GENETICS OF CEREBROVASCULAR DISEASE.
Edited by Mark J. Alberts.

Early misconceptions that this would be a volume about a narrow subject written in a dry manner were quickly dispelled. So too was the belief that in a rapidly moving field such as genetics it would be rapidly out of date. In fact this book is
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the role of ACE gene polymorphisms, for example, in stroke.
It is divided into four sections: genetic principles and
techniques, the genetics of risk factors for cerebrovascular
disease, the genetics of specific stroke aetiologies and
syndromes, and clinical applications. Each section comprises
three to seven chapters commissioned from different authors,
although Mark Alberts has played the sole or major part in
several. As with any multi-authored book there is some
overlap; for example, one can read about inherited
thrombophilias in some detail in two of the chapters.
Nevertheless the book has been well edited and a little
repetition is clearly preferable to glaring omissions, of which
there are none.

The first 60 pages discuss genetic concepts, genetic linkage
and the techniques used to identify genes that cause disease.
For those of us with no specific expertise in genetics it is
pitched at just the right level and, most importantly, it is
readable. A reminder about the structure of DNA is followed
by the principles behind linkage analysis and the use of LOD
scores. The chapter entitled ‘Advanced Genetics’ summarizes
the different types of genetic mutations, gene expression and
also the play of genetic factors in the genesis of ‘complex
diseases’, i.e. those such as diabetes mellitus, hypertension
and atherosclerosis which appear to have genetic components
but are not due to the influence of a single mutation acting
alone. The basic ideas developed in this section will suffice
for most cerebrovascular physicians but the chapters are
thoroughly referenced (as indeed they are throughout the
book) for further information if necessary.

It is in the four chapters of Part II that it dawns on the
reader what a potentially vast task it is to describe the
genetics of cerebrovascular diseases. Hypertension, lipid
metabolism, atherosclerosis and coagulopathies each
command separate chapters. Here is a succinct presentation
of the influence of the renin–angiotensin–aldosterone system
and the role of ACE gene and renin gene polymorphisms.
In common with the rest of the book the data are presented as
a personal view as opposed to the more critical analysis now
favoured by some editors. There are occasions when a tabular
or graphical analysis may help the reader to understand better
the role of ACE gene polymorphisms, for example, in stroke.
Thus, we trust the editor or chapter author to have performed
the appropriate literature search and to have provided us with
the correct answer without being exposed to any of the data.
This section of the book will perhaps be viewed by the
clinical neurologist as a reference section as he would not
wish necessarily to read piecemeal about the metabolism of
lipoproteins, the molecular biology of the apolipoproteins,
their enzymes and receptors. The chapter on coagulopathies
is an excellent source for learning, revision and reference
and it is a comprehensive summary of an increasingly
complex area. The factor V Leiden mutation and activated
protein C resistance is discussed in detail and the recently
described prothrombin gene mutation is mentioned. However,
its clinical role (for example, in cerebral venous thrombosis)
is mentioned no further.

It is within Part III that the cerebrovascular neurologist
will find most interest, not least because it contains the
chapter by Chabriat, Tournier-Lasserve and Bousser on
vascularopathies. Brief summaries of CADASIL, fibromuscular
dysplasia, dissections and Moyamoya are provided. My main
regret is that this chapter is not more extensive. Within Part
III are also chapters on subarachnoid haemorrhage and
intracranial aneurysms. Here again we read about
fibromuscular dysplasia, Ehlers Danlos type IV and other
collagen disorders, and the question of screening for
aneurysms in patients with a family history of aneurysmal
subarachnoid haemorrhage is discussed. This is one important
area where a more critical and painstaking analysis of all
available evidence would have been much more helpful than
what again is a somewhat personal view. Nonetheless the
authors’ criteria for screening, together with a reminder that
intracranial arteries and aneurysms are dynamic structures,
are timely. The implications of a screening process every 3–5
years, particularly given the recent results of the International
Study of Unruptured Intracranial Aneurysms clearly require
further thought.

Inherited cardiac diseases such as the hypertrophic
cardiomyopathies, dilated cardiomyopathies and the
cardiomyopathies associated with generalized disorders (e.g.
mitochondrial diseases) command their own chapter. So too
do the inherited systemic disorders that cause stroke. Here
Alberts has limited his discussion to the more common diseases
(e.g. haemoglobinopathies, hyperhomocysteinaemia) rather
than covering every rare syndrome imaginable.

If it is the extremely unusual inherited causes of stroke the
reader seeks then the paediatric chapter (Babban–Zonona
syndrome, Kohlmeier–Degos disease) is the place to look. By
no means is this chapter only a bewildering array of rare
syndromes, there is much to interest the adult neurologist (e.g.
16 inherited causes of the Moyamoya syndrome; nine inherited
causes of mitral valve prolapse) including a brief section on
cerebral venous thrombosis. Other conditions mentioned
elsewhere in the book are again mentioned here.

Although I have hinted at repetition about certain conditions
this is partly unavoidable given the associations with both
haemorrhage and infarction that certain inherited disorders
have. Since the organization of the book, rightly, is to enable
the reader to help determine what may, for example, have
caused a haemorrhage in his adult patient, or ischaemic stroke
in his paediatric patient, it is inevitable that Moyamoya and its
causes and the collagen vascular disorders will be mentioned
more than once. Although the role of thrombophilias in cerebral
venous thrombosis is covered in the paediatric stroke chapter
I feel that this is an area of sufficient importance and
development to be the devotion of a whole chapter. Should the
book be updated in the future I would hope that this addition is made.

The fourth section on clinical applications almost takes the reader full circle. The first chapter describes the evaluation of the stroke patient for genetic disorders of stroke. Here we are reminded about the importance of specific questioning in eliciting a family history, for example, of migraine, thromboses, miscarriages, skin rashes, etc. This is a slightly disappointing chapter in that an opportunity seems to have been missed to dissect carefully some stroke syndromes and lead the reader through potential causes and investigation. Although Alberts makes the proviso that this is not a book about the clinical features of stroke he could perhaps have led the reader through specific syndromes such as posterior circulation infarction or small vessel disease and given clues on how to recognize patients with MELAS or CADASIL, respectively, from the more common causes of stroke.

Finally the subject of genetic counselling and future gene therapies are summarized, the latter bringing the reader back to the genetics laboratory where he started in Part I. These chapters are necessarily brief and the non-US reader will find information on the qualifications of genetic counsellors in the USA redundant.

The book is sparsely illustrated with line diagrams but does not really suffer as a result. I make no apology for again commending each author on the thorough bibliography accompanying their chapter. The broad overview provided together with a comprehensive reference list makes this book a valuable addition to the bookshelf of the neurologist caring for young stroke patients or those with unusual stroke syndromes. Although this is a rapidly evolving field, little of what is contained in this book will necessarily go out of date. Rather it will act as a firm base to which future developments will be added.

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