age his mental age was evaluated as being 5 months.

His feeding difficulty continued and he suffered frequently from dehydration. His abdomen, lumbar region, and pelvis remained remarkably underdeveloped. His maximum lifetime weight was 6.9 kg aged 6 years 2 months. Subsequently, he suffered repeatedly from fever, vomiting, and dehydration and died at the age of 8 years 7 months. His height (crown to rump) at death was 49.0 cm, weight 4.96 kg, and head circumference 48.2 cm. At necropsy, regurgitant oesophagitis, a poorly developed small intestine, a small, thick walled (approximately 9 mm) urinary bladder, and small undescended testes were found.

The ethics of keeping such a child alive for eight years may seem to be questionable. However, passive euthanasia of such a case as this patient would not be readily acceptable in Japan.

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BOOK REVIEWS

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Genetics and Alcoholism. Evelyn Dumont-Damien, Michel Duyme. Paris: Editions INSERM. 1993.

In the latter part of last century many held the view that alcoholism was inherited. The pendulum of opinion swung, and by the 1960s there was little doubt in the minds of the great majority of its investigators that the origin of alcoholism was psychosocial. Today, with the developing knowledge in biology and especially in the genetics of behaviour, it is possible to contemplate some genetic contribution to its aetiology. For this several factors are responsible. Numerous diseases are known which result from a combination of

genetic and environmental elements. For example, one parallel to alcoholism is cancer of the lung, where the environmental factor is clear but only a proportion of heavy smokers develop the disease. Genetic studies have become possible, for the alcoholism phenotype has been better defined, and there are many genetic markers which allow a search for the location of genes producing susceptibility to any disease.

The authors of this book have drawn together almost all the accessible publications on genetic studies of alcoholism and have reviewed them critically. Their object is to make a balanced appraisal of present knowledge. They envisage alcoholism as a complex behavioural feature, and apply to it the methods of genetic analysis of behaviour.

Immediately in chapter 1 the principal problems that hinder genetic analysis are squarely faced: problems of definition, measurement of the phenotype, lack of clarity of the underlying biological mechanisms, and therefore of possible functional markers. It concerns types of alcoholics, aetiological models, measures of alcoholism, and the several hypotheses involving neurobiology. The chapters that follow summarise the different types of study.

Chapter 2 is devoted to family studies, of which there are approximately 200, comparing relatives of different degrees sharing similar family environments. They show familial concentration of alcoholism, so that the risk is greater for a person, particularly for a male, who has numerous alcoholic relatives, and they suggest an aetiological heterogeneity manifesting in variations in the precocity and severity of the condition. The authors identify topics on which future research could most profitably concentrate.

Chapter 3 draws together the numerous twin studies, 34 published in the period 1939 to 1991. These do not exclude genetic influence and indeed strongly suggest to the authors a multifactorial aetiology, the genetic contribution to which is most apparent in male twins who are alcohol dependent.

The next chapter is devoted to adoption studies, usually considered essential for distinguishing genetic and environmental effects. There have been about a dozen such studies, though the authors show that most of these are biased and use research designs that are not very informative. One finding emerges clearly from the subgroup of studies which are less open to criticism, namely a link between the biological father and his son brought up by adoptive parents. These sons knew nothing of the behaviour of their biological fathers; their biological mothers as well as their two adoptive parents were effectively non-alcoholic. These findings do not of course provide formal proof, but they favour the hypothesis of a transmission of some genetic factor from the father to the son. The result supports the suggestion from the family and twin studies that there is a dominating male influence.

The studies in chapter 5 complement these classical approaches, for they deal with sibs and half sibs brought up apart and unrelated children brought up together. There are only four studies of this type. Criticisms can be levelled at all, especially in the small number of variables considered or the lack of rigour in their specification, so their findings can only be taken as indications. But despite their drawbacks they support the interpretation from the investigations in the previous chapters that there is some genetic influence on alcoholism.

The crucial proof that there is a genetic contribution to the aetiology of alcoholism will come from the discovery of one or more markers, genes, or DNA segments. The searches for these have been numerous and the authors restrict their survey to those studies of characters whose chromosomal locations are known. There are 140 such studies, covering more than 50 markers, the majority being searches for association (to establish relative risks) and only a few using linkage (to establish location). The studies as a whole, dealt with in chapter 6, show that to date there is no certainty that any of the characters analysed is a marker for alcoholism. But these studies give valuable pointers to the methodological precautions to be taken and the paths to be followed in future investigations. The book closes with a series of 14 appendices, dealing in detail with key topics mentioned in earlier chapters but where fuller consideration would have interrupted the flow of the argument. These topics include for example the principal definitions of alcoholism, its classification and typologies, clinical and biological indicators, and aetiological models of alcoholism proposed in the period 1972 to 1988, ending with those of Donovan and of Radouco-Thomas. The list of some 850 references covers only those published in English or French.

The conclusions of the authors after their critical examination of hundreds of published works is that it is not yet definitely established that genetic differences between persons account for their variation in behaviour regarding the pathological taking of alcohol. Nevertheless there are strong indications that at least in some persons there is a genetic vulnerability to the abuse of, or dependence on, alcohol, especially males whose father and several ascendant relatives were alcoholic. The task now for genetic epidemiologists is to find the genes that predispose to the different types of alcoholism.

This book is positively written. From its critical appraisal of existing works, and their lack of conclusive findings, it draws lessons as to the points that future studies should attack and the methodological weaknesses that should be avoided. It is moreover carefully written, well balanced, well organised, a meticulous appraisal of the numerous works examined by the authors. It is the most comprehensive survey of the subject yet produced, and one which any investigator of the subject cannot afford to ignore.

D F ROBERTS

Diagnostic Criteria for Neuromuscular Disorders. Editor A E H Emery. (Pp 72.) UK: ENMC Publishing. 1994.

As Research Director for the European Neuromuscular Centre (ENMC), Baarn, The Netherlands, A E H Emery has participated in around 30 workshops designed to co-ordinate and encourage European research groups involved in the isolation and characterisation of the genes responsible for diverse neuromuscular disorders. This publication is introduced as a discussion document and presents, with some modifications, a series of articles which have appeared in *Neuromuscular Disorders* (Pergamon Press) setting out the diagnostic criteria proposed at each workshop. At the times of a number of

the workshops, the relevant genes had been cloned and this is reflected in the relevant chapters; for instance the diagnosis of Duchenne muscular dystrophy (DMD) is definite "where almost no dystrophin is demonstrable in a muscle biopsy specimen" or there is "a Duchenne-type mutation within the dystrophin gene". Likewise the section on myotonic dystrophy lists amplification (>45) of the trinucleotide repeat sequence in the DM-kinase gene on chromosome 19 in the diagnostic criteria. There is an attempt in some chapters to comment on current diagnostic approaches for DNA analysis, for example, multiplex PCR, SSCP, mRNA(RT-PCR), and most recently the protein truncation test in DMD; the shortened 4q35 linked *EcoRI* fragment detected by p13E-11 in facioscapulohumeral muscular dystrophy and the chromosome 17p11.2 duplication associated with Charcot-Marie-Tooth disease type 1A. In a text of only 72 pages the comments are of necessity brief and the reader is left with the reference lists to identify further reading. The reference lists range from no entries (the section on Rare Neuromuscular Disorders) to 24 (Limb Girdle Muscular Dystrophy) with two (Myotonic Dystrophy, Congenital Muscular Dystrophy) citing single references. The coverage of published reports could have been better standardised across the sections and perhaps one or two key clinical references could have been included in each section.

It is unfortunate that some "chapters" begin with tables or lists (Duchenne/Becker dystrophies, myotonic dystrophy, spinal muscular atrophy). The more traditional introduction to Limb Girdle Muscular Dystrophy (K M Bushby) is eminently more readable. Likewise the use of the abbreviations "I", "E", and "C" for inclusion criteria, exclusion criteria, and comments re-

spectively, in only some of the chapters is irritating. Putting aside these comments on format, the answer to the question of whether this slim volume "will be useful to clinicians and scientists engaged in this field of research" will depend on the individual person's reason for consulting the chapters. The chapters are not intended to be reviews of the clinical manifestations nor of the application of molecular techniques to the diagnosis of these disorders. Unified clinical criteria for the diagnosis of disorders are useful, particularly in studies using linkage analysis, although the availability of computer programmes such as the HOMOG series allows, to an extent, for genetic heterogeneity. The chapters do present some fairly fundamental features on which the diagnosis of these disorders can be made but the layouts of the chapters do not make an easy format for use by a junior doctor faced with a patient with a neuromuscular problem.

The contribution made by the ENMC to furthering collaborations between the disparate research teams working on these disorders in Europe should not be underestimated. The standardisation of the diagnostic criteria to be used by these groups when identifying affected persons and families and when making resources available to others was important. The publication of such criteria (in *Neuromuscular Disorders*) enabled them to be used as a standard reference by the research groups and thus to cut down on unnecessary duplication in subsequent reports. This publication aims to make these criteria available to a wider audience. Unfortunately the format and content of the chapters makes it difficult to identify who it will best serve.

J C MACMILLAN

NOTICES

Call for Patients

Osteopetrosis. We are interested in finding the genetic causes of osteopetrosis. If you know of cases that could be available for DNA analysis, please contact Wim Van Hul, Department of Medical Genetics, University of Antwerp, Universiteitsplein 1, 2610 Antwerp, Belgium. Tel (32) 3 820 25 85; fax (32) 3 820 25 66.

European School of Medical Genetics - 8th course

This will be held in Sestri Levante (Genoa) on 19-25 March 1995. **Directors:** Professor V A McKusick (Baltimore), Professor G Romeo (Genoa). **Topics:** Introduction to human molecular genetics, linkage analysis, cytogenetics, population genetics, molecular genetics, multifactorial diseases, clinical genetics, cancer genetics. **Registration fee:** 420 000 Italian Lire. **Applications:** send your CV, a brief description of your research interests, a letter of presentation (if you wish to present a clinical case during an evening session and to apply for a travel fellowship in case there are some available, please state it clearly in your covering letter), and a certificate of your knowledge of English to: Paola Quattrone, Laboratory of Molecular Genetics, Istituto G Gaslini, 16148 Genova, Italy. Tel: +39/10/5636370-400, fax +39/10/391254.

Fourth International Conference on Systemic Lupus Erythematosus (SLE)

This conference will be held in Jerusalem, Israel on 26-31 March 1995. For further information contact Professor Yehuda Shoenfeld, SLE Conference, PO Box 50006, Tel Aviv 61500, Israel. Tel: 972 3 5140014, fax: 972 3 5175674 or 972 3 660325, Email: 100274.2665@CompuServe.COM.