69 m/sec (mean 54 m/sec) in the distal and from 55 to 76 m/sec (mean 64 m/sec) in the proximal segment of the median nerve (Fig. 1, A, E). A reduction of the maximal sensory nerve CV in the median nerve was also found but to a lesser degree, in patients for whom the clinical evidence of sensory neuropathy was confined to the lower limbs. In these 17 patients, the maximal sensory nerve CV fell beneath the normal value in the fingers-to-wrist segment: it ranged from 26 to 47 m/sec (mean 39 m/sec). Proximally, the maximal sensory nerve CV was found within the normal range in 8 of these 17 patients. It ranged from 46 to 64 m/sec (mean 52.1 m/sec) (Fig. 1, G).

The patients with mononeuropathy exhibited

decreased maximal sensory nerve CV in both the distal and proximal segments of the seemingly normal median nerve, except for one patient in whom it fell within the normal range in the proximal segment (Fig. 1, C, G: black squares).

More unexpected were the findings in the 26 diabetic patients without clinical evidence of neuropathy in the four limbs, since the maximal sensory nerve CV was between 36 to 58 m/sec in the distal segment of the median nerve (mean 46 m/sec) (Fig. 1, B). In 11 of the patients it was beneath the lowest value found in the normal subjects. However, in the proximal segment, only two patients exhibited decreased maximal sensory nerve CV: 48 and 53 m/sec. For the whole group, the maximal sensory nerve CV ranged from 48 to 72 m/sec with a mean value of 61 m/sec (Fig. 1, F).

TABLE
SENSORY NERVE CONDUCTION VELOCITY IN FOUR GROUPS OF PATIENTS

Maximal sensory nerve CV (m/sec)		Normal subjects	Diabetic patients			
			Group I	Group II	Group III	Group IV
Distal segment (fingers to wrist)	Range	48 to 69	48 to 57	50 to 58	35 to 46	18 to 46
	Mean	54	52	52	42	37
Proximal segment (wrist to elbow)	Range	55 to 76	55 to 72	55 to 64	56 to 68	31 to 55
	Mean	64	64	60	60	46
Proximal segment (elbow to axilla)	Range				61 to 70	31 to 71
	Mean	64	64	64	65	49

NERVE ACTION POTENTIAL (NAP): AMPLITUDE AND SYNCHRONIZATION Studies of the shape and amplitude of the nerve action potential (NAP) recorded at various sites along the nerve course are essential in the evaluation of a neuropathy. In normal subjects the amplitude of the triphasic nerve response was 15 to 45 μ V at the wrist.

Fifty-three patients were separated in four groups of increasingly severe nerve involvement (Table).

GROUP I: NORMAL RESPONSE IN UPPER LIMB A 35 year old male had been diabetic and treated with insulin for two years. Clinical examination disclosed no sign of neuropathy. The NAP evoked at the wrist by stimulation of digits II and III was triphasic, without a late component. Its amplitude was 32 μ V (Fig. 2, B). More proximally, its shape was not altered but for a slightly augmented duration due to the normal desynchronization of the afferent volley. The

FIG. 2. Male patient, 35 years. Insulin-dependent diabetes. Negative neurological examination. Average median nerve responses evoked by electrical stimulation of digits II and III, recorded at the wrist (B), in the mid forearm (C), at the elbow (D), axilla (E), and supraclavicular notch (F). The initial negative deflection (arrow) is taken as the latency. Sensory nerve maximal CV evaluated by comparing the latency of the response with the distance of the recording electrode from the stimulation site (A).

FIG. 3. Male patient, 45 years. Insulin-dependent diabetes. Negative neurological examination. Median nerve responses recorded at the wrist (B), in the forearm (C), at the elbow (D), and axilla (E). Maximal sensory nerve CV evaluated in the diagram (A).

FIG. 4. Female patient, 40 years. Insulin-dependent diabetes. Clinical signs of neuropathy confined to the lower limbs. Median nerve responses recorded at the wrist (B), in the forearm (C), at the elbow (D), and axilla (E). Maximal sensory nerve CV evaluated in the diagram (A).

amplitude of the NAP was 12 μ V at the elbow (Fig. 2, D), 6.5 μ V at the axilla (Fig. 2, E), and 2 μ V at the supraclavicular notch (Fig. 2, F). The maximal sensory nerve CV was 64 m/sec in the hand and 71 m/sec in the wrist-to-supraclavicular notch (Fig. 2, A).

Similar results were found in eight other patients, none of whom presented symptoms or signs of neuropathy in any limb.

GROUP II: NORMAL MAXIMAL SENSORY NERVE CV WITH DESYNCHRONIZATION OF THE RESPONSE A

45 year old diabetic male showed no clinical evidence of neuropathy. The duration of the disease was thought to be three years. The maximal sensory nerve CV was normal in the fingers-to-wrist segment (49 m/sec) and the wrist-to-axilla segment (65 m/sec) (Fig. 3, A). The amplitude of the NAP at the wrist was 15 μ V, still within the normal range, but late components were conspicuous and the minimal sensory nerve CV may be evaluated at 13 m/sec (Fig. 3, B). Proximally, the NAP desynchronization increased so that the amplitude of the late com-

FIG. 5. Male patient, 38 years. Insulin-dependent diabetes. Absent Achilles reflexes and diminution of vibration sensation in the lower limbs up to the ankles. Median nerve responses recorded at the wrist (B), in the forearm (C), at the elbow (D), and axilla (E). A: Maximal sensory nerve CV.

FIG. 6. A. Histogram comparing the degree of sensory conduction impairment in the median nerve with the clinical status of 53 diabetic patients. Groups—I: normal nerve conduction. II: normal maximal sensory CV and desynchronization of the nerve action potential (NAP). III: maximal sensory nerve CV decreased in the fingers-to-wrist segment only. IV: maximal sensory nerve CV decreased in the fingers-to-wrist and in the proximal segment. □ = patients without clinical evidence of neuropathy. ◻ = patients with clinical signs of neuropathy in the lower limbs. ■ = patients with clinical signs of neuropathy in the lower and upper limbs. Known duration of diabetes: (B) groups I and II patients, (C) group III patients, (D) group IV patients.

ponents were not different from the amplitude of the initial peak. At the elbow, the amplitude of the initial peak was $6 \mu\text{V}$ (Fig. 2, D). Such findings were characteristic of six patients.

GROUP III: REDUCED MAXIMAL SENSORY NERVE CV IN DISTAL SEGMENT ONLY This group included 19 patients (Fig. 4). A 40 year old woman with diabetes of three years' duration had slight but unequivocal signs of neuropathy confined to the

lower limbs. The maximal sensory nerve CV was decreased to 41 m/sec in the finger-wrist segment of the median nerve but within the normal range proximal to the wrist, 60 m/sec (Fig. 4, A). The NAP was polyphasic at the wrist and the minimal sensory nerve CV was 16 m/sec. Its amplitude was reduced: $8 \mu\text{V}$ (Fig. 3, B). In the forearm (Fig. 3, C), and at the elbow (Fig. 3, D) the response was respectively 6 and $3 \mu\text{V}$. At the axilla late components were hardly recognizable,

probably because of inadequate location of the electrode.

GROUP IV: REDUCED MAXIMAL SENSORY NERVE CV IN BOTH DISTAL AND PROXIMAL SEGMENTS In 19 patients, the maximal sensory nerve CV was also decreased proximal to the wrist (Fig. 5). In a 38 year old diabetic patient with a moderate to severe neuropathy in the lower limbs, the maximal sensory nerve CV was 37 m/sec in the hand, 57 m/sec between the wrist and the elbow and 72 m/sec in the upper arm (Fig. 5, A). At the wrist, the minimal sensory nerve CV was 13 m/sec, the response was polyphasic and its initial peak was 4 μ V. The reduction of the maximal sensory nerve CV was always more marked distally. In the upper arm, the CV tended to reach a normal value.

CORRELATION WITH CLINICAL DATA (Fig. 6) In the nine patients of group I, no evidence of

neuropathy was found on careful clinical examination.

Two of the six patients of group II presented signs of mild sensory neuropathy confined to the lower limbs. In group III, clinical neuropathy in the lower limbs was a common occurrence. It was found in 12 of 19 patients. Moreover, the upper limbs were involved in one additional patient in this group. In group IV, clinical evidence of neuropathy was the rule. It was present in 17 patients, affecting the upper limbs in eight of them. The mean duration of the diabetes was seven years for group I and II (Fig. 6, B), nine years for group III (Fig. 6, C), and nine years for group IV (Fig. 6, D). The distribution of the patients in each group is roughly similar in cases of diabetes of less than 15 years' duration (Fig. 6, B-D).

In each group, the ages of the patients were in the same range: 25 to 68 years for group I, 29 to 65 years for group II, 18 to 67 years for group III,

FIG. 7. Male patient, 50 years. Insulin-dependent diabetes. Pseudo-tabetic syndrome in all limbs. Absence of median nerve response at the wrist by supramaximal stimulation of digits II and III (B). Evaluation of maximal sensory nerve CV from the latency of the cerebral evoked potentials (A). C, D, E: average cerebral responses from the contralateral parietal hand focus and evoked by electrical stimulation of digits II and III (C) or median nerve at the level of the wrist (D) or axilla (E).

and 26 to 64 years for group IV. The mean age showed a gradual increase from group I to group IV; it was respectively 46, 48, 50, and 52 years.

CEREBRAL EVOKED POTENTIALS (CEP) The latency of the average cerebral potential evoked by stimulation of the fingers and recorded at the contralateral focus of the hand (CEP) is fairly constant and shows little variations in successive runs on the same subject. It varies between 17.5 and 20.5 msec in normal subject and may be evaluated to about 0.5 msec (Desmedt, 1971; Desmedt *et al.*, 1973).

In 28 diabetic patients the latency of the CEP ranged from 18 to 29.5 msec. When delayed, the latency seemed related to the decrease in maximal sensory nerve CV, the cortical delay being very similar to the delay of the peripheral response recorded at the most proximal site.

In two patients, no sensory NAP could be recorded even at the wrist. One of them, a 50 year old man, had poorly controlled diabetes of 10 years' duration. Deep reflexes were abolished. He presented a pseudo-tabetic syndrome in the lower limbs: touch and proprioceptive sensation were severely impaired, deep reflexes were absent. Painless ulcers were present on the soles. In the upper limbs, the position sensation was impaired and deep reflexes were weak. The early components of the cortical potential evoked by stimulation of the fingers were small: 0.55 μ V (normal: 2 to 5 μ V). The latency of the first negative component (N_1) was 26.5 msec (Fig. 7). By stimulation of the median nerve trunk at the wrist and axilla, the cortical responses recorded at the contralateral hand focus exhibited a latency of respectively 18.8 msec and 11.8 msec. The shapes of the three responses were very similar, so that the afferent volleys elicited at the different levels of stimulation in the upper limb can be considered to be fairly comparable. The latencies of these responses can thus be compared to evaluate the peripheral CV of the afferent volley. By this technique, the CV was evaluated at 21 m/sec from fingers to wrist and at 47 m/sec from elbow to axilla. It must be emphasized that the latency of the central response evoked by stimulation at the axilla is abnormally long: 11.8 msec against a normal value ranging from 9.5 to 11 msec (Desmedt and

Noël, 1973). This points to an impaired propagation of the afferent volley proximal to the axilla.

In the other patient of this group, a 55 year old diabetic whose upper limbs were amyotrophic and paretic, the latency of the cerebral response was 28.8 msec when evoked by stimulation of the fingers and 13.4 msec by stimulation at the axilla. The mean sensory nerve CV was estimated at 36.5 m/sec in the segment fingers-to-axilla.

DISCUSSION

The recording of a nerve action potential of normal latency, amplitude, and wave form requires synchronous conduction in the large myelinated fibres (Dawson, 1956; Gilliatt and Sears, 1958; Debecker and Desmedt, 1964; Buchthal and Rosenfalck, 1966). In diabetic neuropathy, the sensory nerve potentials are characterized by a reduced amplitude, a polyphasic shape and an increased latency of the initial peak. These alterations can also appear, though to a lesser degree, when a careful clinical examination of the nervous system is negative (Downie and Newell, 1961; Gilliatt and Willisson, 1962; Chopra *et al.*, 1969; Lamontagne and Buchthal, 1970; Noël *et al.*, 1971).

Such subclinical sensory neuropathy may be an early accompaniment of diabetes as substantiated by the finding of abnormal nerve potentials in patients with diabetes of recent onset (Noël *et al.*, 1971, Fig. 3). These alterations are probably related to segmental demyelination, which is the main, though by no means unique, pathological finding in diabetic neuropathy (Dolman, 1963; Thomas and Lascelles, 1966). Of particular significance are the findings of Chopra *et al.* (1969) who described myelin breakdown in sural nerves of diabetic patients without clinical signs of neuropathy, thus affording an anatomical background to subclinical neuropathy.

The anatomical studies were performed on biopsy materials from distal nerves so that available data on more proximal nerves remain scarce (Olsson, Säve-Söderbergh, Sourander, and Angervall, 1968).

Averaging with fast computers now permits demonstration of very small responses (Gilliatt *et al.*, 1961; Liberson *et al.*, 1965; Buchthal and Rosenfalck, 1971) down to 0.05 μ V in this laboratory (Desmedt, 1971; Desmedt and Noël,

1973) so that the maximal sensory nerve conduction velocity can be measured along the arm up to the brachial plexus, even in pathological cases. Furthermore, the shape of the response gives additional clue to the presence of slower conducting fibres and a minimal sensory nerve conduction velocity can be estimated (Buchthal, 1973). The present data on 59 patients, at various stages of the disease, illustrate in a way the natural history of diabetic sensory neuropathy.

A normal maximal sensory nerve CV and triphasic response at the wrist suggest the integrity of the investigated nerve. In the patients presenting such characteristics (group I), no clinical evidence of neuropathy was found in the upper or lower limbs.

In normal subjects, slow components are occasionally disclosed at the wrist with optimally located recording electrodes. Their amplitude is inferior to $0.5 \mu\text{V}$ and the minimal CV remains above 20 m/sec (Buchthal and Rosenfalck, 1971). In our group II patients, the nerve response was desynchronized at the wrist with late components of 1.2 to $5 \mu\text{V}$ and a minimal CV between 10 and 20 m/sec. These findings indicate hampered conduction in the distal segment of the nerve. A number of sensory fibres remain functionally intact as indicated by the normal latency of the initial peak. However, the temporal dispersion of the fibre action potentials accounts for a slightly reduced amplitude of the potential to 50–60% (Gilliat, 1961; Buchthal and Rosenfalck, 1971). These mild abnormalities remain frequently subclinical and represent the earliest stage of diabetic neuropathy. Nevertheless, clinical signs restricted to the lower limbs are occasionally found (Fig. 6), evidencing a widespread involvement of the peripheral nerve at an early stage of the disease.

Eventually, more and more large fibres are affected until most afferent fibres are involved. The maximal sensory nerve CV is then decreased in the distal portion of the limb and the desynchronization of the response is enhanced (group III).

In group IV, the maximal sensory nerve CV is reduced in the forearm and arm. It is not equally low along the whole course of the nerve. The CV is very low in the fingers-to-wrist segment, gradually increases, and reaches a normal value in the arm or at the axilla (Fig. 5). Such findings

are frequently associated with a clinical neuropathy in the four limbs. Indeed, proximally decreased CV is present in 10 of the 19 patients with signs referring to the lower limbs and not unexpectedly in each patient for whom clinical examination discloses signs of neuropathy in both lower and upper limbs.

Thus the reduction of sensory nerve CV seems to start at the periphery and eventually to progress towards the root of the limb. This process cannot be ascribed solely to ageing, since it is much more marked in diabetic patients than in the normal elderly (Buchthal and Rosenfalck, 1966; Noël *et al.*, 1971, Fig. 1). Moreover, it seems to be rather independent of the known duration of the diabetes, which is at variance with the well-known fact that severe neuropathy is mostly encountered in patients with poorly controlled and longstanding diabetes (Pirart, 1965).

The proximal extension of neuropathic involvement is clearly related to the appearance and increasing severity of clinical signs of neuropathy, first in the lower and then upper limbs. This proximo-distal gradient is similar to the observed in motor nerves (Lawrence and Locke, 1961; Lamontagne and Buchthal, 1970).

From these data, it may be proposed that segmental demyelination should be most marked in the distal part of the peripheral nerves, which is in keeping with the anatomical findings of Olsson *et al.* (1968).

In patients presenting a severe neuropathy, the amplitude of the nerve potential is reduced to such a degree that a loss of active fibres must be postulated. This could be the result either of a conduction block in fibres demyelinated for a long distance or of the degeneration of a number of axons (McDonald, 1963; 1973; Dyck and Lambert, 1966; Dyck, 1973). Both mechanisms appear to be at work. While in diabetic neuropathy of recent onset, segmental demyelination may be the only abnormal finding (Thomas and Lascelles, 1966), combined axonal and myelin changes suggesting Wallerian degeneration are found in chronic or severe cases (Chopra *et al.*, 1969). Both histological and electrophysiological evidence point to an initially demyelinating process with subsequent loss of nerve fibres.

Of particular significance are the two patients suffering from a severe neuropathy affecting all

limbs in whom no sensory response was recorded even at the wrist. A large reduction of the number of active fibres can be postulated if the recording electrodes were accurately located. This is assessed by the presence of the cerebral potentials evoked by stimulation of the fingers and of the median nerve through the same electrodes as used for the fruitless recording of the nerve potential. The latencies of these potentials were significantly increased, indicating a very slow conduction more marked in the distal segment of the limb (Fig. 5). Moreover, stimulation of the nerve at the axilla elicited a cerebral response with abnormally long latency in both cases, which suggests that diabetic neuropathy eventually involved the nerve proximal to the axilla.

There are other examples of the usefulness of the cerebral evoked potentials for providing evidence on pathological afferent conduction in nerves with severe lesions (Desmedt, 1971; Desmedt and Noël, 1973).

While sensory polyneuropathy is widely held to be the result of metabolic impairment of the Schwann cell (*cf* Bruyn and Garland, 1970; Eliasson, 1971), it was proposed that diabetic mononeuropathy (multiplex) was due to a specific angiopathy affecting the vasa nervorum (Fagerberg, 1959). The five patients who presented a clinical mononeuropathy, affecting either the lower or upper limbs, exhibited abnormal sensory nerve action potential in the median nerve. Mild clinical signs of sensory neuropathy restricted to the lower limbs were present in three of them. These data point to a widespread involvement of the peripheral nerves which may be assumed to predispose them to further local injuries, thus leading to the clinical impairment. That such local injuries may be of ischaemic origin is evidenced by the observations of Raff *et al.* (1968) who described infarctions in the involved nerves of diabetic patients with mononeuropathy. On the other hand, minor traumas may well be precipitating factors in revealing a latent neuropathic involvement, as substantiated by the frequent observation that the affected nerves in diabetic mononeuropathy are those commonly involved by mechanical neuropathies (Mulder *et al.*, 1961; Gilliatt and Willison, 1962). We think that the diabetic nature of a so-called mono-neuropathy occurring in a

diabetic patient can generally be substantiated by the finding of subclinical involvement of other nerves in nerve conduction tests.

The author wishes to thank Professor J. E. Desmedt for advice in the preparation of this paper and Dr. J. P. Lauvaux who referred the patients for investigation.

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