BOOK REVIEWS

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This book by Ida Bianco Silvestrini presents a concise description of the clinical management, pathophysiology, and molecular pathology of the thalassaemia syndromes with particular emphasis on β thalassaemia. The book clearly 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 whole, of course, the chapters on molecular pathology, molecular diagnosis, and prenatal detection are not 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 co-inheritance of terminators, 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, 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.

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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 metabolic disorders. It is a 'tour de force', packed with detailed and authoritative articles covering the entire range of these fascinating diseases.

Following an introductory overview of diagnostic approaches to these often under-diagnosed disorders there follows a total of no less than 27 separate articles covering the following disease categories: leukodystrophies, gangliosidoses, Niemann-Pick type C disease, sialic acid storage diseases, ceroid-lipofuscinoses, Gaucher's disease, and cerebroside storage diseases. 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 evident.

Federico reviews the clinical and investigatory 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 various features (axia, myoclonus epilepsy, peripheral neuropathy) is provided. In some cases, late onset appears to be a manifestation of heterozygosity in various childhood recessive disorders. Conzelman 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 neurolidays. Suzuki reviews the neuropathology of late onset gangliosidoses, noting that in adult GM1 and GM2 gangliosidoses it is almost limited to the basal ganglia and in adult GM3, gangliosidosis storage neurons are more widely distributed.

The leukodystrophies occupy 69 pages, with articles on metachromatic leucodystrophy, globoid cell leucodystrophy (Krabbe disease), leuko-araiois, adrenoleucodystrophy, and Schilder's diffuse sclerosis; Bau- mann provides a masterly account of the adult forms. The fascinating phenomenon of 'pseudodeficiency' of aysul- phatase A and galactocerebrosidase is considered by Wenger and Louie, and its molecular basis described in detail by Gieselmann et al. Some healthy subjects have low ASA activities and are homozygous to 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 genetics of the ASA pseudodeficiency are described, Cheong and Martin report that the deficiency is associated with multiple sclero- sis are reported.

The term 'leuko-araiois' (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 the brain, and 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 peroxiso- mal fatty acid β oxidation by Wanders and Djozlija, and a discussion of the clinical and management aspects 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 gangliosidoses comprise the second largest section, with four papers totalling 19 pages. At least three genes are involved in the pathology of the activity of bound asialo gangliosides. Federico et al review the clinical aspects of adult Hex deficiencies (GM1, gangliosidosis), pointing out the wide range of conditions which it may resemble: Ramsay-Hunt syn- drome, olivopontocerebellar ataxia, Fried- reich ataxia, amyotrophic lateral sclerosis, Kugelberg-Welander disease, Fazio-Londe disease, and Charcot-Marie-Tooth disease. Suzuki and Varnier discuss the BI 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 dis- tinct phenotype of Jewish adult Tay-Sachs disease. The latter is discussed in a paper dealing with an alteration in cholesterol esteri- fication from exogenous cholesterol: the prim- ary 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 bio- chemical review by the late Nicholas Hall and co-authors which focuses mainly on the recent exciting advances concerning the ac- cumulation of subunit C of mitochondrial ATP synthase in human tissues from patients with the juvenile and late infantile variants.

The Norrbottian type of Gaucher disease is the best characterised late onset neuro- pathic form. All the patients hail from the provinces of Norbotten and Vasterbotten 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 develop- ment of Gaucher disease.

Finally, the pathogenesis and treatment of the biochemical problems in cerebrotendi- nous xanthomatosis are considered by Salen et al., and Dotti et al present 10 Italian cases with the rarest of the premature ageing in CTEX, ataxia, ischaemic heart disease, and osteo- porosis.

In conclusion this is a superb volume of a 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 advances in molecular genetic analysis of these conditions.

R M GARDINER
Microcitemie e Anemia Mediterranea

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