Book reviews


The increasing interest in associations between HLA and various disorders has produced an outpouring of papers and reviews in most major journals, both general and specialised. This is now being added to by the appearance of specific texts dealing with the whole area or small fragments. Except for those who have been involved with HLA antigens previously, there must be an ever-increasing sense of confusion, accompanied by the inability to sort wheat from chaff.

To bring hope to the helpless, we now have at least one text which aims to present not only hard facts on frequencies and statistics, but a generous quota of thoughtful papers, which provide excellent background information on HLA antigens, their genetics, and their possible relevance to disease. In addition, for the real seeker after truth, many of the flaws in the analytical approach are examined and criticized in a clear and informative manner.

HLA and Disease is a rare specimen in scientific book publishing these days. It followed the First International Symposium on HLA and Disease, held in Paris in 1976, under the auspices of INSERM (Institut National de la Santé et de la Recherche Médicale, Paris) and supported by the EEC. Yet, thanks to its joint authors, it is not yet another undigested volume of ‘congress proceedings’. Instead, this is a collection of skilfully edited essays, contributed by major participants at the symposium, which bring together both the factual presentations made at the time of the meeting and the considered opinions of individuals who have devoted much skill to the presentation of the consensus of current opinion. The list of contributing authors reflects the broad nature of the subject, ranging from HLA serologists, through geneticists and clinicians from many different specialties, to the ‘mouse’ researchers from whom so many of these ideas originated.

The text is introduced by a mass of data, which it was most appropriate to bring back into focus, about the search for disease associations with the red cell blood groups; this information is ably summarised by the doyen of the subject, A. E. Mourant. As an introduction to the HLA system and its genetics, the succeeding chapter by Rose Payne is a model of clarity, and recommended reading for those who want a succinct account of the HLA system. The mouse H-2 system is used by Don Shreffler to give the reader the necessary background to understand the concept of genetic control of immune response. This material is perhaps relatively more difficult for the non-geneticist, dare I say non-immunologically minded, clinician, but it is worth perseverance, if only because so much of the succeeding argument in this book depends on understanding these concepts. It is here that the new student will meet the exciting possibility that the major histocompatibility complex of genes (MHC) may have a very central function in disease mechanisms, quite apart from producing what may seem only a complicated series of serological conjuring tricks.

The main chapters, which deal with the final outcome of the Paris symposium, are introduced by Svejgaard and Ryder, who also provide a ‘child’s’ guide to the (relatively) simple statistics and arithmetic needed to analyse HLA and disease studies. As the individuals who instituted and run the HLA and disease registry in Copenhagen, these authors would be expected to provide a clear and careful record of the current reviews, which is indeed the case. There are carefully tabulated data, and an extensive bibliography of all reported studies on HLA and disease that were available to the computerised registry.

The problems of possible genetic models, which might explain the observed associations, are dealt with in the succeeding three chapters, which examine the probabilities of various explanations. These are invaluable contributions to the text but present some contradictions to those who are new to the subject, presenting, as they do, two rather different methods of dealing with the analytical problems. However, the argument over mechanisms is such a crucial part of the study of HLA and disease that the time is not yet ready to crystallise methods into rigid formulae. For those who believe (incorrectly) that they require mathematical training to grasp the concepts dealt with by Ceppellini, Kidd, Thomson, Bodmer, and their colleagues, the chapter by Glensh Thomson and Walter Bodmer might be the less intimidating of this triad. It emphasises the value of family studies and illustrates, by specific examples, how the genetic explanation may differ from one disease to another, even when HLA associations are postulated for both. This approach is timely, because there is a prevailing tendency to seek a single ‘unified theory’ to explain all the reported associations, with a tendency which may be too restrictive and is bound to lead to inconsistency when diseases as diverse as ankylosing spondylitis, juvenile onset diabetes, and multiple sclerosis are considered.

The central section of the text deals with the information available both prior to, and presented to, the symposium. Rheumatology, neurology, dermatology, endocrine diseases, gastrointestinal disease (including liver disorders), allergy, malignant disease, and the immune disorders are dealt with in separate sections. The method of approach to each varies a little, depending on the co-ordinating authors of each section and the type of material to be presented. However, in addition to the factual information on antigen frequencies, relative risk of disease, etc, each section contains an assessment of the possible specific mechanisms for the associations as well as, in many cases, a very pertinent comment on the pitfalls to be encountered in designing and analysing disease association studies. Problems of sample selection and size, of choice of control subjects, and of the serological difficulties that can be encountered are fully dealt with, together with observations on the value and the limitations of HLA association studies. In particular, several sections emphasise the need for further research before HLA antigen determination is considered as yet another ‘routine’ test. The margin of error (ie, of false-positive and false-negative results) is clearly too great to allow HLA
typing to be considered as a suitable diagnostic tool even if the scarce reagents and resources were available. This problem is dealt with most lucidly by Brewerton and Albert in the section on rheumatology.

The book concludes with a series of thoughtful essays on possible mechanisms and the long-term value expected to be derived from such studies. The prospects for understanding precise disease mechanisms are summarised by McDevitt, who has contributed so much to the subject by his elucidation of many features of the mouse MHC and the existence of specific immune response genes.

This is a forward-looking book, which summarises existing knowledge and suggests stimulating approaches to unsolved problems. It may lack depth in some sections, because of the need to provide so much data in a reasonable size of format. Some dogma is questioned, some concepts are ignored, but in a new, rapidly advancing field this book provides an acceptable compromise. The indexing system is unusual and not entirely satisfactory: specific topics are listed in the contents section, and no final index is provided. In view of the complexity of the material, one might forgive the editors for not following usual practice, and HLA and Disease is otherwise highly recommended.

A second publication devoted to HLA associations deals with a more restricted field of study, and is entitled HLA and Malignancy. This is a much less satisfactory book and suffers from many of the failings of 'edited proceedings', including typographical errors, incorrect nomenclature, and a disjointed text. It was a difficult subject to focus on, because malignancy is the one major area where expectations of an HLA association (raised by the positive findings with H-2 in the experimental inbred mouse) have not yet been realised in the study of human malignant disease. This volume, based on the proceedings of a symposium held at Roswell Park Memorial Institute, does not leave one with any real sense of conviction in the demonstration of direct, significant association between HLA antigens and most types of malignant diseases. This is sad, because the initiating studies on HLA and disease were made in Hodgkin's lymphoma by Amiel in the days when HLA typing was in its infancy. Few, if any, of the recognised associations between HLA and human malignant disease are of the order of magnitude of those described for non-malignant disease. The commonest malignancies still seem to have no strong associations; those that do exist are for diseases like nasopharyngeal carcinoma, Hodgkin's disease, and, possibly, some forms of leukaemia. What is the current state of the art?

This book does not supply the answer nor does it reduce the sense of frustration at not being able to define a connection between histocompatibility antigens and malignant disease in man, comparable to the association so clearly distinguished in the mouse leukaemias. The introductory sections are probably too condensed for the general reader, attempting to compress a series of complex serological and genetic matters into a few pages. A further section is devoted to work in the leukaemias, where a glimpse of light may have been cast by the observation that survival, not susceptibility, is the important phenomenon—an observation which was reported as long ago as 1971 for Hodgkin's disease. The picture in the leukaemias is confused by the serological problems of HLA typing leukaemic cells, and the papers in this section are a mixed bag of technical reports and association studies, which might have been better separated and identified as representing quite different facets of the problem.

The section on 'Selected solid tumor and other neoplasias' (what a deal of confused thinking is buried in that title!) is initiated by what is probably one of the most useful chapters of this book. This is a critical view of the present (1976) situation by the pioneer of HLA, Jean Dausset, who contributes a thoughtful and provocative essay, which might well have been the keynote of the whole presentation rather than being hidden away in an otherwise undistinguished section. The book is completed by a series of unconnected papers, which have been capriciously grouped together as 'Transplantation antigens and malignancy', although at least two of them, on Hodgkin's disease, would have been happier in the preceding section. This strange juxtaposition of material in the last section, where pure biochemistry is arranged cheek by jowl with a study of HLA in spontaneous retinoblastoma, is a failing of the book as a whole. Arrangement of a text is a major part of the editorial task in presenting any symposium proceedings: HLA and Malignancy fails badly on that score, with an unhappy mixture that does not present a coherent view of the subject and is certainly not easy reading for those who are not already experts in the field of HLA. The problem of finding the elusive association between HLA and malignancy will not be solved using this book as a guide. It does include a good deal of information but skill is needed to dissect it out of the text. What is particularly lacking, except in Professor Dausset's contribution, is an evaluation of the possible reasons why this aspect of HLA association is still in such an unsatisfactory state, and a long, cool look at the possibilities for future, productive studies. Anyone who needs help regarding what kind of studies are likely to be useful will have to work hard to extract it from this book.

HEATHER DICK


It is 11 years since the first edition of this book was published. Since then there have been many significant developments and advances in the neurological sciences, changes that are reflected in this revised edition.

The text has been considerably enlarged with the addition of a separate chapter on the neuronal system degenerations. Most of the other chapters deal with the major categories of developmental and acquired diseases that affect the spinal cord and the structures of the spinal canal. The last chapter gives details of how the spinal cord is examined post mortem in Oxford. Some 14 new illustrations have been added, and an updated list of references is appended to each chapter.

In many respects this book is a synopsis of neuropathology but with particular emphasis on those conditions that affect the spinal cord. Commonly encountered diseases are described fully, and the rarer conditions briefly. It is perhaps surprising that the opportunity has not been taken to give a more detailed account of the pathology of the diseases of the autonomic nervous system that affect the spinal cord, and of trauma, since recent experimental work (blood flow, electrophysiology, etc.) has greatly added to the knowledge and understanding of these conditions. Nevertheless this book gives a useful account of the subject and is recommended to neurologists, neurosurgeons, clinicians with a particular interest in the pathology.