HANDBOOK OF ATAXIA DISORDERS.  
Edited by Thomas Klockgether.  

This is Volume 51 of the Marcel Dekker (http://www. dekker.com) handbook series ‘Neurological Disease and Therapy’, which attempts to collate the increasing contributions from recent molecular advances of the ataxic disorders. The pace of these advances can create disadvantages in a book of this kind, with an inevitable lag between compilation and publication. It has contributions from a number of respected authors in the field, but with a European and particularly German dominance.

There are 32 chapters, organized within seven themed sections, although three sections have only one chapter each. In general the book is well constructed with comprehensive summaries and generates some interesting points of discussion. The first two chapters of the Introduction examine the architectural and functional aspects of the cerebellar system. Chapter 1 deals with the complex organization of the cerebellum and its connections, and efforts are made to integrate this complexity with clinical classification. The attempt to summarize the complex physiology of the cerebellar afferent and efferent fibres seems a little brief and is placed before the details of embryology. The second chapter provides a competent and understandable picture of the normal functions of the cerebellar system and some helpful insights into the pathophysiological basis for the cerebellar syndrome.

Chapter 3 deals with historical aspects of ataxia research as well as the long-running controversies in the ataxia field: its nosology and disease classification. The influence of recent advances in the past decade of molecular analyses is aptly collated in this chapter. The Introduction is closed with Chapter 4, written by the editor, on rational routes in the clinical approach to patients presenting with ataxia as a
predominant feature. It is of interest that the three suggested
diagnostic steps rely heavily on historical points (age of
onset, possible mode of inheritance and associated symptoms)
following decisions on focal or diffuse cerebellar disease and
recognition of established subgroup phenotypes, raising the
issue of whether clinical neurology has made any recent
advances or whether we simply rely more heavily on
laboratories. The discussions on these diagnostic steps are
coherent and clear in style, and will provide a useful guide
to clinicians dealing with such patients.

Section two, comprising only Chapter 5, entitled
‘Developmental disorders: cerebellar malformations’ is well
illustrated, particularly with neuroimaging, a feature that is
lacking in other parts of this book. Relatively rare conditions
are discussed in adequate length, and congenital dysgenesis
is well covered. There is an awareness of the difficulty of
clinical identification of these disorders in early life and the
extent of the influence of imaging technologies on diagnosis.
Despite such technology, many of these disorders have
genetic bases to them about which little is known.

Section three takes on the main diagnoses in the ataxias:
autosomal recessive ataxias, mitochondrial disorders,
autosomal dominant ataxias and transmissible spongiform
encephalopathies. The reader is immediately aware of the
limitations involved in elaborating aspects of epidemiology,
neuropathology and the management of these distinctive
disorders, with some exceptions. Nevertheless, attempts are
made towards a rational analysis that is well supported by
clinical experience. A strength of all the chapters in this
section is the molecular pathogenesis (even though many
issues are still unclear) and the thorough description of
clinical features of various groups of disorders. Undoubtedly
these positive features make the book worth consulting when
standard neurology textbooks fail to satisfy.

The majority of the chapters spanning this 689-page
book (Chapters 6–15), are on recessively inherited ataxias.
Beginning with useful discussions on a disorder that was
first described by Nicolaus Friedreich (1825–1882) in Chapter 6,
similarly interesting issues are considered with Madame
Louis Barr (1941), and ataxia telangiectasia in Chapter 7.
Interestingly, attempts are made to move from the commonly
encountered one or two paragraph discussion on the
management issues, and to shed some light on what can be
done to alleviate the disability, as well as looking forward to
future therapeutic approaches with our increasing knowledge
of the disorder at molecular level. Chapter 8 deals with early-
onset cerebellar ataxia (EOCA) with retained tendon reflexes,
nosology coined by Harding (1981), which is recognized for
being distinct, clinically and genetically, from Friedreich’s
ataxia. Despite some limitations, due to a degree of
uncertainty about this disorder, the authors have presented a
wide differential diagnosis which supplements their
recognition that only a small proportion of these patients are
identified with laboratory testing.

Chapters 9–13 introduce the reader to ataxia associated
with metabolic disorders, the majority of which are, not
surprisingly, of autosomal recessive inheritance. These
include abetalipoproteinaemia, ataxia with isolated vitamin E
deficiency, Refsum’s disease, cerebrotendinous xanthomatosis
and ataxias associated with rare metabolic disorders. Chapters
14 and 15 cover infantile-onset spinocerebellar ataxia and
autosomal recessive spastic ataxia of Charlevoix–Saguenay,
respectively. Perhaps because of the single racial heritage
known for both conditions (the former with a Finnish
family and the latter with Charlevoix French ancestors), the
respective authors have the advantages of being able to
produce a more detailed account of the neuropathology that
is lacking sometimes in other chapters.

Section four has only one chapter to it, attending to a
variety of mitochondrial disorders. Following the discovery
of an abnormal mitochondrial genome in 1988 and the link
diagnostic steps rely heavily on historical points (age of
onset, single or multiple) and point mutations for various mitochondriopathies.
Despite the absence of any epidemiological data, some credit
should be given to the author for the accounts of the
other essential clinical aspects of these disorders, which are
sometimes overlooked.

Autosomal dominant ataxias are discussed in Section five,
consisting of nine chapters (Chapters 17–25). The absence
of any Japanese contributor becomes apparent from the
omission of DRPLA as a subject heading. With the amount
of information now known about this disorder, and its
prevalence in Japan, it would seem appropriate for some
more detailed attention in this handbook. The terms used for
distinctive disorders in this section relate to the clinical
classification proposed by Harding (1983), which remains
useful despite the increasingly used mutation-based
classification. The coherent chapter styles in this section are
useful and allow easy comparison. There are some useful
insights into possible pathophysiological mechanisms.
Chapter 26 discusses the transmissible spongiform
encephalopathies (TSE) or, simply, prion diseases. This group
of progressive, chronic, disabling and fatal disorders remains
poorly understood.

The final theme is covered in Section seven and comprises
Chapters 27–32, which look into the non-hereditary ataxias.
The title of Chapter 27 (Idiopathic cerebellar degeneration)
is rather misleading since the main theme is multiple system
atrophy (MSA), and it seems probable that only 15% of the
idiopathic late-onset cerebellar ataxia cases actually progress
to develop the clinical features of MSA. Certainly this group
of disorders poses a considerable diagnostic challenge to
most neurologists since the diagnosis is often only confirmed
at autopsy. Frequent references are made to the consensus
published in 1999 (Journal of Neurological Sciences) for
the diagnosis of MSA in the discussions of the clinical features,
variably in an attempt to assist the reader in trying to
distinguish idiopathic late-onset cerebellar ataxia from MSA
clinically at presentation. With the importance of glial
cytoplasmic inclusions, there appears to be a certain lack
of neuropathological discussion, in which case there is a
considerable pathological overlap between MSA and other degenerative late-onset ataxias in sharing the features of olivopontocerebellar atrophy (OPCA). Nonetheless, the discussion of recent advances in using the supplementary tests is promising and fulfils one of the aims of the handbook.

Chapter 28 discusses the features related to alcoholic cerebellar degeneration as well as other toxic causes such as heavy metals, drugs and solvents. As the exact mechanisms for such degeneration are unknown, the chapter is a rather quick read, hastily reaching its comprehensive references list. In Chapter 29 (Paraneoplastic cerebellar degeneration), it is shown that recent molecular advances have greatly influenced the detection of auto-antibodies among cancer patients. However, these antibodies have not been shown to cause cerebellar degeneration, and some studies suggest immunopathogenesis mediated by cytotoxic T cells to be the culprit. Despite this, it is recognized that the absence of these anti-neuronal antibodies does not rule out paraneoplastic cerebellar involvement. The variable responses to treatment strategies are also mentioned. The following chapter deals with cerebellar encephalitis including gluten ataxia (a term proposed by one of the authors recently), infective causes of cerebellar encephalitis, Miller–Fisher syndrome and the controversial link between cerebellar ataxia and anti-glutamic acid decarboxylase antibodies. Equally interesting are the final chapters, where there are organized discussions on ataxia related to acquired vitamin deficiencies or endocrine disorders and heat-induced cerebellar insult, respectively. Both chapters give adequate discussions of these distinctive disorders, with also some insights to their management.

This is another book that deserves to make its way to any neurology library bookshelf. Despite some sense of urgency to complete the book, resulting in a rather unattractive layout with one or two omissions, it provides a comprehensive summary of the ataxias useful for neurologists of all grades, as well as clinicians in related disciplines, to aid in understanding this heterogeneous group of disorders. With the knowledge that many of these patients and their families still face unmet needs, our current increasing understanding of the aetiology and pathogenesis will, in the near future, permit us to identify more therapeutic avenues as well as setting up improved designs of clinical trials and more effective management plans. Last but not least, it should be remembered that any attempt to compile such a book on ataxia is difficult at best, as the information gathered about the ataxias has rapidly expanded with new advances that have transformed the attitudes towards degenerative cerebellar ataxias.

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