Professor Harper has written two widely acclaimed editions of a book on myotonic dystrophy, with the second edition published in 1989. Since then, identification of the causative triplet repeat has transformed diagnosis, genetic counselling and biological understanding of the disease. His computer has been busy with cutting and pasting for the new edition published in 2001. How does it look in 2002?

In any genetic text there will almost inevitably be advances between the writing of the script and publication, making it impossible to optimize timing. The major advance since publication of the latest edition has been the discovery of the DM2/PROMM quadruplet expansion in the Zinc finger protein 9 (ZNF9) gene on chromosome 3. This has implications for many aspects of myotonic dystrophy. There is already a better definition of the DM2/PROMM phenotype, which is close enough to classical myotonic dystrophy (DM1) to make it virtually indistinguishable clinically (except for the absence of congenital cases). The new data also has implications for the pathogenesis of myotonic dystrophy. For example, disruption of neighbouring genes to the DM1/DMPK expansion site would seem an unlikely disease mechanism if the same clinical effects were precipitated by an expansion elsewhere in the genome. With respect to DM2/PROMM the 2001 edition is, sadly, already obsolete. The first few pages of Chapter 3 concerning PROMM now serve to confuse, and the reader would do best to ignore this and seek out a more recent review, while sympathizing with the author on being outflanked by genetic advances.

Fortunately, history does not change as fast as molecular genetics. The introduction provides a fascinating historical perspective on the emergence of myotonic dystrophy with Steinert’s and Batten and Gibb’s descriptions. It is interesting that genetic controversies over the separation of myotonic dystrophy and myotonia congenita persisted until the above papers in 1909, and that there is still room for debate over DM1/DM2/PROMM today.

Chapter 3 reviews ‘other myotonic disorders and muscular dystrophies’. I am not sure that this chapter fully addresses the modern clinical differential diagnosis of myotonic dystrophy. Other myotonic disorders are described, but the text does not provide an updated comprehensive genetic classification of the channelopathies, which provide an important differential diagnosis of myotonia. This difficult area would benefit from a clearer guide to pertinent investigations. Some of the photographs posed questions rather than answers. An 8-year-old with eyelid myotonia and no muscle hypertrophy is said to have myotonia congenita, but it would be instructive to summarize the evidence against the differential diagnosis of paramyotonia congenita. Later, a 49-year-old woman with total ophthalmoplegia is photographed. She is said to have ocuolpharyngeal muscular dystrophy (OPMD). This may be correct, but complete ophthalmoplegia is very unusual in OPMD, and therefore might not be a good example to use. Readers of this book would probably regard descriptions of dystrophinopathies and Emery–Dreifuss Dystrophy as unnecessary.

The diagnosis of myotonic dystrophy is most difficult at the extremes of the phenotype, a point well made by the author. Accordingly, more emphasis could be allocated to diagnostic dilemmas on the neonatal unit, which are given two pages. I would feel that this was a more germane subject than dystrophinopathies, which are allocated six pages. The third chapter ends with brief descriptions of Charcot–Marie–Tooth Disease, polymyositis and myasthenia, which perhaps could be discarded.

The book is very strong on the systemic features of myotonic dystrophy, with chapters on the central nervous system, cardiorespiratory, endocrine, smooth muscle and ocular manifestations of this disorder. The reader will need help from these chapters if he uses the Cardiff myotonic dystrophy questionnaire at the end of the book. It is seldom that direct questioning of a myotonic dystrophy patient does not provide a generous quantity of previously undisclosed symptoms. I suspect these chapters will be useful sources of reference for interested neurologists. The sad fact is that if neurologists are not able to guide myotonic dystrophy patients in explaining and palliating non-neurological symptoms, there are few other informed sources of medical help for these patients.

Perhaps the best chapter in the book concerns genetic counselling. The author robustly summarizes the approach to a number of situations, showing the experience he has in this area. The challenge of amalgamating previous clinical experience with new genetic studies is dealt with well. In
most cases the reader will receive authoritative advice on issues concerning recurrence risks and other genetic advice. Ethical issues are well discussed. I particularly enjoyed the analysis of the role of clinical examination of at risk subjects and how the information derived was related to, but distinct from, genetic analysis. For example, it is noted that clinical examination of an asymptomatic adult subject is more likely to indicate the presence of the gene than subsequent genetic analysis of an adult without signs.

Any reviewer will test a book by trying to resolve their own uncertainties. I have been worried about providing the best advice to parents at risk of having a child with congenital myotonic dystrophy. Some parents wish a prenatal test, with a termination of pregnancy only if the expansion was sufficiently large to predict congenital (or severe) disease. The evidence of the relationship of expansion size with phenotype is clearly stated in the book. Although this relationship is not perfect, the author agrees that an expansion of over 1000 repeats is likely to predict congenital or severe childhood disease. Despite this it is stated that individual predictions are ‘unwise’. I think this will still leave me with uncertainty on how to best advise parents who would still wish a ‘conditional’ prenatal test.

There remains a chapter entitled ‘Diagnostic Tests in Myotonic Dystrophy: Studies of Muscle Pathology and Myotonia’. Certainly there should be space in this book for detailed myopathology and neurophysiology. However, providing space in a chapter on diagnosis, which can now only be justified historically, mars the otherwise comprehensive coverage.

From the clinical viewpoint a useful summary exists within a chapter on management and therapy of myotonic dystrophy, which might prove to be the most used part of the book. I noticed only one flaw. A frequent management problem is the treatment of myotonia. My own practice is to use phenytoin, when necessary, since this is known not to impair conduction through the AV node, and therefore unlikely to exacerbate heart block. I use mexilitine for other myotonias without cardiomyopathy. On page 415 it is stated ‘Mexilitine is now the first choice ...’. Readers may not have noticed that on page 117 the author states ‘Mexilitine ... does not seem to have been studied systematically for its cardiac effects in myotonic dystrophy, but since its primary use has been for cardiac arrhythmias it would seem likely that effects will occur and it cannot be assumed that these will always be beneficial rather than harmful’. In the relevant chapter in Engel and Frazini-Armstrong’s book Myology, published in 1994, Harper and Rudel state that ‘... mexilitine should not be used in myotonic dystrophy’. For the time being I will take the advice offered in 1994!

Brook and Newman write a chapter devoted to the molecular and cell biology of myotonic dystrophy. Such reviews encounter difficulty in catering for the likely disparate genetic knowledge of the audience. The right balance is achieved by the authors, only losing me at one point in listing the evidence for involvement of a gene downstream from DMPK. The authors wisely include a brief conclusion for those clinicians feeling ill-equipped to deal with the whole chapter. I would have enjoyed hearing the authors put the recent DM2 genetic findings into context.

Despite my few reservations about this book the latest edition will remain the encyclopaedia of myotonic dystrophy, carrying more collated information than even the most detailed of internet sources. One can also feel the interest and motivation of the author to help a population of patients who put up with much and complain little. I do hope there is a fourth edition, perhaps on an occasion when the pace of genetic advances allows the author sufficient pause for some further cutting and pasting. Every neurological library needs a copy of this book, and physicians with an interest in muscle disease or neurogenetics will want their own copy.

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