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book reviews

Neurodegenerative diseases: neurobiology, pathogenesis and therapeutics

Edited by M Flint Beal, AE Lang and AC Ludolph.
Cambridge University Press, Cambridge 2005. 1008pp.
£195.

We have come a long way from Gowers' definition in 1893 that in 'old age the brain wastes, like many other organs'. By 1940, Kinnier Wilson included in his textbook many of the neurodegenerative disorders that we now know – Alzheimer's disease, paralysis agitans (Parkinson's disease), progressive lenticular degeneration (Wilson's disease), cerebellar and spinocerebellar degenerations, progressive spinal muscular atrophy (including motor neurone disease) and Huntington's chorea amongst others.

This modern reference work proves to be a mine of information covering many aspects of degenerative diseases affecting the nervous system. There has been a gap between the works dealing largely with neuropathology, like *Greenfield's neuropathology*, and this edition, which adds far more detail including clinical aspects, neurobiology, knowledge of genetics and therapeutic approaches. The editors are to be complimented on their choice of contributors, although there is a heavy bias towards those from the USA.

The early chapters, the first third of the work, cover the basic aspects of the degenerative processes exploring, for example, apoptosis and the role of a number of factors in producing and protecting against cell death. These factors include the influence of various proposed genetic pathways, possible toxic factors and the possible role of inflammatory processes in cell death.

Neuropathology is well covered, particularly in the dementias and movement disorders. Inevitably in a multi-author work there is some overlap. We now have to recognise the disorders caused by

disorders of tau (an axonal phosphoprotein important for the binding and stabilisation of microtubules) and alpha synuclein (a major component of Lewy bodies): the terms tauopathies (eg frontotemporal lobar degeneration, progressive supranuclear palsy) and synucleopathies (eg Parkinson's disease, multiple system atrophy) have appeared. It is useful to know the changes found in normal ageing as opposed to those found in a confirmed neurodegenerative disorder. Emphasis on early changes may allow a better chance of trying new therapies to slow up or prevent further pathological changes.

To a clinician the last five hundred pages carry a wealth of information. The descriptions of normal ageing and the chapters containing overviews of Alzheimer's disease, Parkinson's disease, motor neurone dysfunction and the ataxias are excellent and include many useful details. They have been written by experts in the field. In the section on movement disorders there are valuable tables helping to identify those patients with a progressive supranuclear palsy (PSP), those with a multiple system atrophy (MSA), and those with the uncommon entity of corticobasal degeneration. These conditions still rely heavily on a clinical diagnosis. The section on prion diseases is also informative and helps the clinician towards making a diagnosis of these rare conditions, although there is no mention of the difficulties that a proposed biopsy may invoke in terms of disposable instruments and the handling of this 'transmissible' material. There is also a detailed discussion on the pathogenesis and mechanisms of prion diseases.

An up-to-date account of the genetics of many of these disorders is given and is most appropriate in such an expanding field. Even nineteen of the spinocerebellar ataxias are described. The genetic links with motor neurone disorders and Alzheimer's disease are comprehensively covered. Other topics are discussed and these include the

hereditary spastic paraplegias, Huntington's disease, disorders of the mitochondrial respiratory chain, neuroanthocytosis and Wilson's disease (an excellent section on confirming the diagnosis). The work is also a good source for many other conditions.

I used this work to examine four difficult areas – the electrophysiological abnormalities found on sphincter electromyography in MSA and the Parkinsonism-plus disorders, the magnetic resonance imaging findings in the various Parkinsonism-plus syndromes, the possible role of non-steroidal anti-inflammatory drugs and the possible use of N-methyl-D-aspartate receptor antagonists in the treatment of Alzheimer's disease, and the genetics of motor neurone disease. The information on all four topics proved to be helpful and readily accessible.

The charge is often made that, once diagnosed, all too often the therapeutic options in many neurological disorders are either very limited or merely supportive. In this edition there are excellent discussions of available therapies and the basis for their efficacy, and also discussions on possible future treatments including gene therapy and stem cell implants. Supportive treatment is also discussed.

Overall this reference work is to be recommended. It should be available on the shelves of any neurological department as an up-to-date and informative source.

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Vintage papers from the *Lancet*

Edited and introduced by Ruth Richardson. Elsevier, Edinburgh 2006. 488pp. £32.99.

This handsome book justly celebrates the achievements of Britain's most famous medical journal, from its first issue in 1823 to 2005. The *Lancet's* present editor, Richard Horton, introduces the book with a foreword, reminding us that Thomas Wakley, the *Lancet's* first editor, was an admirer of William Cobbett whose attacks on the British establishment 200 years ago were so effective.

As Ruth Richardson tells us, in a short but fascinating historical introduction, Wakley was a brave man with a resolute sense of justice and a genial sense of humour. The early issues of the *Lancet* sometimes seem to have been quite close in their approach and their impact to today's *Private Eye*. As a correspondent noted, 'comfortable hospital doctors beheld the journal's appearance with trepidation'. Quacks and dubious practitioners were fearlessly exposed. The *Lancet* believed that the Royal Colleges of surgery and 'physic' were run by self-appointed oligarchies 'bloated with wealth and blustering with power' in which 'musty receptacles of ignorance and imbecility' could be found.

Not all the journal's later editors were as brave or reckless as Wakley, but with few exceptions the *Lancet* has remained a fearless pioneering journal with an international reputation as great as that of the *New England Journal of Medicine*, which was founded only a few years earlier. Both these weekly medical journals have remained fiercely independent and critical of the medical establishments of their times. Charles Dickens became Wakley's friend when he was a jury member at a Marylebone workhouse inquest presided over, as coroner, by Wakley. Dickens at once saw that Wakley was an intelligent, discerning and sympathetic man. Much of the medical

information which appears in his novels must have derived from Dickens' meetings with Wakley.

As Richardson notes, Wakley left behind a 'richly creative journalistic legacy', having published lecture texts, news exclusives, regular and irregular columns of many different kinds, scientific papers, hypotheses, arts and leisure articles, descriptions of new treatments, detailed case histories, satires, announcements, obituaries, 'quips, spoofs and petitions'. Later editors remained original and creative, though inevitably they grew closer to the establishment they had derided. Indeed, I remember an election to select a President for the Royal College of Physicians at which Theodore Fox (then the *Lancet's* editor) was *proxime accessit!*

Richardson's book contains an impressive number of original papers, articles and commentaries. Nowadays there are not so many 'firsts' as there used to be, because new original material today inevitably appears initially in *Science* or *Nature*, but in early years many papers had enormous clinical as well as social or political impact. Each of the four sections in the book takes a period of 30 or 40 years and lists the papers of special interest in those years. *Vintage papers*, however, does not just list the papers: its (Chinese) printer has produced photographically accurate and perfect copies of the relevant journal pages, at their original size. This has made the book large and heavy (12 inches tall, 10 inches wide, nearly an inch thick). It is an ideal 'coffee table book', but I don't want to imply that it is trivial. It is packed with fascinating original material. Every doctor will want to have it in their waiting room, though it will be difficult to tear patients and colleagues away from its pages.

Such a huge compilation of material cannot be summarised, but a few papers specially interested and excited me: the detailed exposure of the barbarity of flogging in the services; an appeal for the provision in poor districts of public baths and clean water for washing; the (disapproving) revelation that Queen Victoria had been given chloroform for her latest childbirth; an account of the antipyretic action of salicylate; the first British clinical X-ray photograph (of a bullet lodged in a boy's wrist); a protest against the forcible feeding of suffragette prisoners; a plea in support of the state provision of family allowances; a correspondent's letter suggesting thrombosis; the preliminary results of the Medical Research Council trial revealing that combining two anti-tuberculosis drugs (PAS and streptomycin) reduces the appearance of streptomycin-resistant strains; the first confirmation that thalidomide given during pregnancy could cause congenital abnormalities; the first note by James Black and his colleagues at ICI of the syntheses of propranolol (pronethalol's successor); Tudor Hart's celebrated 'inverse care law'; two adjacent papers by Warren and Marshall (both later Nobel Prize laureates) of 'curved bacilli' in gastric epithelium associated with active chronic gastritis.

My only complaint about the book is that (of necessity) most entries do not finish at the end of the page. Inevitably one begins to read in another column on the page another unrelated but almost equally fascinating article. But we must be grateful to all the editors of the *Lancet*, and its publishers, for making possible this fascinating and endlessly entertaining collection.

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