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BOOK REVIEWS

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Microcitemie e Anemia Mediterranea. I Bianco Silvestroni. (Pp 327.) Rome: Associazione Nazionale per la Lotta contro le Microcitemie in Italia. 1992.

This book by Ida Bianco Silvestroni presents a concise description of the clinical management, pathophysiology, and molecular pathology of the thalassaemia syndromes with particular emphasis on β thalassaemia. The book largely reflects Ida Bianco's personal experience; she has devoted a large part of her life to the study of prevention and management of thalassaemia. The chapters on haematology, traditional diagnosis, and management are certainly outstanding and will be very helpful to postdoctoral workers who would like to improve their knowledge of thalassaemia. On the other hand, the chapters on molecular pathology, molecular diagnosis, and prenatal detection are neither updated nor well integrated with the rest of the text.

For further editions, the book should be improved by more clear and detailed description of the figures, addition of schematic diagrams to illustrate better the molecular pathology, and elimination of some minor inaccuracies. In describing heterozygous β thalassaemias, for instance, the author states that some of them may present mild clinical manifestations, while it is very likely that these manifestations result from the coinheritance of genetic determinants, such as silent β thalassaemia, the triple α globin gene arrangement, or less common mechanisms. In the chapter concerning silent β thalassaemias this phenotype is subdivided into several subcategories. However, the differences in HbA_2 levels and haematology between these subtypes are too subtle to be clinically useful. Molecular analysis is needed to substantiate the subdivision presented. According to the author, globin chain synthesis analysis is not capable of identifying heterozygous β thalassaemia at birth. However, it is known that this technique may detect heterozygous β thalassaemia as early as 18 weeks' gestation.

As stated in the introduction, the purpose of the book is to give a simple, popularised, practical workbook for general practitioners, paediatricians, and obstetricians concerned with thalassaemia and in this sense the author has reached her aim brilliantly.

A CAO

Late Onset Neurometabolic Genetic Disorders. Ed N Baumann, A Federico, K Suzuki (Pp 376; £53.10.) Basel: Karger. 1992.

This special issue of *Developmental Neuroscience* arises from a meeting held in December 1990 at the University of Siena of clinicians, pathologists, biochemists, and molecular biologists involved in research on late onset genetic neurometabolic disorders of lysosomes and peroxisomes. It is a 'tour de force', packed with detailed and authoritative articles covering the entire range of these fascinating disorders.

Following an introductory overview of diagnostic approaches to these often underdiagnosed disorders there follows a total of no less than 27 separate articles covering the following disease categories: leucodystrophies, gangliosidosis, Niemann-Pick type C disease, sialic acid storage diseases, ceroid-lipofuscinoses, Gaucher's disease, and cerebrotendinous xanthomatosis. The emphasis throughout is on the adult varieties of these diseases, and the powerful inroads being made by the new DNA based analyses is strongly in evidence.

Federico reviews the clinical and investigative approaches to diagnosis in this area and considers current theories concerning the mechanisms by which expression of the disease phenotype is delayed. A useful tabulation of investigations by presenting feature (ataxia, myoclonus epilepsy, peripheral neuropathy) is provided. In some cases, late onset appears to be a manifestation of heterozygosity in what is an autosomal recessive childhood disease. Conzelmaan and Sandhoff present a kinetic model for the correlation between residual activity of a deficient lysosomal enzyme and the degradation rate of its substrate to explain the biochemical basis of late onset neurolipidoses. Suzuki reviews the neuropathology of late onset gangliosidoses, noting that in adult GM_1 gangliosidosis neuronal storage is almost limited to the basal ganglia and in adult GM_2 gangliosidosis storage neurones are more widely distributed.

The leucodystrophies occupy 69 pages, with articles on metachromatic leucodystrophy, globoid cell leucodystrophy (Krabbe disease), leuko-araiosis, adrenoleucodystrophy, and Schilder's diffuse sclerosis; Baumann provides a masterly account of the adult forms of MLD. The fascinating phenomenon of 'pseudodeficiency' of arysulphatase A and galactocerebrosidase is considered by Wenger and Louie, and its molecular genetic basis described in detail by Gieselmann *et al.* Some healthy subjects have low ASA activities and are homozygous for a so-called pseudodeficiency (PD) allele which only encodes 5 to 10% of the normal ASA activity. The ASA PD allele is characterised by two mutations, the second of which causes loss of the first polyadenylation signal downstream of the termination codon. Mutations causing MLD can occur in association with PD alleles, and the recognition and evaluation of this problem is a vital responsibility in providing genetic counselling for these families. Initial studies exploring the possibility that ASA pseudodeficiency is associated with multiple sclerosis are reported.

The term 'leuko-araiosis' (Greek for white matter thinning) refers to a "diminution of the density of representation of the white matter" on CT scan and MRI. It arises from a reduction in myelin fibres per unit volume rather than reduction in the total volume of white matter. Its prevalence and significance is considered in an article by Vermy *et al.*

Adrenoleucodystrophy is considered in three papers: an authoritative review by the Mosers, a detailed consideration of peroxisomal fatty acid β oxidation by Wanders and Tager, and a discouraging account of experience with treatment using dietary erucic acid (C22:1) by Uziel *et al.* Martin and Guazzi bring down the curtain on another eponym (Schilder's disease) which has sadly outlived its usefulness.

The gangliosidioses comprise the second largest section, with four papers totalling 19 pages. At least three genes are involved in the full activity of hexosaminidase (Hex). Federico *et al* review the clinical aspects of adult Hex deficiencies (GM_2 gangliosidosis), pointing out the wide range of conditions which it may resemble: Ramsay-Hunt syndrome, olivopontocerebellar ataxia, Friedreich ataxia, amyotrophic lateral sclerosis, Kugelberg-Welander disease, Fazio-Londe disease, and Charcot-Marie-Tooth disease. Suzuki and Varnier discuss the B1 variant as a prototype for juvenile Tay-Sachs disease, and the mutation (a single base pair change in the α subunit gene of Hex) causing the distinct phenotype of Jewish adult Tay-Sachs disease is discussed separately by Navon.

The remaining five conditions are each considered rather more briefly. Three articles focus on the type C variety of Niemann-Pick disease. This is a distinct disease characterised by an alteration in cholesterol esterification from exogenous cholesterol: the primary defect remains unknown. The sialic acid storage disorders are reviewed, one of which, Salla disease, is of course one of the so-called 'Finnish' diseases. Although the defect in lysosomal sialic acid accumulation is clear, the transport protein involved has yet to be identified. The neuronal ceroid-lipofuscinoses are dealt with in a paper by Martin on the adult type (Kufs' disease) and a biochemical review by the late Nicholas Hall and co-authors which focuses mainly on the recent exciting advances concerning the accumulation of subunit C of mitochondrial ATP synthase in human tissues from patients with the juvenile and late infantile varieties.

The Norrbottnian type of Gaucher disease is the best characterised late onset neuronopathic form. All the patients hail from the provinces of Norbotten and Vasterbotton in Sweden: it cannot be described as a disease of major socioeconomic importance. There is a single base substitution in exon 10 of the gene encoding cerebroside-β-glucosidase. Children have been successfully treated with bone marrow transplantation. Levey *et al* review the molecular genetic basis of Gaucher disease and consider the possible role of the prosaposine gene in the development of Gaucher disease.

Finally, the pathogenesis and treatment of the biochemical problems in cerebrotendinous xanthomatosis are considered by Salen *et al*, and Dolti *et al* present 10 Italian cases with features of premature ageing in CTX: cataracts, ischaemic heart disease, and osteoporosis.

In conclusion this is a superb volume of specialist appeal. It would certainly be a useful volume to refer to for a clinician confronted with the possible diagnosis of one of these relatively rare conditions. It will soon be rendered at least partially out of date by the rapid pace of advance in the molecular genetic analysis of these conditions.

R M GARDINER