References

Reversible dementias
The concepts of potentially reversible cognitive impairment in general, and the reversible dementias in particular, remain controversial. The prevalence of these conditions depends to a great extent on the definitions used and on the population studied. Also, the definition of those cases with potentially reversible conditions that actually do reverse remains a critical aspect in assessing these conditions.

In their article, Hejl et al. present the results of a prospective study to investigate the prevalence of potentially reversible causes of cognitive decline in consecutive patients presenting to a tertiary medical centre memory clinic. The description that they provide of a large cohort study provides an important contribution to our understanding of this condition. However, as was mentioned by the authors in the discussion, the rather high prevalence (19%) of potentially reversible causes detected must be regarded with some caution. Also, while no data are presented regarding the follow up of those patients where a potentially reversible cause was identified, the authors nevertheless conclude “that treatment may improve or restore intellectual functions.”

As was mentioned by the authors, one of us (AHC) has previously described the prevalence of reversible dementias, with 13.2% of cases having a potentially reversible cause, while only 3% fully resolved on treatment. In that review of the literature, as in the study by Hejl et al., most of the studies originated from secondary or tertiary centres. In a recent meta-analysis by AMC, where a much higher proportion of studies than previously emamated from either outpatient departments or were community based, it was shown that regardless of potential reversibility, the true prevalence of reversed dementias is actually less than 1%.

We thus feel that although it is important to diagnose and treat concomitant conditions in patients suffering from cognitive decline, one should exercise great caution in describing possible causes of cognitive decline and dementia as either potentially or fully reversible.

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Authors’ reply
We are grateful for the opportunity to comment on the important issue raised by Dr Dvolatzky and Dr Clarfield regarding the true prevalence of reversible dementias. In our paper we investigated the prevalence of potentially reversible aetiology and comorbidity in 1000 consecutive patients referred to an outpatient memory clinic based in neurology. In the whole group of cognitive symptoms, with a potentially reversible condition, which was evaluated as the primary cause of the symptoms leading to referral. However, in patients meeting the clinical criteria for dementia via the prevalence only, the potentially reversible concomitant conditions the prevalence was 23%. Thus, potentially reversible conditions are most common in patients with cognitive symptoms, less common in patients meeting the criteria for dementia, and comparatively common as comorbidity in both groups.

Dr Dvolatzky and Dr Clarfield report that in their future meta-analysis for publication in 2003 the “true” prevalence of reversed dementias is less than 1%. With reference to our results in patients with dementia we are not surprised about the very small prevalence of truly-reversed dementias.

As we have already discussed in our report, both the setting of the study and the definition of potentially reversible conditions may influence the prevalence found. Also a systematic search for potentially reversible conditions in other settings, the study provides evidence that potentially reversible conditions are not rare. They were most common in younger patients and in patients with mild cognitive symptoms not sufficiently severe to meet international criteria for dementia.

The most frequent potentially reversible conditions were depression, hydrocephalus, alcohol dependence syndrome, metabolic disorders, and space occupying lesions. Even if treatment of these conditions may not always lead to full reversal of cognitive symptoms, or dementia, the identification of the disorders is crucial to the management of the patient and important to prevent a misdiagnosis of Alzheimer’s disease. In conclusion, a systematic search for potentially reversible conditions is relevant and important, even when full reversal of the cognitive symptoms may be unlikely.
Neuropathology of Hashimoto's encephalopathy

Doherty et al have recently reported in this journal on a case of Hashimoto's encephalopathy clinically mimicking Creutzfeldt-Jakob disease and performed a neuropathological analysis of a brain biopsy in this case revealed spongiform change and sparse mononuclear infiltrates in perivascular spaces, the authors suggested that Hashimoto’s encephalopathy is an encephalitic process. We have previously described a necropsy case of Hashimoto’s encephalopathy showing lymphocytic vasculitis of veins and venules of the brain stem, supporting the hypothesis that vasculitis represents the morphological substrate of Hashimoto’s encephalopathy.1 Doherty et al have challenged our diagnosis and stated that the term vasculitis should be reserved for lesions with inflammation and fibrinoid necrosis of arterial vessels.

Lymphocytic vasculitis is a generally accepted pathological subtype covered by reviews and standard textbooks.2,3 It is characterised by the presence of lymphocytes within the vessel wall and is encountered in Wegener’s disease, systemic lupus erythematosus, and Behcet’s disease, to name but a few conditions.4 The diagnosis is more difficult than for necrotising arteritis,3 however, implies that lymphocytic vasculitis does not exist, and our case certainly belongs in this vasculitis category.

Additional support for the vascular basis of Hashimoto’s encephalopathy comes from other reports on this condition where there has been angiographic demonstration of vasculitis.5 More recent experimental evidence for a vasculitic pathogenesis involves the identification of α-enolase as an autoantigen in Hashimoto’s encephalopathy.6 Because anti-α-enolase antibodies are present in various autoimmune vasculitic diseases such as systemic lupus erythematosus and ANCA associated vasculitis, and because α-enolase is highly expressed in the endothelium, based on the histological figure and the description provided by Doherty et al, we express some reservations over the presence of these changes. True spongiform changes, usually encountered in prion disease, are present in the neuropil between nerve cell bodies, whereas the perineuronal spaces described by Doherty et al more closely resemble shrinkage artefacts which may be particularly pronounced in small biopsy specimens. In addition, we would like to point out that vasculitis is typically focal and may have been missed in this case.

In conclusion, we feel that the available clinical, pathological, and experimental evidence suggests that vasculitis underlies a substantial proportion of cases of Hashimoto’s encephalopathy. However, additional careful necropsy studies are required to determine whether other pathological entities contribute to the clinical picture.

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References

Authors’ reply
We thank Drs Paulus and Nolte for their interest in our case report, which we offered as a lesson in to a certain extent pathological, similarities between Creutzfeldt–Jakob disease (CJD) and Hashimoto’s encephalopathy on small biopsies. Of course, in established CJD—as the correspondents rightly mention—spongiform change is easily recognised by vacuoles in the neuropil; in contrast to their contention, these are regularly accompanied by neuronal cytoplasmic vacuoles displacing surrounding neuropil (simply as those we illustrated), as described in standard textbooks1 and in clinicopathological cases.2 The difficult judgment is in the brain biopsy in early CJD, in which these changes are minimal and indeed nearly impossible to distinguish from artefact or oedema. The concurrence of astrogliosis with the spongiform appearance (no matter what the cause) in our case further lowered our threshold for submitting the tissue for definitive prion protein studies in the clinical setting of rapidly evolving cognitive decline. We hope the correspondents would agree that such would be simply good clinical practice, especially in a patient like ours without a helpful history of Hashimoto’s thyroiditis or anti-thyroid peroxidase antibodies.

As to their assertion that we “challenged” their diagnosis of vasculitis (which we point out was followed by a question mark in the title of their own report!), we felt that the previous subarachnoid haemorrhage and apparently diffused infiltration of the leptomeninges that they described suggested that the venular lymphocytic infiltrates could be secondary to the haemorrhage, or be a manifestation of a meningoencephalitis (possibly autoimmune) not a primary true vasculitis. According to the textbook they cite, the entities of Wegener’s disease, systemic lupus erythematosus, and Behcet’s disease, to use their examples, are all characterised primarily by true arteritis with necrosis, not by the lymphocytic venulitis which Nolte may accompany it. Drs Paulus and Nolte are correct in that our small biopsy, vasculitis may have been missed. They may also be correct that the pathogenesis of Hashimoto’s encephalopathy involves vasculitis. We stand firm in our position, however, that to make a histological diagnosis of vasculitis requires the exclusion of other factors, such as haemorrhage or tissue inflammation, in which lymphocytic diapedesis through vessels is physiological. Moreover, the novel finding in our case of perivascular inflammation does raise the prospect of an encephalitic process in Hashimoto’s encephalopathy, independent of any effect on blood vessels, whether primary or secondary.

We thank Drs Paulus and Nolte for pointing out the interesting paper by Ochi et al, and look forward to future elucidation of the role of α-enolase in Hashimoto’s encephalopathy. Perhaps those of us with tissue from cases of Hashimoto’s encephalopathy will need to collaborate in that regard, to expand their studies on serum from patients with this condition.

Finally, we want to reiterate the importance of a broad differential diagnosis in evaluating patients with rapid decline in cognition, and with vacuoles, astrogliosis, microgliosis, and perivascular chronic inflammatory cells on brain biopsy. That was the overarching point of our paper.

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References

BOOK REVIEWS

Management of stroke: a practical guide for the prevention, evaluation and treatment of acute stroke, 2nd edition


This textbook exemplifies the recent and dramatic changes in the approach to the management of acute stroke. Whereas in the past stroke was seen as untreatable, this book sees stroke as an emergency warranting acute treatment. As the authors state in the introduction, “A positive attitude towards stroke is critical. Patients with cerebrovascular disease should be considered to have an illness that can be treated successfully.” This admirably emphasises the approach that sees stroke not as an untreatable “cerebrovascular accident” (a term that should be expunged from medical texts) but as a “brain attack.” The term the authors use to emphasise the need for rapid diagnosis and evaluation of acute suspected stroke.

Despite giving the impression of being a brief book, almost all aspects of emergency stroke treatment are covered, starting with organisation of stroke services and proceeding to diagnosis and emergency treatment. There is also a chapter devoted to stroke prevention. The text is divided into 13 chapters, followed by a reference list and an index, which includes the tables and figures. The text is illustrated with computed tomography and magnetic resonance imaging scans and is interspersed throughout with very helpful...
Diseases of the nervous system: clinical neuroscience and therapeutic principles


The third edition of this well known book is subtitled Clinical neuroscience and therapeutic principles. This signifies that it is not a textbook of clinical practice, but a reference book founded in pathophysiology. So how well does it succeed? With 221 authors writing 129 chapters some unevenness is inevitable. It is a tribute to the editors’ tight grip that the overall coverage of neurological disease is suitably comprehensive.

I particularly liked the introductory section which highlights contemporary trends in understanding neurological disease processes, the principles of restoring function after damage, and “windows on a working brain”. This is the section of the book that I chose to read for pleasure, simply for a succinct and thoughtful view as to where neurology is going outside our specialty. And throughout the book, there is excellent coverage of background issues ranging from the chemical bases of addiction and alcoholism, to host responses to infection, to pathophysiology of cerebral circulation, to the cellular basis of epilepsy, and to repeat trimucleotide expansions.

Inevitably one can take issue with aspects of subject matter coverage, particularly in one’s own subspecialty. For instance, within the neuromuscular disease section, the scientifically interesting and clinically important multifocal motor, CIDP paraproteinaemic, and vasculitic neuropathies, lie buried incognito in a chapter entitled “Guillain-Barré syndrome”. I imagine that the lack of coverage of mononeuropathies deliberately reflects the lack of sexy science underlying this topic, despite its commonness as a clinical encounter. Most welcome, is the coverage of how channelopathies and metabolic derangements affect muscle function.

Although extending to two hefty volumes, totalling over 2000 pages, this text has a refreshingly light and accessible feel. The index is reasonably good. Many of the illustrations are line drawings, and are beautifully clear. This enhances the notion of scientific principles which imubes the text. A superb book to have at hand in one’s office alongside a textbook of clinical practice. It is pretty expensive, but probably worth it if you need a succinct summary of the myriad bases and their treatment with antipsychotic drugs.

This short book is an update of the two chapters from the second edition of Stahl’s larger textbook Essential pharmacology that deal exclusively with psychosis and schizophrenia and their treatment with antipsychotic drugs. The author argues that this new book is justified by the rapidly expanding knowledge base of psychopharmacology for psychosis and schizophrenia.

This book has the same qualities as its big brother. The simple and beautifully conceived layout makes the book highly readable while conveying information that is at the cutting edge of contemporary neuroscience. The latest theories of mechanisms of “atypicality” are presented, including Kapur’s rapid dissociation theory, as are the modes of action of the new generation of so-called dopamine system stabilisers, exemplified by aripiprazole. Given that the latter has not yet been launched in the UK, this volume can be seen as a first attempt at addressing each of these three themes. There is a wealth of stimulating, challenging, and elegant argument used in so doing, and whether one agrees or disagrees with any particular premise the clarity of thought is enviable. Inevitably in a collection such as this there is some degree of repetition and, to some extent, a difficulty in maintaining a focus on the overarching themes and concepts. Nevertheless the book amply repays the time spent in reading each essay carefully and thoughtfully, and it is a great pleasure to recognise Professor Sartorius’ passion for the wellbeing of people with mental health problems. Each chapter of the book is illustrated by a carefully selected painting and each of these adds another dimension to the work.

At the end of his introduction Professor Sartorius urges psychiatrists to “fight the social and political battles that are necessary to improve the fate of people struck by mental illness, and make psychiatry and related disciplines and sciences useful to society and responsive to its ethical duties”. This is a rallying call which I hope will be heard and responded to by many.

J Hollyman

Essential pharmacology of antipsychotics and mood stabilizers


This short book is an update of two chapters from the second edition of Stahl’s larger textbook Essential pharmacology that deal exclusively with psychosis and schizophrenia and their treatment with antipsychotic drugs. The author argues that this new book is justified by the rapidly expanding knowledge base of psychopharmacology for psychosis and schizophrenia.

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