PERIPHERAL NEUROPATHY IN CHILDHOOD. Second edition.
By Robert A. Ouvrier.

Peripheral neuropathies in childhood are a not uncommon part of paediatric neurology practice. Of my last 5000 cases, 99 have had one of the conditions dealt with in this book, making them collectively the tenth most common diagnosis I see. This is a slightly artificial grouping, however, as one does not think of or manage the hereditary, motor and sensory neuropathies (of which I have seen only seven) in the same way as one does Bell’s palsy (20) or brachial plexus lesions of the new-born (18).

Thus, individually, they are not a prominent part of clinical practice either. Consequently, few paediatric neurologists have taken a special interest in this group of disorders. We are therefore fortunate to have the accumulated wisdom of one of the few groups that has. Ouvrier and his team wrote the first edition of this monograph in 1990. Up to 1983, they had studied 125 cases over a 17-year period. Since then, the number has risen to more than 300. Uniquely, these are all biopsy-proven cases. Hence they speak with considerable authority on histopathological correlations of the hereditary neuropathies, which, unlike adult practice, constitute the majority (71% of this series). Since the first edition, diagnosis by DNA analysis is now available for five of these, and the need for biopsies will correspondingly decrease. This is therefore a fitting moment to review this experience, which is unlikely to be repeated.

The study of hereditary motor and sensory neuropathy type I and III (HMSN I and HMSN III) is the study of the formation and maintenance of peripheral myelin, recently fuelled by the advances in molecular biology. Alterations in PMP22 [22 Dalton Peripheral Myelin Protein (PMP) gene at 17p11.2-12] are designated HMSN Ia. This can be caused by duplication, point mutation and rarely deletion of the gene. Although PMP22 constitutes only 2.5% of peripheral myelin protein, defects in it contribute 70–90% of the cases of HMSN. Differences between the different defects begin to emerge. About 18 different point mutations have so far been described. The point mutation cases tend to have a greater increase in the total transverse fascicular area with earlier ‘onion bulb’ formation, than do the duplications.

Changes in myelin protein 0 (MPZ or P0) gene are designated HMSN Ib. P0 is a glycolipid which represents about 50% of membrane protein. It appears to be important for myelin compaction. These cases tend to be more severely affected both clinically and on nerve conduction velocity testing than 1a.

Cases with unknown mutations are designated type 1c, although here also mutations in different genes are beginning to be implicated (e.g. Early Growth Response gene 2, and Knox 20 gene). It is difficult to escape the conclusion that HMSN III, the Dejerine-Sottas phenotype, is not a severe
form of HMSN I. Thus it too may be caused by point mutations of the MPZ gene. It appears that substitution of arginine at position 69 of the MPZ molecule by cysteine causes HMSN III but by histidine or serine causes HMSN Ib—presumably the result of differences in the conformational folding of the molecules. Similarly, HMSN III and Ia can both be caused by point mutations or homozygous duplications of PMP22 gene. Homozygous point mutations of PMP22 have not yet been described. Although HMSN III can be caused by compound heterozygotes of PMP22 deletion and/or mutations, severity is not simply a case of homozygosity. Indeed some homozygous point mutations of MPZ are less severely affected than others heterozygous at the same allele, but with a different basepair deletion.

That other factors must be responsible for severity is borne out by a number of other observations. Thus the condition of hereditary neuropathy with liability to pressure palsies (tomaculous neuropathy)—HLPP—is also caused by deletions and point mutations on the PMP22 gene. Furthermore, the same point mutations can apparently cause HLPP or HMSN Ia in the same kindred. MPZ mutations can also cause a severe congenital hypomyelinating neuropathy.

Thus the peroneal muscular atrophy syndrome can be caused by HMSN I, II and III, Refsum’s, metachromatic leukodystrophy, chronic inflammatory polyneuropathy, HLPP, myotonic dystrophy, congenital myopathies, tumours of the cauda equina and atypical case of spinocerebellar degeneration and cerebral palsy. The dominant forms of HMSN I can be caused by changes in a number of genes, different forms of which in turn may cause different syndromes. The molecular biology information has both solved a number of questions and not surprisingly raised others, whilst promising to increase our understanding of pathogenesis at myelin structural level. Linkage for HMSN II (the axonal form) to four sites has been achieved, but further progress awaits gene identification and sequencing.

Treatment of the ataxic, autonomic, toxic and post infectious neuropathies is dealt with in similarly comprehensive style. The chapter on neuropathies in metabolic and degenerative disease is a tour-de-force. Peripheral nerve involvement occurs in surprisingly many neurodegenerative conditions—although it may not always be clinically apparent. This chapter usefully summarizes all of this whilst maintaining a clear clinical perspective. Neuropathies in systemic disease and focal lesions of peripheral nerves are not neglected. The only condition I could come up with which seems to have been omitted was shingles.

The text is succinct and unambiguous, and well supported by 47 pages of references that are usefully gathered together at the end of the book. A monograph of this authority has no competitor. Consulting the internet is no substitute, first because as a source of references, it is far from comprehensive, and second because the authors are not afraid to use their experience to make arguments and draw conclusions from a mass of what could otherwise be confusing material.

The one disadvantage of this format is the pace of change. Already the molecular biology of Rett’s syndrome and Friedreich’s ataxia have advanced; I have to warn the authors, their families, colleagues and friends that 10 years will be too long before the third edition will be needed. Meanwhile, the patients of any paediatric neurologist attempting to practise without this book will be at a significant disadvantage.

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