Book reviews

reviewing arthropathies, multiple sclerosis, diabetes mellitus, coeliac disease, liver disease, acute leukaemia and Hodgkin's disease, and finally trophoblastic tumours. Unfortunately, the genetic linkage between HLA and 21-hydroxylase deficiency was discovered too late for inclusion in the Bulletin. 21-hydroxylase deficiency is a paradigm of genetic disease as the genetics, biochemistry, and treatment are so well worked out. Never before have we had such razor-sharp dissection of a segment of a human chromosome and been able to discern, even if we do not always fully understand, the interactions of closely linked genes, the effects of linkage disequilibrium, and the emergence of disease associations. Without doubt, HLA will be of the greatest practical importance in the prediction of those at risk of developing many diseases with a clear genetic basis but which depend on environmental triggers. As our understanding of this system increases, we will be able to detect and potentially remove offending environmental agents thus allowing true prevention.

This issue of the British Medical Bulletin is first rate and is obligatory reading for every clinical geneticist. It is remarkable value at £5.00 and is perfectly complementary to 'Basic Immunogenetics' by Fudenberg and his colleagues which is reviewed below.

**R. Harris**

**Basic Immunogenetics**


Since the first edition was published in 1972, a great deal has happened in the field of immunogenetics and it is remarkable that Dr Fudenberg and his colleagues have managed to limit the expansion of the second edition to only 48 pages. The use of finer quality paper has also kept the overall dimensions of the book about the same. One has to confess at the outset that immunogenetics is difficult. I wonder, for example, how many immunologists feel at home in the new and rapidly expanding sister-field of cell immunology? Taken together, the subject matter of this book, which covers the chemistry and genetics of antibody molecules, cell mediated immunology, and human blood group serology, is a highly concentrated collection of facts and theories. One should not, however, succumb to the temptation of leaving immunogenetics to the experts in the hope that it will become easier as time goes by, for already the subject has produced a number of unexpected observations with wide relevance to genetics as a whole, as a few examples will show. Single immunoglobulin polypeptides are coded for by two or more genes; families of multiple closely linked genes are characteristic of immunology, but may well be a basic phenomenon of mammalian germ lines; immunoglobulins demonstrate the importance of somatic mutations; the interaction between different lymphocyte types exerts control over protein synthesis, presumably by some form of genetic feedback. Last, but not least, allelic exclusion (involving autosomes) was discovered in a study of antibody molecules.

Fudenberg’s book covers all these areas with great clarity, tackling with skill a plethora of experimental data from both comparative and human studies. An abundance of tables and diagrams is a particularly praiseworthy feature of the book. As in the first edition, chapter 1 is an introductory essay which is well worth reading. Chapter 2 describes immunoglobulin structure and evolution and goes on to a lucid exposition of the admittedly complicated genetics of immunoglobulin molecules. Chapter 4 tackles the generation of antibody variability and describes what is known of the genetics of antibody specificity. Chapter 5 deals succinctly with lymphoid membrane antigens including their genetic control and relation to immune response, T and B cells, and lymphocyte interactions. The potted version of mouse H-2 is excellent. Chapter 6 is an adequate review of the human blood group systems and the book finishes, as before, with a number of useful appendices.

The index is generally good, though there are occasional omissions. For example, I encountered 'Fd' in the text but could not find an entry in the index or in the appendices. This edition went to press before the Seventh International Histocompatibility Workshop and before most of the new information on HLA-DW and -DRW loci became available. (This gap is filled admirably by 'The HLA System' in No. 3 of Vol. 34 of the British Medical Bulletin which should be read in parallel with this book and is reviewed above.) The section on HLA will no doubt be extended in a third edition. These criticisms do not detract significantly from 'Basic Immunogenetics' which remains an essential for the library of geneticists of all persuasions, both graduate and undergraduate.

**R. Harris**

**The Genetics of Aging**


Homer likened the generation of man to the fall of leaves. Addison introduced a continuous stochastic
model in his Bridge of Mirzah. In the intervening two and a half millenia most that could be said at the non-cellular level has been said, and said well and clearly. This book aims to provide all that gerontologists need to know about age, so that they can become 'biogerontologists', and goes direct to the novel and obscure with very little respect for the obvious. The well-known is frequently burdened with recent references.

As a many-authored book, aiming to cover the whole range of genetic influence on aging and survival in man, with occasional references to mammals, a few to flies, and almost none to plants, invertebrates, or ciliates, it has ambitions which are not easily bounded within a single volume. Whether the aim is realistic is the editor's problem; whether it has been achieved sufficiently to justify reading, with or without the burden of purchase, is the reviewer's.

On the whole, I do not think it has succeeded. Only one essay, by Murphy, shows aim, clarity, and vigour and one has to plough through 260 pages of assorted chapters reviewing various specific aspects, fairly equally divided between the platitudinous, the obvious, and the useful. The bibliographic dragnet has rarely gone deep, and fails to distinguish between papers which present new observations, new interpretations, or reviews. The idle hand of the computerised abstract is much in evidence, and many authors seem either to believe that scientific publishing followed the transistor, or that what is obvious to anyone who has either a parent or a child needs chapter and verse, in English or American, in this decade. Except for Murphy's chapter on the genetics of longevity in man, there is little new or original, all the remaining chapters being reviews. There are several useful papers, including one of the longest (43 pages) and most relevant, on somatic mutations and aging by Hirsch.

There seem to be some surprising omissions. There is nothing on age-specific death rates, nothing on the familial tendency to cause of death, nothing on the effect of work on longevity (which seems good for men and bad for horses), and little on the obvious greater longevity of women (one reference 1972). The fact that life is terminated by death, that most deaths have a single cause, and that most causes show both age-dependence and a familial predisposition, is hardly mentioned. Even Murphy does not mention Haldane's lucid contribution based on data and Lotka is not mentioned. The clear capacity of some individuals to reach advanced age with little evident physical or mental weakening is not mentioned.

Even the clinical parts seem to be based unduly on libraries. Patients with mongolism (Down's syndrome, here called Down syndrome), and with Turner's syndrome look old; those with ataxia-telangiectasia do not. The description of ataxia-telangiectasia includes 50% mental deficiency and a high proportion of an unusual form of diabetes. The Table on page 186, which includes diabetes as a human genetic disorder, asserts that in this condition, as in Turner's syndrome and ataxia-telangiectasia, epithelial tumours are increased. Mosaicism occurs in a minority of Turner's syndrome, not a majority (page 190).

Some of the psychological problems presented to the aged might well task the young. For example:

'The important Stroop factor for women was shown to be colour difficulty, a task in which the name of a colour (eg, red) is printed in ink of a different colour (eg, green), and the subject must then report the colour of the ink, rather than read the name of the colour (eg, green, not red); no particular Stroop factor emerged as salient for men'.

Twin studies are included in detail, but, since twins are concordant for date of birth, these are difficult to interpret, even without advanced statistical aids. While the difficult attempt to interpret what is going on inside the head by psychometric means covers many pages, there is almost nothing on the direct approach of the pathologists to the brain or its attendant sense organs.

The more obvious possibilities of studying the outside of the head for greyness and baldness, which would seem simple and relevant, are not considered. Nor is there anything on the eye and the ear, though a timely death unencumbered by accurately prescribed glasses is now becoming rare, and a failure in hearing sufficient to influence social activities, or to need an aid, is common.

It is very difficult either to plan such a book, or to execute such a plan, but even allowing for these difficulties the proportion of papers which seem to be based on mere reviewing, uninspired by any clear aim or balanced by any robust biological common sense, seems high. It is difficult to see why those who study age should be so dependent on young references.

The genetics of fatal disease is even more difficult than the genetics of those inborn and other disabling disorders which kill, if at all, by second intent. The genetics of childhood disease is difficult enough, but at least children have accessible sibs, and are rarely lost by death or migration; nor do they confound pursuit by changing their names. It is quite possible that genetic disorder of a simple genic origin is common in the aged.

The book can, at most, be recommended on the
basis of a single essay which repays reading, and a few reviews supported by a balanced and rich bibliography. What is needed is a ‘benchmarks in aging’ to include the papers of Price, Farr, Pearl, Lotka, Haldane, Medawar, and others, which will deserve the company of Murphy, supported with some descriptive papers on the lives and deaths of a wide variety of species, and of human and other cells in culture.

J. H. Edwards

Blood Groups and Diseases. A Study of Associations of Diseases with Blood Groups and Other Polymorphisms

Oxford Monographs on Medical Genetics.

This book is a natural companion to the authors’ other large work, the second edition of ‘The Distribution of the Human Blood Groups and Other Polymorphisms’ (1976), and together they represent an unrivalled source of information on blood groups and other polymorphisms as they occur in populations, both healthy and diseased.

Two-thirds of the book is taken up with the Tables that bring together data from virtually the whole of the world literature on the subject, express it in a uniform way, and add appropriate published control samples where these were not included in the original source material. Each Table documents the frequency of the different alleles of a particular polymorphic system in people with and without a particular disease, and calculates the relative incidence (risk) with a $\chi^2$ for the difference from unity. The data from each published study of a particular association are tabulated and a $\chi^2$ for homogeneity is provided. The basic arrangement of the Tables is by polymorphic system (ABO, MN, Rhesus, ABH secretor, haptoglobin, and PTC tasting), with each subdivided into disease type (infectious and parasitic, neoplasms, endocrine and metabolic diseases, etc).

Having set out all the raw data with complete bibliographical details, the book then provides summaries and analyses of various kinds, starting with tabular summaries that allow the overall trends to be seen more clearly. The 1976 report from the HLA and Disease Registry of Copenhagen is also reproduced at the end of the book as an appendix.

The remaining third of the book is concerned with synthesis and interpretation, and it is these 15 short chapters that give the book such a wide appeal. Obviously it was essential to include the histocompatibility antigens in any general discussions of disease associations and there is a clear explanation of linkage, association, and that trendy merger of the two, linkage disequilibrium, but the appendix on HLA association does not discuss the findings in any depth. Readers seeking this information would do better to turn to ‘HLA and Disease’ (1977) edited by Jean Dausset and Anne Sveigaard, Munksgaard, Copenhagen, a volume that also has an appendix to the main theme, a summary of blood groups and disease by Dr Mourant!

There is no-one better equipped to assess and then distil the evidence contained in the thousands of entries in the Tables, and though the associations are slight compared to what we have come to expect of HLA associations, the evidence is often very impressive. The association of carcinoma of the stomach with blood group A (A/O relative incidence 1.21) is now based on 161 surveys and over 63 000 cases. Heterogeneity between different studies can sometimes be very revealing as in the case of peptic ulcers, where the association with group O turns out to relate primarily to duodenal ulcers and in particular to ones that bleed. It is typical of the book that an interesting piece of information like this is not allowed to rest as an ‘isolated fact’. It crops up again when considering thrombosis and haemorrhage generally, because haemorrhage of various kinds is associated with group O, and thrombosis with group A, and factor VIII levels are higher in people of group A than group O. I could describe many such trains of thought that enliven the text and produce a flurry of hypotheses that the interested clinician could investigate.

It is, however, the broader ideas on what selective factors maintain the balanced polymorphisms, or account for the variations between populations, that are likely to provoke the most discussion. With probably at least a third of conceptions ending in miscarriage, pregnancy has always demanded attention from those interested in selection. Mourant concludes that there certainly is selective loss of A and B fetuses carried by group O mothers and seeks an opposing selective effect preventing populations from becoming entirely of group O. He turns his attention to the major epidemic infections and is disappointed that documented associations with particular infections are more often with A than O. This disappointment seems premature, for influenza infections are associated with group O and this is probably a general tendency for most viral infections. William McNeil’s ‘Plagues and Peoples’ documents devastating epidemics in the past that were probably virus infections, and it may be that there has been