Journal of Neurology, Neurosurgery, and Psychiatry 1984;**47**:699–703

Prognosis of alcoholic peripheral neuropathy

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SUMMARY Ten male alcoholics aged 38–72 years with clear clinical and electroneurographical signs of peripheral neuropathy were re-examined three to five years later. Conduction velocities, latencies and nerve action potential amplitudes were measured from median, peroneal and sural nerves on both occasions and the results were compared with age-matched reference values from 80 healthy men. Seven of the alcoholics showed normal or nearly normal scores in electroneurographical and clinical examination and they had all managed to stop drinking alcohol. The results suggest that the prognosis of alcoholic peripheral neuropathy is good and independent of age provided that intake of alcohol is discontinued and other causes of neuropathy (malignancy, diabetes, nerve trauma) are carefully excluded.

The data collected so far have failed to establish the prognosis of alcoholic polyneuropathy.[1–4] This may be due to frequent dropout of alcoholics from their rehabilitation programmes and poor diagnostic accuracy. We were able to follow up a small group of alcoholics with clear clinical and electroneurographical findings of peripheral neuropathy. This report shows that the prognosis of the disease is usually good provided that the intake of alcohol is discontinued.

Patients and methods

Two hundred and ten randomly selected alcoholics admitted to our in-patient alcoholism programme for detoxification and rehabilitation were studied between 1977 and 1979. Twenty-four of these patients (11%), all men, had clinical and electroneurographical signs of peripheral neuropathy and ten of them could be followed up and re-examined 1982. The age of these ten men ranged from 38 to 72 years, and they had all been drinking heavily for several months or years immediately before the initial admission in 1977–79. Their daily alcohol consumption averaged 3·6 ± 0·3 g/kg of absolute ethanol (mean ± SE) and their alcoholic career ranged from 10 to 30 years.

These patients regularly attended our out-patient department. Their consumption of alcohol was controlled by direct questioning, measurement of breath alcohol and assay of various enzymes (GGT, ASAT, ALAT) and mean corpuscular volume.

Electroneurography was performed on three nerves at both occasions: median, peroneal and sural nerves, and the following 10 electroneurographical parameters were measured: *Median nerve:* (1) Motor nerve conduction velocity between elbow and wrist, (2) motor conduction latency between wrist and test muscle (opponens), (3) conduction velocity and (4) amplitude of the mixed nerve action potential recorded at the elbow, elicited by stimulation of the nerve at the wrist, (5) conduction velocity and (6) amplitude of the sensory nerve action potential recorded at the wrist, elicited by stimulation of the digital nerves at the base of the index finger. *Peroneal nerve:* (7) Motor nerve conduction velocity between knee and ankle, (8) motor conduction latency between ankle and test muscle (extensor digitorum). *Sural nerve:* (9) Conduction velocity and (10) amplitude of the sensory nerve action potential recorded behind the lateral malleolus, elicited by stimulation of the nerve at the middle part of the lower leg.

The distal motor conduction latencies (parameters 2 and 8) were converted into a factor = conduction distance (cm) / conduction latency (ms). Figure 1, shows the electrode positions. All stimulations were made in the conventional way by electrical square pulses of 0·2 ms duration with surface electrodes. All recordings were made by surface electrodes, the nerve action potentials bipolarly with the electrodes along the nerve 2 cm apart. Skin temperature was not measured.

The electroneurographical parameters showed a considerable inter- and intra-individual variability due to technical as well as biological conditions. This means that quite a large deviation from normal mean values were required before detecting significant pathological values when

Received 27 September 1983 and in revised form 25 January 1984. Accepted 30 January 1984

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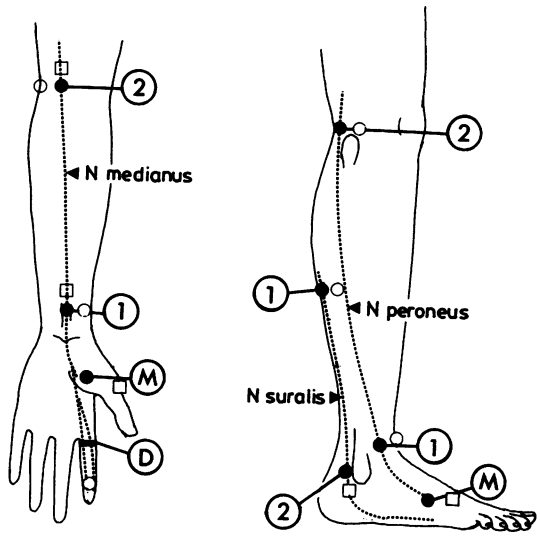

Fig 1 *Positions of stimulating and recording electrodes. M = Muscle response recording electrode, D = Digital nerve stimulating electrode. Filled circle indicates position of cathode or position of first recording electrode (nearest to the stimulus). Open circle indicates position of anode. Open square indicates position of second recording electrode (all nerve action potentials were recorded bipolarly with the recording electrodes (all nerve action potentials were recorded bipolarly with the recording electrodes 2 cm apart).*

1 and 2 = stimulating or recording electrodes

examining single parameters. Therefore a score was made in which the values of all the above mentioned ten electroneurographical parameters are taken into consideration. All these values were then expressed in equal units. The deviation of the values from their corresponding normal mean values expressed in standard deviations were used as a basis for a score. Two standard deviations (2 SD) are usually regarded as a statistically significant ($p < 0.05$) deviation from a mean value. If the standard deviations of ten independent variables are used to calculate a mean deviation, the corresponding level of significant deviation from the normal mean values will be ± 0.63 ($= \pm 2.0/\sqrt{10}$). We assumed that such a score would be more reliable as a basis for electroneurographical neuropathy diagnosis than regarding the different electroneurographical parameters separately.

In some cases a supramaximal nerve stimulation did not elicit a measurable nerve action potential or a muscle response. In such a case the value zero was used for the amplitude parameters but not for the conduction velocities, as this would give unreasonably low scores. In cases of axonal neuropathy, conduction velocities below 30 m/s are rarely found. We have therefore arbitrarily used 30 m/s as a substitute value for peroneal motor nerve conduction velocity and 35 m/s for sural sensory nerve conduction velocity in those cases where no muscle response could be elicited.

Electroneurographical normal values and standard deviations for calculation of the scores were taken from a group of 80 healthy male workers from two electronic plants, that was used as a reference group in another study[5] concerning effects of organic solvents on peripheral nerves. When calculating the electroneurographical score, the age of the subject was taken into consideration.

The clinical neurological findings were scored according to a numerical index. A value of zero was assigned if the finding was normal. For a patient who could not walk unaided because of weak muscles the score was 4 points. If the patient could not squat down and/or get up without the help of hands or had difficulty in walking on heel or toe the score was two. Muscle atrophy was scored one if slight and two if prominent, and the biceps, patellar and ankle jerks were scored one if uncertain and two if absent.

Sensitivity to figure writing was tested on the forefoot. The score was zero, if five centimeter high figures were perceived, one if only higher figures were perceived and two, if the patient failed to perceive the figures correctly. Vibration measurements were made with a standard tuning fork (128C) beginning from the tips of the toes and fingers and if absent the score was one. If absent on the medial malleoli of the feet or on the metacarpophalangeal eminences of the hands the score was two. Diminished or altered sensitivity to hair touch was scored one, and two if it was absent. Finally, sensitivity to passive movements was tested in toes and fingers. If small flexions or extensions were correctly perceived the score was zero but if some mistakes were made it was one and if the patient did not at all perceive movements at least in his toes the score was two. This semi-quantitative evaluation scale had a maximum range from zero to twenty.

Results

All electroneurographical parameter results are given in table 1. The electroneurographical scores based upon these values are given in table 2. In addition to the *All Nerves* score, separate scores are given for the three nerves examined.

Table 2 also gives the clinical scores. According to clinical criteria most of the patients had only mild to moderate signs of polyneuropathy. For example, none of the patients had severe muscle weakness and none was chairbound. The scores are all shown of a patient (case 11) who was initially free from neuropathy, but developed it during the follow-up when he continued to drink daily.

Figure 2 shows the *All Nerves* electroneurographical scores plotted against the age of the patient. All the patients underwent two (in one case, No. 11, three) examinations and the results for each patient are joined by a straight line. Thus, the direction and the slope of the line indicates to what extent the electroneurographical neuropathy score of a particular patient changed with time. In another study[6] it was found by repeated examination of volunteers that score variations of less than 0·67 in a single

Table 1 *Electroneurographical parameter values*

Pat no	*Age (yr)*	*Parameter No*									
		1	*2*	*3*	*4*	*5*	*6*	*7*	*8*	*9*	*10*
1	69	44	1·7	54	10	42	5	27	0·7	29	2
	72	51	1·9			47	4	45	1·1	39	4
2	57	56	1·7	58	16	50	20	35	1·0	—	0
	61	55	2·0	64	8	55	15	19	0·7	54	5
3	57	52	1·7	56	10	53	4	41	0·9	45	4
	61	51	1·6	55	5	50	5	—	—	—	0
4	33	55	2·0	63	22	52	10	32	1·6	—	0
	38	51	2·0	53	24	36	15	30	1·3	—	0
5	45	46	1·7	58	8	46	18	41	0·5	42	6
	50	58	1·8	65	16	47	12	41	1·2	51	13
6	67	42	2·1	54	12	45	10	35	1·1	—	0
	72	53	2·1	55	9	43	7	30	0·7	42	4
7	35	47	0·8	52	12	42	42	53	1·3	49	10
	38	53	2·0	62	48	58	13	48	1·7	43	6
8	46	57	1·7	59	9	58	13	49	2·0	—	0
	50	44	2·0	53	8	53	3	47	2·0	39	8
9	48	52	1·8	56	4	54	12	34	0·8	—	0
	53	54	1·7			51	3	45	1·5	44	1
10	36	55	1·3	57	8	44	34	—	—	—	0
	40	50	1·2	70	15	61	5	53	1·7	51	13
11	44	56	2·5	53	54	53	8	46	1·6	46	2
	49	50	2·2			50	3	48	1·2	44	7
	49	49	2·1			45	8	37	1·0	33	5

Notes: Parameter numbers refer to the numbers presented in the text, that is Median nerve:
(1) motor nerve conduction velocity (m/s)
(2) peripheral motor conduction latency factor
(3) mixed nerve action potential, conduction velocity (m/s), and
(4) amplitude (microvolt)
(5) sensory nerve action potential, conduction velocity (m/s), and
(6) amplitude (microvolt)
Peroneal nerve:
(7) motor nerve conduction velocity (m/s)
(8) peripheral motor conduction latency factor
Sural nerve:
(9) sensory nerve action potential, conduction velocity (m/s), and
(10) amplitude (microvolt).

Table 2 *Clinical and electroneurographical neuropathy scores*

Pat No	*Year of examination*	*Clinical score*	*Electroneurographical neuropathy score*			
			All Nerves	*Median*	*Peroneal*	*Sural*
1	1979	6	−1·87	−1·17	−3·60	−0·97
	1982	1	−0·29	−0·20	−0·70	−0·08
2	1978	4	−0·83	−0·16	−2·32	−1·34
	1982	3	−0·44	+0·39	−4·67	+1·27
3	1978	7	−0·87	−0·82	−1·96	−0·87
	1982	11	−1·54	−0·89	−3·52	−1·52
4	1977	4	−1·20	−0·79	−1·52	−2·13
	1982	5	−1·84	−1·61	−2·38	−1·98
5	1978	4	−1·51	−1·25	−3·25	−0·55
	1982	0	−0·13	−0·20	−1·31	+1·25
6	1977	3	−1·00	−0·72	−1·83	−1·01
	1982	0	−0·67	−0·11	−3·29	+0·27
7	1979	3	−1·28	−2·22	−0·04	+0·28
	1982	0	−0·10	−0·20	+0·74	−0·63
8	1978	3	−0·32	−0·50	+1·63	−1·75
	1982	0	−0·62	−1·34	+1·42	−0·49
9	1977	4	−1·39	−0·44	−3·08	−1·60
	1982	1	−0·46	−0·72	+0·03	−0·43
10	1978	5	−2·01	−1·33	−3·99	−2·05
	1982	0	−0·20	−0·94	+1·04	+0·80
11	1977	0	−0·05	+0·01	+0·17	−0·39
	1982 (april)	6	−0·45	−0·57	−0·58	−0·06
	1982 (nov)	8	−1·34	−0·83	−2·24	−1·47

Notes: Due to missing values (cf table 1) the All Nerves scores for Pats Nos 1, 9 and 11 are based on 8 parameters. In these cases the level of significant neuropathy is 0·71 ($= 2·0/\sqrt{8}$) instead of 0·63.

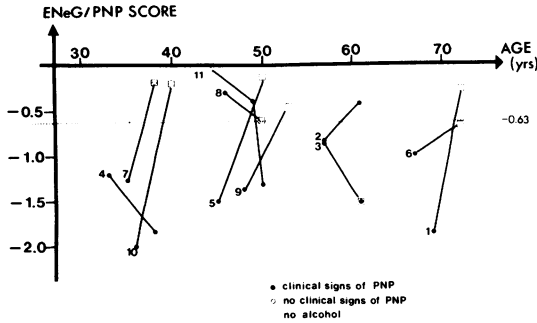

Fig 2 *The electroneurographical All Nerves polyneuropathy scores plotted against the age of each patient at the time of examination. The figures (1–11) refer to the patient numbers. The lines join the results of the same patient at the two (or three) examinations. The horizontal, broken line indicates the border between "normal" and "neuropathic" score.*

subject cannot be regarded as a significant change of the electroneurographical status. Thus in the present study the electroneurographical status was not significantly changed in cases No. 2, 4, 6 and 8. Among the remaining cases, No. 1, 5, 7, 9 and 10 did show regress of the neuropathy while No. 3 and 11 had deteriorated.

Three patients continued to drink (cases No. 2, 4 and 11) in amounts similar to those before the initial examination. Two others (cases No. 1 and 8) could not abstain totally but were able to cut down their drinking to a few drinks per week and six totally abstained. Those three who continued to drink showed elevated mean corpuscular volume and gammaglutamyl transpeptidase values during follow-up and at the time of re-examination. On the other hand, these values became normal in those eight patients who stopped drinking or diminished markedly their alcohol intake for periods varying from six months to several years preceding the re-examination.

Figure 2 indicates that both electroneurographical and clinical neuropathy disappeared in the majority of the eight patients who were able to cut down or stop drinking. A remarkable exception was case No. 3 who, however, also had diabetes. Recovery was found in all age groups, and even though some of the patients had used aversive drugs (disulfiram, calcium carbimide) for several weeks or months. In addition, two patients (cases No. 6 and 9) had lowered serum albumin suggesting liver disease.

One of the three patients who continued heavy drinking, showed electroneurographical and clinical deterioration (No. 11). The other two (No. 2 and 4) did not change significantly in their *All Nerves* scores but they were significantly deteriorated in their peroneal nerve scores (cf Table 2).

An *All Nerves* score of less than − 0·63 implies a statistically significant ($p < 0·05$) deviation from normal (reference) electroneurographical, that is a neuropathy. As can be seen from fig 2, most cases with a score above − 0·63 were free from clinical signs of neuropathy while below this level all cases but one (No. 6, 2nd exam.) had a clinically verified neuropathy.

Discussion

The findings indicate that the prognosis of slight and moderate alcoholic polyneuropathy is good and independent of age provided that the patient stops drinking. We have also seen two initially chairbound cases, not included in this series, where rehabilitation and abstinence resulted within six months in a marked clinical improvement. This included good ambulation, and almost complete disappearance of muscle weakness and sensory symptoms. Similar observations have also been reported by others.[1 3 7]

It was previously thought that if alcohol has a direct neurotoxic effect on peripheral nerves, the alcoholic polyneuropathy should become progressively worse with continued drinking. However, although reinnervation may be poor in this condition compared with other neuropathies, regeneration does seem to occur at least in the distal parts of the nerves. Alcoholic neuropathy may remain subclinical or unchanged for several months or years despite continuous drinking.[4 8–10] In general, the degree of recovery after toxic nerve damage varies with different agents as was emphasised in a recent article by Le Quesne.[11]

The data available so far do not unanimously suggest a single cause for alcoholic polyneuropathy. Already five decades ago it was concluded that alcoholic polyneuropathy may be regarded as similar to the polyneuropathy of beriberi and treated accordingly.[1] However, the conclusion was based on studies with poor control material, short follow-up periods and poor diagnostic criteria. Later on, a more comprehensive study showed that alcoholics as a group have a high frequency of combined vitamin B deficiencies, but these patients do not always have polyneuropathy.[12]

The results cannot answer whether our patients had neuropathy of nutritional or toxic aetiology. Even nutritional neuropathies usually recover although the most severe cases may remain permantently disabled.[13] The three patients who continued drinking in our series were given adequate vitamin therapy, but despite this, their signs and symptoms were not markedly improved. On the other hand, four of the eight patients who managed to abstain

did not receive vitamins at all, but they all recovered. In contrast, two of them received calcium carbimide or disulfiram for several months.

Although good prognosis of polyneuropathy in the alcoholics who stop drinking was clearly evident, we cannot determine the prognosis if heavy alcohol intake continues. However, a bad prognosis was suggested by a previous study.[14]

Interestingly, the neuropathy of the patient with diabetes became worse although he was abstinant for at least six months before his re-examination. It has been reported that early effective control of diabetes will lead to a reduction in the incidence of serious nerve damage.[15] Our records revealed that this patient could not, however, treat his diabetes adequately.

Finally, we want to emphasise that the diagnosis of alcoholic polyneuropathy cannot be made without a long enough follow-up of each individual patient. Alcoholics may have many other causes of neuropathy, for example, malignancy, nerve trauma, cervical or lumbal spondylosis, infections, diabetes mellitus. All of these must be carefully excluded before the diagnosis is made. Perhaps a poor diagnostic accuracy represents the most important cause of controversy surrounding alcoholic neuropathies.

This work was supported by the Karolinska Project for Research and Treatment of Alcoholic Dependence (KARTAD).

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