(Cases 3 and 4) were thought to have had a deficient diet, and one (Case 5) was an Asian immigrant child and we see rickets frequently in this immigrant community. All of our patients were living at home and attending the outpatient clinic when they developed rickets.

The place of vitamin D prophylaxis for patients taking anticonvulsant therapy has been debated, but it seems reasonable to suggest that such prophylaxis may be particularly indicated in tuberous sclerosis. The amount of vitamin D required is uncertain, but is probably of the order of 500–1000 units as a daily supplement to a normal diet (Hahn *et al.*, 1975; Silver *et al.*, 1974).

Summary

Five children with tuberous sclerosis and anticonvulsant-associated rickets have been seen in a general paediatric clinic over the last 5 years. It is suggested that vitamin D prophylaxis is particularly indicated in patients with tuberous sclerosis taking anticonvulsant medication.

I thank Dr. J. S. Oldham for permission to publish details of Cases 3, 4, and 5.

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D. P. Addy
Department of Paediatrics, Dudley Road Hospital, Birmingham B18 7QH.

Motor nerve conduction velocity in spinal muscular atrophy of childhood

Spinal muscular atrophy is a hereditary disease characterized by degeneration and loss of motor neurones in the spinal cord and brain stem. Three clinical forms are recognized. The severe infantile form of the disease usually has an early onset, either *in utero* or within the first 2–3 months, and death usually occurs within the first 2 years from severe respiratory involvement. The intermediate form is characterized by normal motor development up to the age of about 6 months, with the infants usually achieving the ability to sit, but unable thereafter to take weight on their legs or to stand and walk. In the mild form the children have normal milestones in the first year of life and are able to walk but show evidence of muscle weakness. Not all cases of spinal muscular atrophy fall neatly into these three categories; many borderline cases are also encountered.

The motor nerve conduction velocity is generally considered to be normal in diseases of anterior horn cells, including spinal muscular atrophy (Munsat *et al.*, 1969; Hausmanowa-Petrusewicz, 1970). However, Gamstorp (1967) found borderline or slow nerve conduction velocities in 6 infants with spinal muscular atrophy, all severely affected. Buchthal and Olsen (1970) noted 'slightly decreased' peroneal nerve conduction velocities in 3 of 9 patients with infantile spinal muscular atrophy. In an extensive study of motor and sensory conduction velocities in Werdnig-Hoffmann disease, Raimbault and Laget (1972) found slow velocities for both motor and sensory fibres of ulnar and posterior tibial nerves in several of the patients. Hausmanowa-Petrusewicz *et al.* (1975) found motor nerve conduction velocities below normal in the ulnar, peroneal, and median nerve in 15, 7, and 3 cases of Werdnig-Hoffmann disease respectively.

This report describes the results of motor nerve conduction velocities in children with spinal muscular atrophy of different severity.

Materials and methods

This study comprises 29 children with spinal muscular atrophy in whom the diagnosis was subsequently confirmed by electromyography (EMG) and muscle biopsy. Their ages ranged from 3 months to 12 years. 12 were male and 17 female. For the purposes of this study they were placed into one of the following groups. (1) Severe (14 infants): this included all those infants with onset at birth or within 3–4 months of age, with severe paralysis and death usually within the first year.

(2) Less severe (15 infants): this group comprised all other children with the intermediate or mild form of the disease, with later onset and ability to sit or walk.

Nerve conduction measurement. The conduction velocities of the motor fibres of the ulnar and posterior tibial nerves were determined in each patient as previously described (Moosa and Dubowitz, 1971). Surface electrodes were used to stimulate the nerves and record the evoked response from the appropriate muscle. The stimulus intensity was varied until maximal response was obtained. The stimulus duration was usually 0·1 ms but often had to be increased to 0·5 ms to obtain a suitable response. The latency of the response was calculated to the peak of the response and the difference in latencies between the two points of

TABLE I

Motor nerve conduction velocities in spinal muscular atrophy of severe form

Case no.	Sex	Age at assessment (m)	Conduction velocity (m/s)		Age of onset	Age at death (m)
			Ulnar	Posterior tibial		
1	M	3	21·6	15·5	Birth	4
2	F	4	22·3	18·3	Birth	8
3	F	8	25·0	*	Birth	9
4	F	7	39·6	22·2	4 m	11
5	F	3	29·6	28·9	Birth	7
6	F	7	18·9	*	Birth	8
7	M	8	28·0	17·0	1 m	11
8	M	6	21·0	16·6	1 m	8
9	F	6	22·0	18·3	1 w	7
10	M	2	21·0	13·0	1 m	—
11	F	6	27·0	19·0	3 m	—
12	F	6	36·0	22·0	3 m	—
13	M	2	22·0	19·5	Birth	3
14	M	6	21·0	18·4	1 m	6
Normal mean (±1 SD)						
Birth			28·3±2·70	22·0±2·36		
3 m			35·5±2·50	26·3±2·25		
6 m			41·7±2·56	32·0±3·06		
1 yr			46·1±3·00	38·2±3·30		

*Not possible to measure because of inadequate response.

TABLE II

Motor nerve conduction velocities in spinal muscular atrophy of less severe type

Case no.	Sex	Age at assessment (yr)	Conduction velocity (m/s)		Age of onset	Present age (yr)
			Ulnar	Posterior tibial		
15	M	2½	60·0	*	<4 m	3½
16	M	1½	*	66·6	?8 m	3½
17	F	1½	21·7	*	<8 m	2½
18†	M	4	67·0	43·8	<13 m	6
19†	F	5	45·3	46·9	>1 yr	7
20†	F	8	54·4	44·4	Birth	10
21†	F	11	70·0	42·0	<18 m	13
22†	M	5	54·8	39·1	18 m	7½
23†	M	5	67·7	42·4	2 yr	7½
24†	F	6	58·3	48·0	1 yr	6½
25	F	12	44·2	*	<11 m	13
26†	F	3½	52·0	45·0	<1 yr	4½
27†	F	4	58·3	48·3	<6 w	5
28†	F	1¾	48·0	43·0	18 m	2½
29	M	6	53·0	*	? Birth	7
Normal mean (±1 SD)						
3 yr			52·5±3·5	44·4±1·9		
Adult			56·3±4·4	45·2±3·2		

*Not possible to measure because of inadequate response.
†Ambulant.

stimulation along a particular nerve was divided into the distance between the points to give the mean velocity of the motor fibres of that nerve. The results were compared to those of a group of normal children of similar ages.

Results

The results for the ulnar and posterior tibial nerve conduction velocities of children in the severe and less severe groups are given in Tables I and II and plotted in Figs. 1 and 2. Suitable responses were obtained in all but one of the ulnar nerves examined but no responses were obtained from posterior tibial nerve stimulation in 6 patients.

Ulnar nerve conduction velocity was slower than normal (i.e., more than 2 SD below mean for age) in 12 of the 14 infants with severe disease, whereas it was slow in 3, fast in 4, and normal in 7 of the patients less severely affected (Table III). The posterior tibial conduction velocity was slow in 11 infants and normal in one infant with the severe disease. In the 11 patients who were less severely affected in whom it was possible to obtain a velocity measurement, it was normal in 10 and fast in one (Table IV).

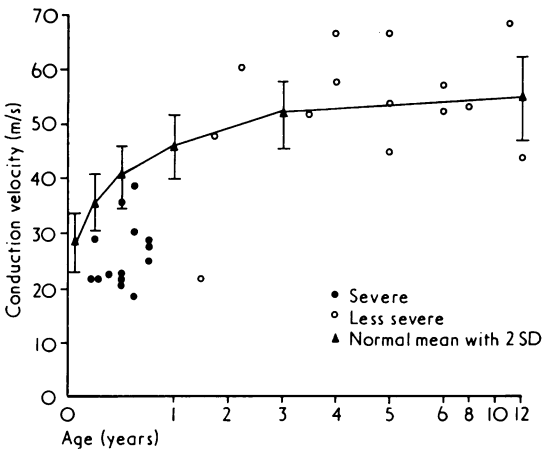

FIG. 1—*Ulnar nerve conduction velocities of children with spinal muscular atrophy.*

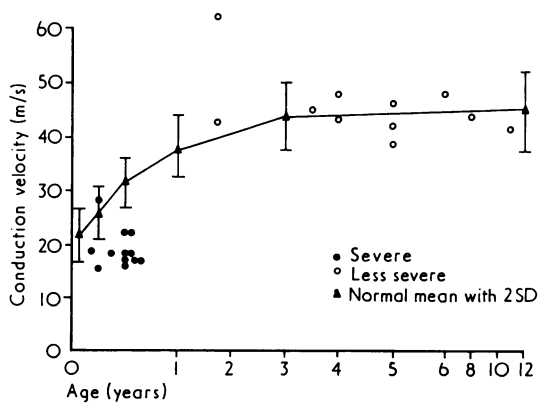

FIG. 2—*Posterior tibial conduction velocity in children with spinal muscular atrophy.*

TABLE III

Ulnar nerve conduction velocity in spinal muscular atrophy

	Group of patients	
	Severe	Less severe
Normal	2	7
Slow	12	3
Fast	0	4

TABLE IV

Posterior tibial conduction velocity in spinal muscular atrophy

	Group of patients	
	Severe	Less severe
Normal	1	10
Slow	11	0
Fast	0	1

Discussion

The striking finding in this study was the slow ulnar and posterior tibial nerve conduction in almost all patients with spinal muscular atrophy who were severely affected, whereas those less severely affected had normal or even faster than normal conduction velocities. One possible explanation for the slow nerve conduction is a selective loss of fastest conducting fibres arising from the largest motor neurones, which in turn would mean that in the less severe forms of spinal muscular atrophy there is selective loss of the slowest conducting fibres in some and random loss in others. Chaco (1970), using double pulse stimulation technique, has found a predominant loss of slow conducting fibres in the adult form of spinal muscular atrophy.

An alternative explanation has been proposed by Hausmanowa-Petrusewicz *et al.* (1975) who found an increased number of unmyelinated fibres in the sural nerve and a decreased density of myelinated

fibres in the ulnar nerve from patients with Werdnig-Hoffmann disease but no evidence of demyelination with teased fibre preparations. They suggested that the slow motor nerve conduction may be due to arrested myelination brought about by the fetal onset of the disease.

The finding of slow conduction in the severe but not in the other forms of spinal muscular atrophy suggests that the severe infantile form of spinal muscular atrophy as a group are different from the other forms of the disease and this might support the views of those workers who believe that different genes are involved (Hausmanowa-Petrusewicz, 1970; Fried and Emery, 1971; Pearn, Carter, and Wilson, 1973). However, the difference may be explained by the early onset in the severe form with secondary effect on myelination.

The presence of slow motor nerve conduction in Werdnig-Hoffmann disease makes it difficult to distinguish it from severe peripheral neuropathy (Karch and Urich, 1975). Recording of sensory action potential may not help either as it has been reported as being absent in Werdnig-Hoffmann disease (Raimbault and Laget, 1972), though our own preliminary studies have failed to confirm this (Schwartz and Moosa, 1976). Difficulties of interpretation may also be encountered in the muscle histology, especially in the very early stages of the disease. The EMG appears to be the only sure way of diagnosis with the finding of the characteristic repetitive discharges described by Buchthal and Olsen (1970). These have not been described in other neurogenic conditions.

Summary

The ulnar and posterior tibial conduction velocities were measured in 29 children with spinal muscular atrophy, 14 of whom had the severe form of the disease. The ulnar nerve velocity was slow in 12 of the 14 severely affected infants, but normal or fast in 11 of 14 children less severely affected. The corresponding results for the posterior tibial nerve were slow velocities in 11 of 12 infants in the severe group and normal or fast in all 11 infants less severely affected. The difficulty in distinguishing infantile spinal muscular atrophy from peripheral neuropathy is emphasized.

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A. MOOSA* and V. DUBOWITZ

Department of Paediatrics and Neonatal Medicine, Institute of Child Health, Hammersmith Hospital, Du Cane Road, London W12.

*Present address: Department of Paediatrics, Somerset Hospital, Beach Road, Green Point, Cape Town, South Africa.

Failure to thrive and death in early infancy associated with raised urinary homovanillic and vanillylmandelic acids

'It is not always possible to find why certain infants fail to thrive. Such instances are regarded as due to some congenital weakness of constitution, a concept which is still far from satisfactory' (Holt and McIntosh, 1933). An enigmatic case of failure to thrive in an infant is here reported.

Case report

A 2½-month-old White boy was brought to the Mayo Clinic for evaluation of failure to thrive. The infant was born at term to a 35-year-old White woman (gravida IV, para 3) whose other 3 children are alive and well. Pregnancy was complicated by polyhydramnios, noted after the fourth month of gestation. Also, at the seventh