individuals of different kinships, or more importantly within the same kinship, such differences would be considered “minor variations” and would not warrant separate classification. In most patients with Refsum’s disease MCV is substantially reduced.1 However, Ulrich et al.11 have found MCV of 45 m/s in the ulnar nerve of a patient but few details were given. In a further case studied in depth by Sahgal and Olsen,10 MCV was 40 and 45 m/s in the ulnar and median nerves respectively. Barolín et al.14 reported in detail the clinical features of two sisters with Refsum’s disease where the MCV in the median nerves of case I were 45 and 50 m/s. In these latter three cases the diagnosis was supported by phytic acid estimation. Thus Refsum’s disease may present with normal or only slightly reduced MCV. In addition, the sister of case 1, that is case 2, had median nerve MCV of 23 and 27 m/s.

In our view, the above data on Charcot-Marie-Tooth disease and Refsum’s disease cast serious doubts on the value of MCV as a means for “genetic” classification.

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References

Thomas replies

Sir: Salisachs et al have raised some interesting questions. Essentially two points are being made. The first is that the estimation of motor nerve conduction velocity is not a fully satisfactory way of separating the different genetic disorders that present clinically as Charcot-Marie-Tooth disease. With this I would entirely agree. The second is that the proposed separation of Charcot-Marie-Tooth disease into two or more genetically distinct types has lost credibility. With this I would not agree.

As there appears to be some difficulty in the interpretation of the available evidence, a brief recapitulation is necessary. Amongst cases diagnosed clinically as peroneal muscular atrophy are patients with distal denervation atrophy in the limbs and without sensory involvement, either clinically or electrophysiologically. These can be designated hereditary distal spinal muscular atrophy.1 2 Probably both autosomal dominant and autosomal recessive inheritance occurs.3 The remaining cases display additional sensory involvement, sometimes only detectable by nerve conduction studies. These can be designated hereditary motor and sensory neuropathy (HMSN).3 4 If median motor nerve conduction velocity in the index cases from such families is plotted against the values obtained in affected relatives, there is a highly significant positive correlation.5 This is strongly suggestive of genetic heterogeneity and supports the view, originally advanced by Dyck and Lambert,6 7 that there are two genetically different forms of the disease, one (type I) with markedly reduced nerve conduction velocity, the other (type II) with velocities within the normal range or only modestly reduced. The value of 38 m/s chosen by Harding and Thomas8 as a dividing line was purely empirical; it gave the best separation between the type I and II clusters in that particular series. It was evident in that study that complete discrimination could not be obtained between families whatever value was taken. Nevertheless, the number of cases misclassified was small.

The median nerve has been chosen for estimates of motor conduction velocity rather than the peroneal or tibial nerves in view of the frequency with which the small foot muscles are totally or almost totally denervated.9 It is of interest that using sensory conduction velocity in the sural nerve as a discriminator, Buchthal and Behse10 obtained complete separation between the hypertrophic (type I) and neuronal (type II) cases; related patients had similar conduction velocities. The two groups thus distinguished were the same
as those separated by changes observed in sural nerve biopsies. The degree of slowing and the reduction in potential amplitude in the sural nerve correlated with the findings for the sensory fibres in the superficial peroneal nerve and the distal sensory branches of the median nerve. It is likely that both types I and II HMSN each display autosomal dominant and autosomal recessive inheritance. 10 11 Conduction velocity in the recessive type I cases is significantly lower than in the dominant cases. 6

In the absence of biochemical markers, confirmation as to the existence of more that one gene responsible for a given clinical syndrome can be obtained from genetic linkage studies. This has recently been undertaken for dominantly inherited HMSN. It has been established that type I HMSN is linked to the Duffy locus on chromosome 1, 12 whereas this is not true for HMSN II. 13 This provides support for the view that there are at least two genetically distinct forms of dominantly inherited HMSN. The clinical features of the two forms, as pointed out by Salisachs et al, are generally similar. This merely reflects the fact that both can be classified as Charcot-Marie-Tooth disease. Individual cases cannot always be distinguished on clinical grounds. Nevertheless, statistical analysis has shown significant differences between the two in the incidence of such features as tremor and ataxia, severity of upper limb motor involvement, tendon areflexia and severity of sensory loss. 5

The concept of Dejerine-Sottas disease is confused as the term has been used widely and imprecisely since its introduction. There is now general agreement that it should be reserved for cases of recessively inherited, childhood onset neuropathy (HMSN III) with hypomyelination in the peripheral nerves as a conspicuous pathological feature. 4 Although nerve conduction velocity tends to be markedly reduced in Dejerine-Sottas disease, it is not feasible to separate such patients from recessively inherited HMSN in this way. They can be distinguished by nerve biopsy. 9 It is difficult to comment on the disparity between the two siblings considered to have Dejerine-Sottas disease included in the paper by Dyck and Lambert 4 and cited by Salisachs et al. This is an early report and documentation is incomplete. For example, for the elder sibling, the results of sensory nerve conduction studies are not given and nerve biopsy was not performed. It is certainly possible that these two cases represent a marked degree of phenotypic variation, which would be unusual for a recessively inherited condition. However, on the evidence presented, it would not be possible to be emphatic that both individuals had the same disorder.

Salisachs et al are quite correct in inferring that at present Refsum's disease appears to be a genetically homogeneous disorder. On the other hand, should future observations indicate clustering of conduction velocities within families, the situation would have to be reconsidered, and investigations undertaken to establish whether this was the result of environmental factors, modifying genes or different main genes.

As is true for inherited disorders in general, detailed study frequently discloses genetic complexity. Charcot-Marie-Tooth disease is likely to be no exception. Indeed, the recently described disorder that clinically resembles type II HMSN but which has an earlier onset and a less favourable prognosis, may be genetically distinct. 18 Classifications can only be provisional, and it is highly probable that the scheme proposed by Dyck and Lambert, 14 which was subsequently supported by the observations of Thomas and Calne, 7 Buchthal and Behse 8 and Harding and Thomas, 9 will require modification in the light of further experience. Nevertheless, at present it still appears to provide the best synthesis of the clinical, electrophysiological and genetic information that is available.

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References

The Babinski Response
Sir: In “The Babinski Response: A Review and New Observations” published in your journal 1955;18:250, the authors PW Nathan and MC Smith quoted, with some misunderstanding, Babinski’s work. For instance, on page 250 it says: “However, when anatomical evidence presented itself, it began to be obvious that Babinski’s statement were wrong.” Babinski himself reported cases which did not accord with his previous statements. For instance, in 1899, he reported three cases of paraplegia in flexion. He stated that in all three there was no histological evidence of degeneration of the pyramidal tract. Yet in the first case, the plantar responses were normal, in the second case, the...