mic slow wave discharges on the right at 1–2 Hz, occasionally associated with spikes, and more clearly epileptiform activity on the left. Intravenous diazepam abolished the activity on the left, but spared that on the right. The initial diagnosis was of pneumonia with complex partial status epilepticus. On the following day the EEG record was dominated by widespread, irregular, repetitive complexes with a period of approximately two seconds. Unenhanced CT scan appearances had not, however, changed since 1988. A lumbar puncture was performed as her conscious level had failed to improve. The CSF was under a pressure of 24 cms and contained $52x10^6$/L leucocytes (93% lymphocytes) with normal CSF protein and CSF: blood glucose ratio. A further lumbar puncture two days later showed worsening abnormality and treatment was started with intravenous Acyclovir, rifampicin, isoniazid and pyrazinamide. Over the following nine days her reflex responses deteriorated and she died.

A polymerase chain reaction for the amplification of HSV-1 DNA was carried out post-mortem using the primer sequences and methods described by Aurelius *et al*,[3] with some modifications. Reaction conditions for first and second round PCR were as described previously.[4] The patient's second CSF sample and the positive controls contained detectable HSV DNA after two rounds of PCR (fig). The first CSF sample, taken two days before, was negative. Neither oligoclonal bands of total IgG, nor antigen specific oligoclonal bands were detected in either CSF sample. Viral culture and viral titres were negative in the first CSF sample; in the second sample viral culture was again negative but a weak IgG response to Herpes simplex virus 1 was detected by ELISA.

Post mortem examination confirmed the presence of a right petrous meningioma. The brain was swollen and soft, with uncal and cerebellar tonsillar herniation. Temporal and insular cortex were involved in a marked meningoencephalitis, with necrotising venulitis and perivascular infiltration by lymphocytes and macrophages. Immunoperoxidase staining revealed a very striking positive reaction for herpes simplex virus antigens in neurons, macrophages, and many cells whose nature could not be identified.

This complex case emphasises the importance of prompt treatment with Acyclovir[5] where there is clinical suspicion of the diagnosis of HSE. In general the diagnosis should be considered in any patient with fever and depression of consciousness: suspicion should be heightened by accompanying abnormalities of behaviour, focal seizures or signs, especially dysphasia, evidence of acute temporal lobe pathology from neuroimaging or EEG, or a CSF lymphocytosis.[1] A number of factors conspired to reduce clinical suspicion in the present case, in particular the patient's long history of epilepsy with pronounced post-ictal confusion and the clinical evidence for a severe pneumonia. In retrospect, the onset of encephalopathy with drowsiness, seizures, fever and new EEG disturbance was fully in keeping with the eventual diagnosis of HSE. It is of course always important, even in the context of a patient with a chronic disorder, to assess an acute illness on its own merits.

Although PCR is highly sensitive and specific, the negative result from the first CSF sample reminds us that all laboratory tests give rise to occasional false negative results: it is advisable to test more than once in difficult cases, and a negative PCR result should not preclude the use of acyclovir where HSE is suspected clinically.

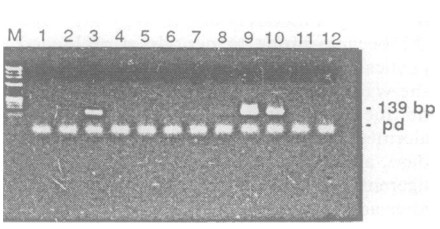

Figure Second round PCR products, on ethidium bromide stained gel, showing a positive reaction in lanes 3 (patient's CSF) and lanes 9 and 10 (positive controls). Lane M contains molecular weight markers. pd = primer-dimer amplification products, 139 bp = herpes simplex virus type 1 second round PCR products.

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1 Whitley RJ, Soong S-J, Linneman C, Liu C, Pazin G, Alford A. Herpes simplex encephalitis: clinical assessment. *JAMA* 1982;**247**:317–20.
2 Whitley RJ, Cobbs CG, Alford CA, *et al.* Diseases that mimic herpes simplex encephalitis: diagnosis, presentation and outcome. *JAMA* 1989;**262**:234–9.
3 Aurelius E, Johansson B, Skoldenburg B, Staland A, Forsgren M. Rapid diagnosis of herpes simplex encephalitis by nested polymerase chain reaction assay of cerebrospinal fluid. *Lancet* 1991;**337**:189–92.
4 Wakefield AJ, Fox JD, Sawyerr AM, *et al.* Detection of herpes virus DNA in the large intestine of patients with ulcerative colitis and Crohn's disease using the nested polymerase chain reaction. *J Med Virol* 1992;**38**:183–90.
5 Skoldenburg B, Alestig K, Burman L, *et al.* Acyclovir versus vidarabine in Herpes simplex encephalitis. *Lancet* 1984;**ii**:707–11.

MATTERS ARISING

Accuracy of clinical diagnosis of idiopathic Parkinson's disease

I read the paper by Hughes *et al*[1] in the journal with much interest and wish to compliment them for their work.

The percentage of inaccurate clinical diagnosis of idiopathic Parkinson's disease (IPD) in their study is identical to that which we reported last year.[2] Their observations, however, are different from our study in several respects. For example, the largest subgroup of patients (6 cases) which were erroneously diagnosed as having IPD by Hughes *et al*[1] had progressive supranuclear palsy (PSP); in contrast, all the necropsy proven PSP cases in our study were recognised before death.[2] The reasons for that difference are unclear. The final clinical diagnosis in all our patients was made by the same neurologist.[2] Hughes *et al*[1] did not indicate the number of neurologists and the geriatricians involved in the evaluation of their patients and those contributing to the brain bank. The larger the number of clinicians assessing the patients, the greater would be the variability and the chance of error.

The second possibility for the misdiagnosis is that the patients may have been evaluated during an early stage of illness, before the features characteristic of PSP were evident. The clinical data in our cases were collected prospectively and we were able to assess the issue of diagnostic accuracy based on each, the initial and the final clinical diagnosis before death. While only 65% of our cases whose initial diagnosis was IPD had Lewy body pathology, the diagnostic accuracy increased to 76% by the time the final assessment was done—mean 12 years after onset. Most cases who had other variants of Parkinsonian syndrome (PS) were recognised within 5 years of onset. It is unclear in the report if they[1] relied on initial or the final clinical diagnosis.

Another aspect that we[2] made a note of but is not clarified in their study[1] is the method used to assign one diagnosis to a patient. We considered the clinical diagnosis correct only if it was the sole diagnosis or the pathological diagnosis was listed at the top of diagnostic possibilities.[2]

Several variants of PS, including PSP[3–5] were clinically and pathologically identified in the early 1960s. Those patients who were evaluated before that would therefore have a larger proportion of inaccurate diagnosis by contemporary standards. Their paper does not indicate if some of the errors in diagnosis may be related to the calendar year of patient assessment.

In addition to our paper, there is a small study by Forno[6] which addressed the issue of the accuracy of clinical diagnosis in IPD.

Hughes *et al* retrospectively analysed patients using the UK Parkinson's Disease Society Brain Bank (PDSBB) clinical diagnostic criteria. By those criteria, 11 patients did not have IPD, yet 3 (27%) of those turned out to have Lewy body pathology. They have not discussed the reasons for this significant error. Whatever the reason, it illustrates that no diagnostic criteria are fool-proof.

I suggest a minor amendment to the PDSBB clinical criteria for consideration by the committee. Postural instability which has been recommended as one of the two major manifestations necessary for making the diagnosis of PS should be deleted as it is present in a large segment of normal elderly people. Most clinicians looking after elderly people recognise that individuals in this age group lose balance rather easily compared with younger age groups. Postural instability, as evaluated in the PS, was carefully studied by Weiner *et al*[7] in the elderly. When all the neurological, mechanical and other possible causes for postural reflex impairment were excluded, they noted that postural instability was an age-related phenomenon.[7] While 43% of those between age 60–69 years had impaired postural reflexes, 70% between 80–89 and 100% of those between age 90–99 years had impaired postural reflexes.[7]

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1 Hughes AJ, Daniel SE, Kilford L, Lees AJ. Accuracy of clinical diagnosis of idiopathic Parkinson's disease: A clinico-pathological study of 100 cases. *J Neurol Neurosurg Psychiatry* 1992;**55**:181–4.
2 Rajput AH, Rozdilsky B, Rajput Alex H. Accuracy of Clinical Diagnosis in

Parkinsonism—A Prospective Study. *Can J Neurol Sci* 1991;**18**:275–8.
3 Steele JC, Richardson JC, Olszewski J. Progressive Supranuclear Palsy. *Arch Neurol* 1964;**10**:333–59.
4 Adams RD, van Bogaert L, Van der Eecken H. Striato-nigral degeneration. *J Neuropathol Exp Neurol* 1964;**23**:584–608.
5 Delay J, Deniker P. Drug-induced extrapyramidal syndromes. In: Vinken PJ, Bruyn GW, eds. *Handbook of clinical neurology*, 6th ed. New York: Elsevier, North Holland, 1968:248–66.
6 Forno LS. Pathology of Parkinsonism: a preliminary report of 24 cases. *J Neurosurg* 1966;**24**:266–71.
7 Weiner WJ, Nora LM, Glantz RH. Elderly inpatients: postural reflex impairment. *Neurology* 1984;**34**:945–7.

Hughes et al reply:

We thank Professor Rajput for his interest and contribution to the discussion of our study.[1] It is unclear why progressive supranuclear palsy (PSNP) comprised such a high percentage of patients clinically misdiagnosed as having Parkinson's disease (PD) in our study, while in his series all necropsy proven cases of PSNP were recognised before death.[2] A pure akinetic syndrome may, however, be the only manifestation of PSNP.[3] The UK Parkinson's Disease Society Brain Bank (PDSBB) receives donor tissue from Parkinsonian patients throughout the UK. Once enrolled in the scheme, patients are examined annually by one of 70 neurologists and geriatricians associated with the Brain Bank and information is recorded according to a standard format. Despite the use of diagnostic criteria it is clearly impossible to completely standardise diagnostic practice across such a group of assessors. The stage of disease when patients are examined is clearly important in studies of this type. The clinical diagnoses used in our present study were all made within 12 months of death, at the time of the last assessment, and during or after 1986. All patients were considered specifically to have PD rather than a less well-defined Parkinsonian syndrome.

We agree that no diagnostic criteria for PD are fool-proof and have subsequently analysed the clinical features of our cases in terms of their diagnostic value.[4] By using selected criteria (asymmetrical onset, no atypical features, and no possible aetiology for another Parkinsonian syndrome) the proportion of true PD cases identified was increased to 93%, but at the expense of excluding 32% of pathologically confirmed cases. Twelve of 100 cases of histologically confirmed PD examined at the PDSBB had atypical clinical features according to Brain Bank diagnostic criteria for this disease.[5] More than half of these cases had no other associated neuropathological findings that could have explained the atypical features.

These findings suggest that studies based on consultant diagnosis of Parkinson's disease will include patients without the disease as well as excluding some who subsequently satisfy the histological criteria, thus results from clinical trials and epidemiological studies may be distorted.

1 Hughes AJ, Daniel SE, Kilford L, Lees AJ. Accuracy of clinical diagnosis of idiopathic Parkinson's disease: A clinico-pathological study of 100 cases. *J Neurol Neurosurg Psychiatry* 1992;**55**:181–4.
2 Rajput AH, Rozdilsky B, Rajput Alex H. Accuracy of Clinical Diagnosis in Parkinsonism—A Prospective Study. *Can J Neurol Sci* 1991;**18**:275–8.
3 Matsuo H, Takashima H, Kishikawa M, Kinoshita I, Mori M, Tsujihata M, Nagataki S. Pure akinesia—an atypical manifestation of progressive supranuclear palsy. *J Neurol Neurosurg Psychiatry* 1991;**54**:397–400.
4 Hughes AJ, Ben-Shlomo Y, Daniel SE, Lees AJ. What features improve the accuracy of clinical diagnosis in Parkinson's disease: A clinicopathologic study. *Neurology* 1992;**42**: 1142–6.
5 Hughes AJ, Daniel SE, Blankson S, Lees AJ. A Clinocopathological study of 100 cases of Parkinson's Disease. *Arch Neurol* 1993;**50**: 140–8.

BOOK REVIEWS

All titles reviewed here are available from the BMJ Bookshop, PO Box 295, London WC1H 9TE. Prices include postage in the United Kingdom and for members of the British Forces Overseas, but overseas customers should add £2 per item for postage and packing. Payment can be made by cheque in sterling drawn on a United Kingdom bank, or by credit card (Mastercard, Visa or American Express) stating card number, expiratory date, and your full name.

Bailliere's Clinical Neurology (International Practice and Research). Vol 1/ No 3. Unusual Dementias. Guest Editor MN ROSSOR. (Pp 689; Price: £27.50). 1992. London, Balliere Tindall. ISBN 0-7020-1631-4.

At the present time there is some fascinating progress in the definition and territorial demarcation of neurodegenerations causing dementia. There is space for splitters among clinicians and pathologists to identify new diseases such as corticobasal degeneration and the causes of frontal lobe degeneration, and primary progressive aphasia. In contrast, molecular genetics is tending to lump diverse phenotypes together in the prion disorders and familial Alzheimer's disease. Real progress in other areas, notably Pick's disease, is to some extent lacking. This condition is finding a more critical definition by the effect of erosion, because some examples of non-Pick body Pick's disease are undoubtedly other things, such as corticobasal degeneration. The remaining chapters in the book cover the neuropathology of unusual dementias, dementia and motor neurone disease and Lewy body dementia: so not, as you might have thought, small print causes of dementia as implied by the title, nor a fully comprehensive account of these disorders, but mostly areas of real progress and new knowledge.

The introduction provides a paragraph on the clinician's approach to a patient with dementia. This is a useful summary, to which collection, storage and analysis of genetic and pathological material could be added. Many of these diagnoses remain neuropathological ones, and their genetic implications are still uncertain. In addition, peculiar phenotypes of these neurodegenerations can mimic almost any other. Future developments should justify this encouragement to obtain a postmortem diagnosis, if not for the family, for future patients and families. Storage of DNA will provide a valuable resource for immediate use in new genetic studies. The chapter dedicated to an overview of neuropathology is valuable as these disorders are sufficiently uncommon to allow a critical mass of cases to be seen clinically and pathologically by one individual, and yet the pathology can be objectively compared by an experienced neuropathologist. Refreshingly, the pathology consists largely of updates, understandable for the newcomer, and extensive reviews are not included.

I found minor inaccuracies in the book, mostly reflecting very recent progress in knowledge. This speed of progress is encouraging, and until recently was not a feature of neurodegenerations. This book is well worth reading by those wanting an update or introduction to the subject; this is best done soon as the book will be superseded in due course.

WRG GIBB

Medico-Legal Assessment of Head Injury. By DAVID S BELL. (Pp 361; Price: $69.75). 1992. Illinois, Charles C Thomas. ISBN 0-398-05814-8.

It has been the experience of most neurologists on appointment to receive instructions from solicitors to examine and give an opinion by way of report on claimants undertaking civil action for injuries sustained in domestic, social or work situations.

Unfortunately most young neurologists when first approached, have had neither advice nor instruction on the preparation of reports and the implications of a medico-legal assessment. Nor have they been warned of the pitfalls which may upset them between writing a report and submitting to a cross examination in the high court. Often the prospect is disturbing. With the increasing civil litigation in the western world and a specific increase in claims of medical negligence, most of us will be invited to undertake assessments of claims. In some departments of neurology, a feature of the post graduate training is an introduction to this aspect of the neurologists work, but these are few.

For many years there has been a need for published advice. This is now provided by David Bell's book. *Medico-legal assessment of head injury*. He addresses the duties of the medical expert and the court's expectations. In a chapter almost certainly written for the lawyers, he describes the anatomy and pathophysiology of head injury and the major consequences of the brain damage. In his chapter on the syndromes of regional brain injury he finds space for a useful account of the effects of extension-flexion injury to the cervical spine and quotes some important figures and references to an acceptable estimation of prognosis. He assesses the literature on the prediction of post traumatic epilepsy both in the adult and child and considers the question of ictal violence and the attribution of serious crime to epileptic activity.