Generalised peripheral nerve dysfunction in acromegaly: a study by conventional and novel neurophysiological techniques

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SUMMARY Twenty four patients with clinical, radiological and biochemical evidence of acromegaly were investigated by a number of independent neurophysiological tests. Two-thirds of the patients showed evidence of generalised peripheral nerve dysfunction. A significant correlation was found between total exchangeable body sodium, an indicator of disease activity, and the severity of the neuropathy. The generalised peripheral nerve abnormality was found to occur independently of the associated carbohydrate intolerance human growth hormone levels and other endocrinological dysfunction in this disorder.

The association of median nerve entrapment at the wrist with acromegaly is well known^{1–5} and is probably due to compression of the nerve by hypertrophic connective tissue.^{3,6,7} Unilateral or bilateral carpal tunnel syndrome is one of the first symptoms in 12% of patients with acromegaly⁸ and later in the course of the disease the incidence may rise to as high as 35–47%.^{8,9} Generalised neuropathy is a much less recognised complication and only occasional reports have appeared.^{10–17} This neuropathy was found to be predominantly sensory in nature¹⁸ but severe muscle weakness and wasting have been described.¹³

Although believed to be related to the disease process, no correlation has been found between this peripheral nerve dysfunction and indices of human growth hormone (HGH) secretion and the associated glucose intolerance.^{8,15} This finding was not based on statistical analysis of this correlation in an adequate number of patients but rather on observations on individual patients.

We have looked for evidence of a generalised peripheral neuropathy in 24 patients with acromegaly and have correlated our findings with measurements

of body composition, circulating HGH concentration, thyroid dysfunction, total exchangeable body sodium and other endocrine data. The relative frequency of involvement of large versus small fibre afferent pathways was assessed using conventional electromyography and nerve conduction studies, our recently introduced technique for the study of thermal thresholds¹⁹ and the technique of Goldberg and Lindblom²⁰ for the quantitative measurement of vibration thresholds.

Methods and materials

THE NEUROPHYSIOLOGICAL TECHNIQUES *Electromyography and nerve conduction studies*

Electromyography (EMG) and nerve conduction (NC) studies were performed using a Medelec MS91 electromyograph. The fastest motor nerve conduction velocity (FMNCV) and the shortest distal motor latency (SDML) for the right lateral popliteal nerve (LPN) and median nerve were recorded from surface electrodes over the extensor digitorum brevis (EDB) and abductor pollicis brevis (APB) muscles respectively by conventional techniques.²¹ The sensory nerve action potentials (SNAPs) were elicited orthodromically in the right median and sural nerves. For each SNAP measurement, 64 potentials were averaged. Sensory latencies were measured from the onset of the stimulus artefact to the peak of the negative deflection. Amplitudes were measured from peak to peak. For median SNAP studies, the method of Gilliatt and Sears²² was followed. The sural nerve was stimulated at the lateral aspect of the foot immediately

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Received 13 May 1986 and in revised form 8 October 1986.
Accepted 10 October 1986

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inferior and anterior to the lateral malleolus and the potential recorded by surface electrodes 12–14 cm proximal to the malleolus and lateral to the tendo achillis. The distance between the recording and the reference electrodes was 4 cm. Electromyographic studies were performed with concentric needle electrodes in the APB and the EDB muscles. The ambient room temperature was kept at $22 \pm 2^\circ\text{C}$. Skin temperature of the limb was maintained at $34 \pm 1^\circ\text{C}$ using a thermostatically controlled heating lamp.

Thermal thresholds measurement

Thresholds for appreciation of heat (HT) and cold (CT) were determined for the volar aspect of the right wrist just proximal to the distal wrist crease and for the medial aspect of the right ankle behind the medial malleolus. These were expressed in temperature change from the basal skin temperature (before application of the stimulus) using a micro-computer controlled system and the two-alternative forced-choice method of psychophysical analysis (The Glasgow Thermal System). The method and control values of threshold measurements have been described in detail elsewhere.^{19 23}

Vibration threshold measurement

Vibration perception threshold (VPT) was measured in all subjects on the dorsal aspect of the middle of the right second metacarpal bone and on the dorso-medial aspect of the middle of the right first metatarsal bone where the overlying subcutaneous tissue is thin. The technique, its physiological basis and normal values have been described.²⁰ Briefly, the vibration stimulus intensity is assessed from the displacement of the skin in micrometres and not from the voltage applied to the vibrometer. The degree of displacement of skin is the physiological stimulus to the vibration-sensitive receptors.^{20 24} The apparatus (Somedic AB Vibrometer type III) consists of an electromagnetic vibrator with a 13 mm diameter probe which vibrates at right angles to the skin. The amplitude of the skin displacement (the vibration amplitude) is measured indirectly by an accelerometer with continuous digital display. The vibrator is held against the skin with a force of 500 ± 100 g by reference to a force indicator on the Vibrometer. The subject is placed in a comfortable position, the right leg is supported by pillows to prevent stimulus spread and a suprathreshold test is applied to familiarise him/her with the sensation produced. The apparatus can deliver two standardised rates of increase in stimulus intensity, slow or fast. The amplitude of vibration is increased using one of these alternatives and the subject is instructed to indicate when he/she feels the stimulus. The vibration amplitude is repeated at the alternative rate of increase of stimulus intensity. The average of three trials is taken as the VPT. In cases where there is more than 10% variation between the values, further trials are performed until 3 consecutive readings are within the 10% limit.

Vibration amplitudes in the range of 0–399.9 μm at 100 Hz can be produced by the apparatus. The VPT determinations are made in a quiet room with a constant ambient temperature ($22 \pm 2^\circ\text{C}$). Skin temperature is kept at $34 \pm 1^\circ\text{C}$ with a thermostatically controlled heat source. On the average less than 5 minutes is required for each VPT determination. All investigations were carried out by the same person (GAJ).

PATIENTS AND CONTROL SUBJECTS

The normal values for various tests come from different control groups. Healthy control groups were drawn from among the staff and their relatives of the Institute of Neurological Sciences, Southern General Hospital, Glasgow. There were 61 control subjects for the thermal thresholds aged 35–73 (mean = 45.5, SD = 11.8) years. The control group for the EMG and NC studies contained 21 healthy subjects aged 23–69 (mean = 46, SD = 12) years. The control group for the vibration threshold measurement consisted of 27 subjects aged 17–64 (mean = 46.2, SD = 11.5) years.

Patients

Twenty four patients with clinical, radiological and biochemical evidence of acromegaly attending the Department of Medicine at the Western Infirmary, Glasgow, were included in this study. Their ages ranged from 26 to 78 (mean = 48, SD = 15.4) years. There were 14 female and 10 male patients. All the patients were informed about the nature and purpose of the study and agreed to participate. Those thought to have excessive alcohol intake or to be taking drugs likely to cause peripheral nerve dysfunction were excluded from the study. All patients had received some treatment for their acromegaly. This and other clinical details are shown in table 1 which include, where available, the hormonal status both at diagnosis and at the time of the neurophysiological studies.

All patients had been admitted to hospital for full biochemical and endocrinological evaluation within 6 months prior to the neurophysiological measurements.²⁵ A standard 50 g oral glucose tolerance test was performed on each after an overnight fast. Blood samples (venous cannula) were taken at the time of glucose ingestion and at 30 minute intervals for 2 hours for blood glucose and HGH estimations. The areas under glucose and HGH curves during the glucose tolerance test were also measured. A "HGH day curve" from blood samples taken during one day at 800, 1100, 1300, 1700 and 1900 hours, was also performed to obtain the mean circulatory HGH concentration. HGH was measured by radioimmunoassay using the 1st international reference preparation (MRC 66/127; 1 mcg/l = 2 mu/l). Each patient, in addition, had a standard intravenous thyrotrophin-releasing hormone test²⁶ during which the thyroid stimulating hormone (TSH) and HGH were measured at intervals of 0, 20 and 60 minutes after intravenous administration of 200 μg of synthetic thyrotrophin-releasing hormone. Total exchangeable body sodium was determined by the method of Davies and Robertson²⁷ and was expressed as a percentage of that expected in a normal individual of the same body surface area and sex. Total body water was measured by tritium dilution.

Results

Table 1 shows a summary of the clinical findings. Clinical evidence of a generalised neuropathy was present in eight patients while two other patients had typical distal sensory symptoms but without objective clinical evidence on examination. Four of the eight patients had wasting of EDB muscle on both sides

Table 1 Summary of the important clinical data in 24 patients with acromegaly at diagnosis and at the time of the neurophysiological assessment

Case No.	Sex	Age (yr)	Clinical* polyneuropathy	CTS	Clinical nerve hypertrophy	At diagnosis		GTT
						Mean "HGH day curve"	Nae	
1	F	68	+	+	+	43	147	
2	F	48	+	—	+	67	126	
3	F	38	—	—	+			
4	M	52	+	—	+			
5	M	30	+	+	+			
6	M	46	—	—	—	39	133	
7	M	66	+	—	+	17	126	
8	F	30	—	+	+			
9	F	68	+	—	—			
10	M	26	—	—	—	618	118	
11	M	43	—	—	—	135	132	
12	F	52	—	—	—	19	120	
13	F	62	—	—	—			
14	F	29	—	—	—	36	114	
15	M	30	—	+	—		139	
16	F	56	—	+	—	63	134	
17	F	65	—	+	—	109	134	
18	F	54	—	+	—	97	120	
19	M	65	+	+	+	140	155	
20	F	42	—	—	+	36	108	
21	M	78	+	+	+	80	153	
22	M	37	—	+	—	38	131	
23	F	35	—	—	—	29	115	
24	F	33	—	—	—	16	107	

*All patients with (+) had signs of weakness and/or wasting of small muscles of the foot and hyposensation to one or more of the following in a stocking-glove distribution: pinprick, light touch, vibration with or without symptoms (paraesthesiae, numbness, abnormal heat or cold sensation) or a generalised neuropathy.

Abbreviations: F: female; M: male; +: present; —: absent; N: normal; Abn: abnormal; H: hypophysectomy; I: irradiation; CTS: carpal tunnel syndrome; Nae: total exchangeable body sodium; GTT: glucose tolerance test; HGH: human growth hormone; TRH: thyrotrophin-releasing hormone.

accompanied by weakness of toe flexion and extension and cupping of the sole of the feet while the power of ankle joint or more proximal movements were not reduced. Reflexes were diminished in all the eight patients; in one patient all reflexes were lost whereas in the remaining seven ankle jerks were lost and knee jerks were either absent (four patients) or only present on reinforcement (three patients). Clinical abnormality of reflexes in these eight patients was accompanied by abnormalities of H-reflex on electrical testing. All the eight patients had distal sensory changes in both lower limbs in the form of hyposensation to pinprick (6/8), light touch (7/8) and vibration (7/8) in a stocking distribution. Distal sensory symptoms including numbness, paraesthesia and abnormal heat or cold sensation were present in only five of these eight patients with objective sensory changes. In 10 patients, mostly with clinical evidence of neuropathy, the ulnar and/or the lateral popliteal nerves were considered to be enlarged clinically.

The results of the neurophysiological assessments of the control subjects and the patients with acromegaly are summarised and compared in table 2. The statistical significance of the results was evaluated using Student's *t* test. It is clear from table 2 that all but one (the sural SNAP latency) of the neurophysiological parameters are significantly abnormal

in the patients with acromegaly compared with the normal control groups. The mean values of the upper and lower limbs thermal and vibration thresholds, the median SNAP latency, the SDML for the LPN and median nerve were all significantly higher than corresponding means for the control groups. The mean values of the FMNCV for the LPN and median nerve and the median and sural SNAP amplitude were significantly lower than those of the control group.

The figure shows the distribution and the relative frequencies of the abnormalities for the neurophysiological tests. Values above the 95th percentile were abnormal for sensory and motor conduction and vibration threshold studies while thermal threshold values in excess of the 99th percentile were considered abnormal. The SDML and/or the FMNCV for the LPN were abnormal in 50% of the patients. The sural SNAP amplitude and/or latency were abnormal in 14% of the patients with acromegaly. A smaller number of patients had abnormalities in the sensory and/or motor median nerve conduction studies (table 3).

Thermal thresholds for one or both sites were abnormal in 67% of the patients studied. The thermal threshold abnormalities were generally more marked and more frequent at the ankle (62%) than at the wrist (42%) (table 3). Abnormal VPT at the tarsal site

At present					Treatment	
Mean "HGH day curve"	Nae	GTT	Mean HGH during GTT	TRH test	Type	Duration (yr)
6.1	125	Abn	3.9	Abn	H	5
9.3	107	N	16	N	H & I	4
1.8	96	N	1.9		H	6
1.8	109	N	1.9		H & I	19
1.6		N	0.8	N	H & I	10
7	112	Abn	6.8	Abn	H & I	3
4.1	125	Abn	3.2	Abn	H	10
4.5	121	N	4.5	Abn	H	2
22.2	138	N	20.4	Abn	H	14
115.8	115	N	24.6	Abn	I	6
11.4	107	N	11.3	Abn	H	11
4.2	111	N	4.4	Abn	I	10
2.9	93	N	1.4	N	I	10
29.2	109	N	40	Abn	H	6
17.3	118	Abn	15.8	Abn	H & I	8
6.7	115	N	6.2		H	2
2.4	107	N	2	Abn	H & I	8
2.5	111	Abn	2.7	N	H	6
2.2	128	Abn	1.6	Abn	H	7
21.8		N	18.8		H	12
17	144	N	28	N	H	30
8	119	N	9.2	N	H & I	3
1.2	93	N	1.2		H	10
2.9	93	N	1.6	N	H	5

Table 2 Neurophysiological data: comparison of normal and patient groups

Parameter	Group	N	Mean	SD	Units	p
Ankle HT	Normal	40	1.59	0.82		< 0.001
	Acromegaly	24	4.17	2.16	°C	
Ankle CT	Normal	40	0.18	0.07		< 0.001
	Acromegaly	24	0.43	0.28	°C	
Wrist HT	Normal	40	0.23	0.07		< 0.02
	Acromegaly	24	0.55	0.62	°C	
Wrist CT	Normal	40	0.16	0.05		< 0.03
	Acromegaly	24	0.26	0.21	°C	
Carpal VPT	Normal	27	0.8	0.41		NS
	Acromegaly	24	1.21	1.51	um	
Tarsal VPT	Normal	27	1.63	0.45		< 0.05
	Acromegaly	24	4.42	6.13	um	
Median SDML	Normal	21	3.54	0.35		< 0.02
	Acromegaly	24	3.98	0.77	ms	
Median FMNCV	Normal	21	58.6	4.8		< 0.05
	Acromegaly	24	54.8	7.66	m/s	
Median SNAP latency	Normal	21	2.92	0.26		< 0.01
	Acromegaly	24	3.52	0.99	ms	
Median SNAP amplitude	Normal	21	17.8	7		< 0.01
	Acromegaly	24	11.7	8	uv	
SDML for LPN	Normal	21	3.59	0.44		< 0.001
	Acromegaly	24	4.5	0.9	ms	
FMNCV for LPN	Normal	21	50.5	4.6		< 0.001
	Acromegaly	24	45.9	3.4	m/s	
Sural SNAP latency	Normal	21	3.62	0.44		NS
	Acromegaly	24	3.53	0.42	ms	
Sural SNAP amplitude	Normal	21	6.8	2		< 0.005
	Acromegaly	24	4.8	2.15	uv	

Abbreviations: HT: heat threshold; CT: cold threshold; VPT: vibration perception threshold; SDML: shortest distal motor latency; FMNCV: fastest motor nerve conduction velocity; SNAP: = sensory nerve action potential; LPN: lateral popliteal nerve.

Fig The distribution of the values of the neurophysiological tests performed in 24 patients with acromegaly. A: in the upper limb; B: in the lower limb. The scales are drawn so that control means and control standard deviations coincide to render comparison easy. The axes of the median and sural SNAP amplitudes and the LPN and median FMNCVs are reversed so that abnormalities are shown as shifts in upward direction for all the parameters. HT: heat threshold; CT: cold threshold; SNAP: sensory nerve action potential; SDML: shortest distal motor latency; FMNCV: fastest motor nerve conduction velocity; LPN: lateral popliteal nerve; VPT: vibration perception threshold.

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Table 3 Frequency of abnormality of neurophysiological parameters in 24 patients with acromegaly

Neurophysiological parameter(s)	Criteria of abnormality	Patients with abnormal values	
		No.	%
Ankle HT	99% CL	14	58
Ankle CT	99% CL	9	37
Wrist HT	99% CL	9	37
Wrist CT	99% CL	5	21
Tarsal VPT	95% CL	9	37
Carpal VPT	95% CL	3	12
Median SDML	95% CL	7	29
Median FMNCV	95% CL	6	25
Median SNAP latency	95% CL	7	29
Median SNAP amplitude	95% CL	5	21
SDML for LPN	95% CL	11	46
FMNCV for LPN	95% CL	3	12
Sural SNAP latency	95% CL	1	4
Sural SNAP amplitude	95% CL	3	12
HT and/or CT at ankle	99% CL	15	62
HT and/or CT at wrist	99% CL	10	42
HT and/or CT at wrist and/or ankle	99% CL	16	67
Carpal and/or Tarsal VPT	95% CL	9	37
SDML and/or FMNCV for LPN	95% CL	12	50
Sural SNAP latency and/or amplitude	95% CL	4	17
Abnormal LPN and/or sural NC studies	95% CL	12	50

Abbreviations: As in table 2.

was encountered in 37% of the patients while 12% had VPT abnormality at the carpal site (table 3).

The diagnosis of carpal tunnel syndrome was made on both clinical and electrophysiological evidence. The clinical criteria of carpal tunnel syndrome included one or more of the following features: paraesthesiae in the distribution of the median nerve; wasting and/or weakness of the APB muscle and sensory impairment in the median nerve distribution of the hand. The electrophysiological criteria of carpal tunnel syndrome included one or more of the following abnormalities: a prolonged median nerve SDML, a prolonged median SNAP latency and a reduced median SNAP amplitude at the wrist. These criteria had to obtain in the presence of normal ulnar nerve and proximal median nerve conduction studies. Ten patients had both clinical and electrophysiological criteria of carpal tunnel syndrome (42%). In five patients, two of whom had bilateral carpal tunnel syndrome, this was the only abnormality in their neurophysiological tests. In the remaining five of the carpal tunnel syndrome patients, there was also evidence, from one or more of the neurophysiological tests performed on the lower limbs, of a widespread subclinical dysfunction of the peripheral nerves and their end organs (table 4).

Table 4 Summary of some of the neurophysiological tests in 10 patients with acromegaly associated carpal tunnel syndrome

Patient No.	Median nerve				Sural nerve			LPN FMNCV	Thermal thresholds					
	Motor		SNAP		SNAP		Wrist		Ankle		VPT			
	SDML	FMNCV	Lat	Amp	Lat	Amp	HT		CT	HT	CT	Carpal	Tarsal	
15	4.7	50	4.5	5	4.5	3	44.2	0.15	0.15	2.85	0.25	0.4	0.6	
16	4.3	49.5	3.2	12	4	5	45	0.15	0.15	2.95	0.75	0.6	2.2	
17	5	53.5	3.8	5	3.3	6	46	0.15	0.15	1.35	0.25	0.2	0.9	
18	4.8	49	6.5	0.5	3.4	5	44	0.15	0.15	3.45	0.35	0.8	1.5	
22	3.6	50	3.6	12	3.8	6	50	0.25	0.15	3.15	0.25	0.6	1.6	
1	6	46	5.4	3.5	4.3	4	43.4	0.35	0.25	5.65	0.35	5.7	45	
7	4.2	54.3	4.5	3	3.6	3.5	41.7	1.45	0.95	6.75	1.15	5.6	10.6	
9	4.6	60	3.3	7	3.3	3	46.4	0.65	0.28	7.35	0.45	0.7	3.5	
19	3.8	55	3.8	4	3.3	3.5	43	1.45	0.35	5.25	0.65	0.8	5.6	
21	5.4	46	5.5	2	4.0	4	46	0.35	0.25	4.20	0.75	0.9	2.6	

Abbreviations: As for table 2. Abnormal values for VPT and thermal thresholds are underlined.

Table 5 Correlations between total exchangeable body sodium and the neurophysiological parameters in 22 patients with acromegaly

Neurophysiological parameter	At the time of diagnosis of acromegaly		At present	
	r	p	r	p
Ankle HT	0.69	< 0.001	0.455787	0.02
Ankle CT	0.4347	< 0.05	0.428333	0.02
Tarsal VPT	0.4282	< 0.05	0.290966	NS
Median SDML	0.689	< 0.001	0.584923	0.01
Median SNAP latency	0.4397	< 0.05	0.447054	0.02
Median SNAP amplitude	- 0.6677	< 0.001	- 0.2489	NS
Sural SNAP amplitude	- 0.679	< 0.001	- 0.424078	0.05
Sural SNAP latency	0.609	< 0.01	0.317485	NS
SDML for LPN	- 0.25	NS	- 0.157554	NS
FMNCV for LPN	- 0.4454	< 0.05	- 0.484736	0.02

Abbreviations: As in table 2.

There was no significant correlation between the neurophysiological parameters and values of fasting blood sugar, two hour post-prandial glucose, the area under glucose curve during GTT, human growth hormone (HGH), mean HGH during the glucose tolerance test (GTT), the area under HGH curve during GTT, mean "HGH day curve" and TSH levels at 20 and 60 minute intervals during the thyrotrophin-releasing hormone test. The neurophysiological parameters also did not correlate with these endocrinological data performed at the time of the diagnosis of acromegaly before treatment. Significant correlation, however, was found between most of these neurophysiological tests and the total exchangeable body sodium (table 5). No correlation was found between duration of diagnosis of acromegaly and the neurophysiological parameters. It is accepted, however, that the lack of correlation may be due to the difficulty of estimation of the actual duration of this disorder.

Discussion

The results obtained in this study using a number of independent neurophysiological techniques, indicate the presence of a generalised impairment of peripheral motor and sensory nerves in acromegaly. One-third of the patients had clinical and two-thirds had neurophysiological evidence of a generalised neuropathy. Local nerve entrapments were present in 10 of the 24 patients.

Several isolated cases of "hypertrophic" neuropathy have been described in association with acromegaly.¹¹⁻¹³ In a small series of patients with acromegaly, 45% were found to have some enlargement of peripheral nerves clinically.¹⁵ Sural nerve histology in some of these patients showed endoneurial and subperineurial tissue hypertrophy.^{11 12 14} These findings were supported by Low and associates¹⁵ who also demonstrated an increase in the fascicular areas of the sural nerves. Ten of our patients (42%) had clinical evidence of enlargement of peripheral nerves on examination.

The sural sensory action potential (SNAP), when measured to the peak, gives information in its latency about the modal peak of the conduction velocity of the large myelinated nerve fibre velocity population.²⁸ The amplitude gives information about the number of nerve fibres stimulated with a wide variety of velocities.²⁸ This test was abnormal in 14% of the patients (table 3). Abnormal tarsal vibration perception threshold was found in 37% of the patients, an indication of involvement of the large fibre afferent nerve pathway.²⁰ The abnormality of VPT was less severe and less frequent at the carpal site compared with the more distal tarsal position. As the method

measures VPT from the displacement of skin rather than the voltage applied,²⁰ local changes of skin and subcutaneous tissue does not influence VPT measurements.

Thermal thresholds are an indication of function in the small nerve fibre afferent pathway.²⁹ In the acromegalic patients abnormalities of thermal thresholds were more severe at the ankle (67%) than at the wrist (42%). The increase in thermal threshold values in these patients is unlikely to be due to soft tissue hypertrophy as the thermode is calibrated before each threshold measurement so that the rate of temperature change is independent on skin thickness.¹⁹ Sural nerve histological studies in acromegaly have demonstrated a decrease in the density of unmyelinated and myelinated fibres with signs of segmental demyelination and remyelination.¹⁵

Our results suggest involvement of both small and large fibre pathways. In addition, the combination of all the neurophysiological and perceptual tests with the greater frequency of thermal and vibration sense abnormalities distally is similar to the pattern of involvement in many metabolic and toxic peripheral neuropathies where the most severe abnormality occurs in the longest nerve fibre.

No significant correlation was found between the values of the neurophysiological tests and the associated glucose intolerance, the level of HGH in plasma, the mean "HGH day curve", the mean HGH during the glucose tolerance test and the 20 and 60 minute TSH hormone levels during the thyrotrophin-releasing hormone test. This is in agreement with Low *et al*¹⁵ and Pickett *et al*⁸ who found no correlation of the peripheral neuropathy with HGH levels and the associated diabetes mellitus in acromegaly. Total exchangeable body sodium is increased in acromegaly^{25 30 31} and may reflect disease activity since it correlates with HGH levels³¹ and with the duration of the disease process²⁵ and also falls following successful treatment.²⁵ Most of the neurophysiological parameters showed a significant correlation with total exchangeable body sodium; the higher the total exchangeable body sodium, the more abnormal were the neurophysiological tests (table 5). This would reflect a generalised neuropathy which increases in severity with disease activity.

The independence of the neurophysiological data from the glucose intolerance and the pituitary thyroid dysfunction suggests that the neuropathy is not aetiologically similar to that of diabetes mellitus or hypothyroidism. In view of the known correlation between total exchangeable body sodium and HGH,^{25 31} the lack of an association between HGH and the neurophysiological data is difficult to explain but may be due to a different rate of change in the two variables following treatment in this heterogeneous

group of treated acromegalic patients. However, the generalised peripheral neuropathy seems likely to be due to an effect mediated through excessive human growth hormone levels the exact mechanism, remains to be determined.

Unilateral or bilateral carpal tunnel syndrome was present in 10 of our 24 patients. This is in agreement with other published series.^{8,9} The results show that in 50% of patients with acromegaly associated carpal tunnel syndrome, there is an underlying generalised peripheral neuropathy but equally there are 50% who develop the entrapment neuropathy independent of any generalised process.

Conclusion

Generalised peripheral nerve dysfunction is common in patients with acromegaly. The peripheral nerve abnormality does not correlate with the associated diabetes mellitus, the circulating levels of growth hormone, and the pituitary thyroid function. A significant correlation exists between the presence and severity of the peripheral neuropathy and total exchangeable body sodium. Compression neuropathies either as part of the generalised dysfunction, or independent of it, occur frequently. The exact mechanism of this peripheral nerve dysfunction in acromegaly remains to be determined.

We thank Professor J A Simpson, Drs J P Ballantyne, I D Melville, I Bone, A M Thomas and S Hansen for their helpful comments about the manuscript. We thank Mrs M McColl for secretarial assistance. The Somic Vibrometer was supplied by Pfizer Limited.

Dr G A Jamal was supported during the later part of the study by Pfizer Limited.

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