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Huntington’s Chorea

This book is primarily directed at the practising clinician and therefore is also useful for paramedical workers such as psychologists and social workers. The stimulus for the work came from a personal study of 120 patients with Huntington’s chorea in South Africa, which prompted Dr Hayden to make a very thorough review of the disease. While the emphasis of the book is on clinical aspects of Huntington’s chorea, Dr Hayden puts these into historical and geographical perspective and discusses recent advances in research and hopes for the future. The result is an enjoyable and comprehensive monograph, where a readable text is accompanied by many helpful tables, figures, and photographs.

The account Hayden gives of the history, geography, and epidemiology of Huntington’s chorea makes fascinating reading. Although the condition was only clearly described at the beginning of the 19th century, studies of the pedigrees of some present day affected cases can be traced back, with probably affected ancestors, to the 17th century. Fifty probands in Hayden’s study were related to a single affected common ancestor, a Dutch immigrant of seven generations earlier. Twenty-nine other probands could also be traced back to ancestors who originated in north-west Europe, and these observations have led to the simple, and I think erroneous, view that the first gene mutations occurred in this part of Europe. Probably the pattern of genetic descent merely reflects the patterns of immigration in the 17th century.

Hayden describes the different prevalences of Huntington’s chorea in different parts of the world and points out that some apparently high prevalence rates are more a reflection of the assiduity with which the data were collected rather than an unusually high prevalence. However, the intriguing fact remains that in spite of keen and interested workers, some races, notably the Japanese and the South African Negroes, still appear to have a low prevalence of Huntington’s chorea.

The next and equally good section is on the clinical picture of Huntington’s chorea. The account of presenting symptoms and signs is useful, and it is important to be reminded that chorea is absent throughout life in 5 to 10% of those possessing the mutant gene, as well as often being absent at the time the patient presents with a psychiatric disorder. The unusual features of juvenile Huntington’s chorea are described from first-hand experience: the presentation with behaviour disturbance or psychosis, the domination of the motor signs by rigidity rather than chorea, and the associated features, unusual in adult patients, of epilepsy and cerebellar signs. The chapter is completed by a description of diagnostic aids and differential diagnosis, and a subsequent chapter describes the pathognomonic pathology of the brain.

Chapters 4 and 7 discuss the genetics of Huntington’s chorea and here there is much of interest, such as the predominance of paternal descent for juvenile Huntington’s chorea, and the use of age of enquirer and age of onset of affected relatives in assessing genetic risks. I should have preferred more discussion of genes modifying the onset of severity of Huntington’s chorea, since these are likely to be responsible for the juvenile form. Haldane’s suggestion1 is of interest here: namely that modifying genes are probably producing a later age of onset in Huntington’s chorea, which could have been a disease of infancy in early man. I should have preferred a more critical approach to published reports of fitness and heterozygote frequency in Huntington’s chorea. The measurement of fitness has to be performed with great care if the presence of an affected relative has influenced the ascertainment of patients. The figures for heterozygote frequency given in table 7.3 are rather different one from another, because they have been estimated in different ways and are based on different prevalence rates. Probably they are all too low; the simplest method for estimating heterozygote frequency at birth is to multiply the prevalence by the average life expectancy in the population (70 years), divided by the average duration of the disease (15 years) (Carter, personal communication, 1981). Using the recent South Wales data,2 the heterozygote frequency becomes 1 in 2830.

Since the book went to press, Newcombe3 has calculated some life tables for Huntington’s chorea which show that previous risk estimates for still being a heterozygote if healthy at certain ages are too low, because calculations based on a knowledge of heterozygotes who have developed signs ignore the fact that some heterozygotes will develop signs later, or indeed will die of other causes before developing.
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In the light of these new risk figures which give a median onset age of 49 years, the section on the use of age of onset in genetic counselling should be revised. However, Dr Hayden is right to emphasise that there is more to the duties of a genetic counsellor than the provision of genetic risks.

The last chapters describe the management of patients with Huntington's chorea, including some precise drug regimens, and discuss new prospects in research. The book thus provides a comprehensive review of Huntington's chorea, written by someone with wide experience of and sympathy towards the disease. It is an excellent monograph, interesting and stimulating, and I also found a it valuable source of reference.

S Bunney

References

1 Haldane JBS. The relative importance of principal and modifying genes in determining some human diseases. J Genet 1941;41:149–57.

Clinical, Structural, and Biochemical Advances in Hereditary Eye Disorders


This is the report of a symposium held by the Society of Craniofacial Genetics. The first three papers are concerned with various aspects of ocular development in birds and in man. The importance of neural crest cells in the development of ocular tissues, supplanting mesoderm as the major mesenchymal component, is a significant advance in our understanding of this topic, as is the contribution of the extracellular matrix which influences the migration of these cells.

These are followed by several short review articles on connective tissue diseases, macular corneal dystrophy, conjunctival biopsy in lysosomal disorders, and gyrate atrophy. Each is succinct, up to date, and easy to read; available elsewhere but conveniently placed in this volume. These are useful sources for the ocular complications in these groups of genetically determined disorders. The last contribution is a genetic survey of a large population with retinitis pigmentosa, an important contribution on this subject and one useful for those concerned with the management of patients with this group of disorders.

Reports of symposia are notoriously patchy and this is no exception. It is useful to have this material in one place, yet no-one will find every paper of interest. The first two papers describe fundamental advances in our knowledge and could easily be overlooked by the majority of clinicians. The remaining papers are useful to refer to when faced with a patient with one of the conditions covered in this volume.

Barrie Jay

Organic Acids in Man. The Analytical Chemistry, Biochemistry and Diagnosis of the Organic Acidurias


In the last 15 years there has been a vast increase in our knowledge of many aspects of the metabolism of organic acids in man. This has largely been made possible because of the development of suitable methods of analysis, particularly gas chromatography and mass spectrometry. However, there are no comprehensive texts covering all aspects of the subject and it is this gap which the authors aim to bridge.

The book is divided into three parts. In the first, the methods of analysis of organic acids are discussed in detail with chapters on extraction, derivatisation, separation, and identification. Part two is devoted to the organic acids that are found in physiological fluids of normal subjects. A good example of the detail in this book is the table of the 'more important' organic acids in urine of normal subjects which has nine sections and lists 93 organic compounds. The final part of this book is largely concerned with inborn errors of organic acid metabolism. This is interpreted widely since not only do conditions such as propionic acidaemia and methylmalonic acidaemia receive their due space, but phenylketonuria and primary hyperoxuryria find their way in. The biochemistry and the abnormal metabolites found in these disorders are discussed in detail. However, neither of the authors is a clinician and the sections on the clinical aspects of these disorders are less satisfactory. The scheme for identifying children with organic acidurias is too vague. For example, it appears to suggest that all babies with a low pH should have blood and urine amino acids measured quantitatively as well as the urine organic acids, a policy which would quickly