British Journal of Psychiatry (1993), **163**, 100–104

Point of View

'Pick's Disease' – 101 Years on
Still There, But in Need of Reform

BOB BALDWIN and HANS FÖRSTL

On 23 April 1892, Arnold Pick reported the case of AH, who died aged 71 years following a two-year history of progressive 'feeble-mindedness', outbursts of rage, fits and, in the later stages, severe aphasia (Pick, 1892). The post-mortem showed cerebral atrophy, particularly affecting the left temporal lobe. Pick went on to describe further cases of circumscribed atrophy affecting the temporal lobe (Pick, 1901, 1904), and parietal and frontal lobes (Pick, 1906). Although he believed the focal pathology represented a local emphasis of 'senile cortical atrophy', he wanted to show that a localised form of cerebral atrophy could nevertheless cause specific symptoms:

> ". . . thereby bringing neuropathology and psychiatry into closer union . . . so that the latter may be brought nearer to medical understanding."

What is the status of Pick's disease 101 years on?

Diagnostic uncertainties in Pick's disease – a brief history

Neither Pick, nor his collaborator Chiari, the pathologist, made any assertions about the nature of the underlying pathology of the disorder which bears Pick's name. This was left to Alzheimer, who drew attention to certain microscopic changes not found in 'senile dementia', or the disease which was to bear his name (Alzheimer, 1911; Förstl & Levy, 1991). These he outlined as 'ballooned cells', 'argentophilic globes' in neuronal cytoplasm, and 'spongy cortical wasting', in the absence of fibrillary tangles or plaques.

Gans (1922) proposed that Pick's disease was a 'heredo-degenerative abiotrophy' with a predilection for the phylogenetically younger parts of the brain. Although later disputed (Ferraro & Jervis, 1936), Gans's work encouraged the use of the term Pick's disease in Europe, although it was not recognised until the 1930s in the US (Kahn & Thompson, 1933).

Despite Pick's original case, the pathology has usually been associated more with the frontal than the temporal lobes, and rarely elsewhere (Kahn & Thompson, 1933; Malamud & Boyd, 1940; Graff-Radford *et al*, 1990).

There has never been agreement as to the minimum pathological criteria for Pick's disease: some accept circumscribed fronto-temporal atrophy on macroscopic examination (Onari & Spatz, 1926; Malamud & Boyd, 1940; Constantinidis *et al*, 1974); others require ballooning of cells in addition (Lindgren, 1952); Ferraro & Jervis (1936) described argentophilia and ballooning as 'quasipathognomonic' while other authors have argued for retaining a triad of progressive dementia, lobar atrophy and neuronal argentophilic inclusion (Pick) bodies (Kim *et al*, 1981; Verity & Wechsler, 1987). We feel that the latter definition is justified.

The pathological heterogeneity of fronto-temporal atrophy

The pathological heterogeneity of fronto-temporal atrophy was illustrated by the Lund group (Brun, 1987). Of 26 autopsied brains (from a series of 158) from people who had had evidence of frontal lobe dysfunction in life, all but one had pronounced frontal degeneration. Of these, four met strict criteria for Pick's disease, three Creutzfeldt–Jacob disease, two Alzheimer's disease, and 16 non-specific neuronal loss with spongy degeneration.

Subdivisions of Pick's disease have been attempted, for example when fronto-temporal degeneration occurs in association with subcortical change, either of atrophy (Munoz-Garcia & Ludwin, 1984) or of gliosis (Neumann, 1949; Neumann & Cohn, 1967). However, the typical Pick inclusion bodies were often absent in these reports, so classifying them as variants of Pick's disease is misleading (Verity & Wechsler, 1987).

Other reports of cortical atrophy with a fronto-temporal emphasis, some familial (Kim *et al*, 1981; Morris *et al*, 1984) and some not (Mehler *et al*, 1987), described pathology which was hard to classify.

Clearly, Pick's disease cannot be diagnosed on the basis of fronto-temporal degeneration alone; the pathology associated with this is too heterogeneous. Nor is the presence of swollen (ballooned) neurons, as described by Alzheimer, pathognomonic, as they occur in a variety of neurodegenerative conditions. Pick inclusion bodies, on the other hand, are rarely

found in other conditions (Clark *et al*, 1986). Only the latter then, in association with dementia and fronto-temporal degeneration, can be considered a hallmark of Pick's disease.

The focal dementias and lobar atrophy

These terms are meant to refer to opposite sides of the same coin: focal dementia being a circumscribed neuropsychological syndrome; lobar atrophy representing its presumed underlying structural correlate. However, the correlation is not exact since a circumscribed neuropsychological deficit suggesting cortical dysfunction may be associated with subcortical damage (Brun, 1987; Strub, 1989; Sandson *et al*, 1991). Nevertheless, presentations of dementia thought to reflect lobar atrophy have attracted much interest.

Although syndromes involving the parietal lobe (De Renzi, 1986) and the occipital lobe (Benson *et al*, 1988) have been described, it is those implicating the *frontal* and *temporal* lobes that have received most attention – the topographical areas usually associated with Pick's disease. Terms applied to the frontal lobe include: 'dementia of frontal-lobe type' (Neary *et al*, 1988); 'frontal lobe dementia of non-Alzheimer type' (Gustafson, 1987); 'frontal lobe dementia' (Jagust *et al*, 1989); 'dementia lacking distinct histologic features' (Knopman *et al*, 1990); and 'frontal lobe degeneration' (Miller *et al*, 1991). Terms applied to the temporal lobe include: 'primary progressive aphasia' (Mesulam, 1987); 'slowly progressive aphasia' (Poeck & Luzzatti 1988); 'semantic dementia' (Hodges *et al*, 1992); and 'progressive language disorder due to lobar atrophy' for cases (Snowden *et al*, 1992) presenting with linguistic disturbance.

The range of terms and the context in which they are used (sometimes referring to a clinical syndrome, sometimes to neuropathological findings) is bewildering. A number of questions arise, not least whether these presentations can be categorised as Pick's disease.

Frontal lobe syndromes

Independent reports from Lund (Brun, 1987; Gustafson, 1987) and Manchester (Neary *et al*, 1988) drew attention to a syndrome presenting with altered behaviour, ranging from disinhibition to extreme apathy, concrete, stereotyped speech, an unremarkable physical examination, normal electroencephalogram (EEG), anterior perfusion deficits on dynamic imaging, and neuropsychological deficits suggesting frontal lobe dysfunction, with relative sparing of memory and visuospatial performance. The psychiatric picture is variable: some patients had antecedent or concurrent major psychiatric symptoms such as depression, mania, or persecutory ideation (Gustafson, 1987; Neary *et al*, 1988). The usual age at onset was in the mid-50s, with an average duration to death of eight years. About 50% of patients had a first-degree relative with a similar disorder.

The clinical description is thus broadly similar to that in earlier case reports of Pick's disease. However, the Lund group found that only a fifth had Pick inclusion bodies, and most had non-specific neuronal loss and superficial cortical spongy degeneration without neuronal inclusions (Brun, 1987), which would not permit a diagnosis of Pick's disease, strictly defined.

Both the Lund and Manchester groups found that frontal lobe dementia (FLD) was the second most common cause, after Alzheimer's disease, of primary cerebral atrophy in the presenium. These were not epidemiological studies, and referral bias is likely. Nevertheless, the disorder seems more common than the literature suggests. How can this discrepancy be explained?

In the past, such cases may have been classified as Pick's disease, broadly defined. Alternatively, Poeck & Luzzatti (1988) have suggested that, earlier in the century, cases of lobar atrophy with circumscribed neuropsychological deficits, but without ballooned cells or neuronal argentophilia, were discussed in the wider context of Alzheimer's disease. Others argue that a tendency to overdiagnose Alzheimer's disease at the expense of lobar atrophy persists to this day (Mesulam, 1987), perhaps encouraged by an over-inclusive approach to the diagnosis of Alzheimer's disease in current operational diagnostic criteria (Neary, 1990). Another reason, which is evident from studying the historical literature, is that case reports usually provide detailed neuropathological information which is not matched by equivalent clinical detail, this reflecting the paucity of clinical investigational tools available at the time in relation to those of pathological enquiry. Finally, related to the latter point, earlier authors often assumed that Pick's disease was inherently difficult to distinguish in life from Alzheimer's disease (Nichols & Weigner, 1934; Ferraro & Jervis, 1936; Neumann & Cohn, 1967), although there were exceptions (Kahn & Thompson, 1933).

In fact, FLD is capable of accurate clinical detection and is clearly distinguishable from the pattern of dementia seen in Alzheimer's disease (Testa *et al*, 1988; Jagust *et al*, 1989; Knopman *et al*, 1990; Miller *et al*, 1991). However, recognition

of the syndrome of FLD does not guarantee knowledge of the underlying pathology; clearly, the pathology is heterogeneous. Furthermore, an association of FLD with motor neuron disease (MND) has been shown (Neary *et al*, 1990). The pathology of the FLD/MND complex may be non-specific, or may correspond to Pick's disease, strictly defined (Constantinidis, 1987; Sam *et al*, 1991).

In summary, FLD is a well delineated clinical syndrome often associated with lobar atrophy. On current evidence, Pick's disease, strictly defined, accounts for a minority of cases.

Temporal lobe syndromes

The first of the modern descriptions was that of Wechsler (1977), who reported a 67-year-old man with aphasia and a strikingly dilated appearance of the Sylvian fissure on a computerised tomography (CT) scan. Mesulam (1982) described further cases, including one in which a biopsy revealed no changes, either of Alzheimer's disease or Pick's disease, and proposed that these represented a new disorder. However, as with FLD, the pathology is heterogeneous. Wechsler's case, for example, proved to be Pick's disease, strictly defined (Wechsler *et al*, 1982) whereas other reports have shown non-specific pathology, similar to that often associated with FLD (Brun, 1987; Kirshner *et al*, 1987). But, unlike FLD, both the clinical *and* neuropathological manifestations are heterogeneous (Snowden *et al*, 1992).

An additional controversy surrounds whether such cases should be classified as dementia at all. 'Progressive aphasia' may merely be a prodrome of global dementia, or may be a discrete disorder caused by lobar atrophy. Both points of view have their advocates. A spectrum of disorder seems much the most likely, with isolated cases of aphasia such as those of Wechsler and Mesulam at one extreme, with the more usual cases of dementia presenting with an aphasic syndrome at the other (Kirshner *et al*, 1984).

In summary, the case reports suggest that there is considerable heterogeneity, both clinically and pathologically, with regard to language disorders and lobar atrophy, and that we are not yet in a position to organise the data into a coherent scheme. A clinical syndrome may reflect a variety of underlying pathologies, and a particular pathological change may manifest clinically in a variety of syndromes. Once again Pick's disease, strictly defined, accounts for a proportion of cases.

Comments and suggestions

Where does this leave Pick's disease? In one sense all the recent cases which reflect a focally pronounced atrophic process could, in historical terms, be regarded as Pick's disease for that is all Pick originally drew attention to. However, it seems wise to retain the pathological distinction that Alzheimer highlighted. Thus Pick's disease is one form of lobar atrophy and should be defined according to the triad of focal neuropsychological deficits in the context of dementia, focally accentuated brain atrophy, and typical argentophilic inclusions.

An important contribution of the Lund and Manchester groups has been to dispel the notion that dementia represents a non-specific or 'global' breakdown of higher cortical function. Rather, by drawing together data from clinical, behavioural, neuropsychological, and imaging sources, they have prompted the successful delineation of distinct neuropsychological syndromes. As Neary comments (1990), such an approach is superior to "submerging differences (in clinical syndromes) under a weight of numbers generated by standard clinical psychological test batteries".

Before further clinico-pathological designations can be accepted, a minimum data set for future research should be established. We suggest three axes.

Firstly, a *clinical* axis should record demographic data, behavioural and personality change, psychopathology, family history, and neuropsychological deficits using neuropsychological analytical techniques, for which the method has been described by Neary *et al* (1988). Admittedly, 'personality change' has no agreed meaning, and descriptions often confound changes in temperament with those of behaviour and psychopathology; but distinguishing between these would be a useful first step. With regard to psychopathology, psychiatrists can play a helpful part, drawing on recent efforts to record psychopathology and behavioural change in brain disease in a systematic fashion (Fairburn & Hope, 1988; Devanand *et al*, 1992).

Secondly, a *gross anatomical* axis would draw upon neuroimaging (CT, magnetic resonance imaging (MRI), single-photon emission computerised tomography (SPECT), or positron emission tomography), and gross pathology.

Thirdly, a *histopathological* axis would document the nature, degree, and distribution of microscopic changes, cell loss, 'sponginess', inclusion bodies, plaques and tangles, and immunocytochemical change.

Operational criteria and check-lists may help detect the various clinical syndromes associated with non-Alzheimer's disease pathologies and are

currently being explored for Binswanger's disease (Bennett *et al*, 1990), and for Lewy body disease (McKeith *et al*, 1992). No criteria exist for 'frontal lobe dementia' or 'progressive aphasia', although they could be developed from the three-dimensional model proposed. For example, in *frontal lobe dementia*, currently the most convincing of the syndromes, criteria might include the following.

(1) *Clinical axis*:

(a) progressive breakdown in social conduct and/or
(b) insidious change in personality
(c) circumscribed frontal lobe dysfunction on neuropsychological assessment
(d) normal neurological examination or primitive reflexes only.

(2) *Anatomical axis*:

(a) anterior hemisphere abnormalities on SPECT or
(b) focally reduced regional cerebral blood flow in frontal hemispheres on xenon inhalation scanning.

(3) *Supportive* (but not essential) *evidence*:

(a) age at onset in mid-50s
(b) family history of similar disorder in a first-degree relative
(c) normal EEG
(d) selective frontal or fronto-temporal atrophy on CT or MRI
(e) atypical presentation of late-onset depression, mania, or psychosis.

Exclusion criteria might include:

(a) neuropsychological assessment supportive of posterior hemispherical deficits (especially visuospatial dysfunction)
(b) posterior or 'patchy' hemisphere abnormalities on dynamic imaging
(c) widespread non-specific abnormalities or discrete focal abnormalities on EEG
(d) lateralising neurological signs.

The *pathological axis* would be invoked for the diagnosis of *lobar atrophy with FLD*, thus:

(a) frontal or fronto-temporal atrophy on gross examination of the brain
(b) significant loss of large frontal cortical neurons
(c) either:
  (i) ballooned cells and argyrophilic inclusion bodies (FLD, Pick type) or
  (ii) superficial frontal cortical microvacuolar degeneration (FLD, non-specific type)
(d) absence of neurofibrillary tangles and senile plaques.

The DSM-III-R criteria for dementia (American Psychiatric Association, 1987) are not included in this scheme because of its criterion (A): definite evidence of memory impairment - memory is variably affected in FLD (Neary *et al*, 1988; Miller *et al*, 1991). An important question is how many patients with FLD would *not* meet DSM-III-R criteria for dementia.

The three-dimensional model proposed seems the best approach for studying the lobar atrophies which Pick so helpfully introduced us to. It encourages a logical framework for data collection and thus the establishment of convincing clusters of cases in the future.

References

ALZHEIMER, A. (1911) Über eigenartige Krankheitsfälle des späteren Alters. *Zeitschrift für die Gesamte Neurologie und Psychiatrie*, **4**, 356–385.

AMERICAN PSYCHIATRIC ASSOCIATION (1987) *Diagnostic and Statistical Manual of Mental Disorders* (3rd edn, revised) (DSM-III-R). Washington, DC: APA.

BENSON, D. F., DAVIS, J. R. & SYNDER, B. D. (1988) Posterior cortical atrophy. *Archives of Neurology*, **45**, 789–793.

BENNETT, D. A., WILSON, R. A., GILLEY, D. W., *et al* (1990) Clinical diagnosis of Binswanger's disease. *Journal of Neurology, Neurosurgery and Psychiatry*, **53**, 961–965.

BRUN, A. (1987) Frontal lobe degeneration of non-Alzheimer type. I Neuropathology. *Archives of Gerontology and Geriatrics*, **6**, 193–208.

CLARK, A. W., MANZ, H. J., WHITE, C. L, *et al* (1986) Cortical degeneration with swollen chromatolytic neurons: its relationship to Pick's disease. *Journal of Neuropathology and Experimental Neurology*, **45**, 268–284.

CONSTANTINIDIS, J. (1987) Syndrome familial: association de maladie de Pick et sclerose laterale amyotrophiqe. *L'Encephale*, **13**, 285–293.

———, RICHARD, J. & TISSOT, R. (1974) Pick's disease: histological and clinical correlations. *European Neurology*, **11**, 208–217.

DE RENZI, E. (1986) Slowly progressive visual agnosia or apraxia without dementia. *Cortex*, **22**, 171–180.

DEVANAND, D. P., MILLER, L., RICHARDS, M., *et al* (1992) The Columbia Scale for psychopathology in Alzheimer's disease. *Archives of Neurology*, **49**, 371–376.

FAIRBURN, C. G. & HOPE, R. A. (1988) Changes in behaviour in dementia: a neglected research area. *British Journal of Psychiatry*, **152**, 406–407.

FERRARO, A. & JERVIS, G. A. (1936) Pick's disease: clinicopathological study with report of two cases. *Archives Neurology and Psychiatry*, **36**, 739–767.

FÖRSTL, H. & LEVY, R. (1991) Classic text no. 5. A. Alzheimer: on certain peculiar diseases of old age. *History of Psychiatry*, **2**, 71–101.

GANS, A. (1922) Betrachtungen über Art und Ausbreitung des krankhaften Prozesses in einem Fall von Pickscher Atrophie des Stirnhirns. *Zeitschrift für die Gesamte Neurologie und Psychiatrie*, **80**, 10–28.

GRAFF-RADFORD, N. R., DAMASIO, A. R., HYMAN, B. T., *et al* (1990) Progressive aphasia in a patient with Pick's disease. *Neurology*, **40**, 620–626.

GUSTAFSON, L. (1987) Frontal lobe degeneration of non-Alzheimer type II. Clinical picture and differential diagnosis. *Archives of Gerontology and Geriatrics*, **6**, 209–223.

HODGES, J. R., PATTERSON, K., OXBURY, S., *et al* (1992) Semantic dementia: progressive fluent aphasia with temporal lobe atrophy. *Brain*, **115**, 1786–1806.

JAGUST, W. J., REED, B. R., SEAB, P. J., *et al* (1989) Clinical-physiological correlates of Alzheimer's disease and frontal lobe dementia. *American Journal of Physiological Imaging*, **4**, 89–96.

KAHN, E. & THOMPSON, L. J. (1933) Concerning Pick's disease. *American Journal of Psychiatry*, **90**, 937–946.

KIM, R. C., COLLINS, G. H., PARISI, J. E., *et al* (1981) Familial dementia of adult onset with pathological findings of a 'non-specific' nature. *Brain*, **104**, 61–78.

KIRSHNER, H. S., WEBB, W. G., KELLY, M. P., *et al* (1984) Language disturbance: an initial symptom of cortical degeneration and dementia. *Archives of Neurology*, **41**, 491–496.

———, TANRIDAG, O., THURMAN, L., *et al* (1987) Progressive aphasia without dementia: two cases with focal spongiform degeneration. *Annals of Neurology*, **22**, 527–532.

KNOPMAN, D. S., MASTRI, A. R., FREY, W. H., *et al* (1990) Dementia lacking distinct histologic features: a common cause of non-Alzheimer degenerative dementia. *Neurology*, **40**, 251–256.

LINDGREN, A. K. H. (1952) The patho-anatomical classification of Morbus Alzheimer and Morbus Pick. *Acta Psychiatrica et Neurologica Scandinavica* (suppl. 81), 118–152.

MALAMUD, N. & BOYD, D. A. (1940) Pick's disease with atrophy of the temporal lobes: a clinicopathological study. *Archives of Neurology and Psychiatry*, **43**, 210–222.

MCKEITH, I. G., PERRY, R. H., FAIRBURN, A. F., *et al* (1992) Operational criteria for senile dementia of Lewy body type (SDLT). *Psychological Medicine*, **22**, 911–922.

MEHLER, M. F., HOROUPIAN, D. S., DAVIES, P., *et al* (1987) Reduced somatostatin-like immunoreactivity in cerebral cortex in nonfamilial dysphasic dementia. *Neurology*, **37**, 1448–1453.

MESULAM, M-M. (1982) Slowly progressive aphasia without generalised dementia. *Annals of Neurology*, **11**, 592–598.

——— (1987) Primary progressive aphasia: differentiation from Alzheimer's disease. *Annals of Neurology*, **22**, 533–534.

MILLER, B. L., CUMMINGS, J. L., VILLANUEVA-MEYER, J., *et al* (1991) Frontal lobe degeneration: clinical, neuropsychological and SPECT characteristictics. *Neurology*, **41**, 1374–1382.

MORRIS, J. C., COLE, M., BANKER, B. Q., *et al* (1984) Hereditary dysphasic dementia and the Pick – Alzheimer spectrum. *Annals of Neurology*, **16**, 455–466.

MUNOZ-GARCIA, D. & LUDWIN, S. K. (1984) Classic and generalised variants of Pick's disease: a clinicopathological, ultrastructural and immunocytochemical comparative study. *Annals of Neurology*, **16**, 467–480.

NEARY, D. (1990) Non-Alzheimer's disease forms of cerebral atrophy. *Journal of Neurology, Neurosurgery and Psychiatry*, **53**, 929–931.

———, SNOWDEN, J. S., NORTHEN, B., *et al* (1988) Dementia of frontal-lobe type. *Journal of Neurology, Neurosurgery and Psychiatry*, **51**, 353–361.

———, ———, MANN, D. M. A., *et al* (1990) Frontal lobe dementia and motor neuron disease. *Journal of Neurology, Neurosurgery and Psychiatry*, **53**, 23–32.

NEUMANN, M. A. (1949) Pick's disease. *Journal of Neuropathology and Experimental Neurology*, **8**, 255–282.

——— & COHN, R. (1967) Progressive subcortical gliosis, a rare form of presenile dementia. *Brain*, **90**, 405–418.

NICHOLS, I. C. & WEIGNER, W. C. (1934) Pick's disease: a review of the literature and presentation of a case. *Archives of Neurology and Psychiatry*, **32**, 241–244.

ONARI, K. & SPATZ, H. (1926) Anatomische Beiträge zur Lehre von Pickscnen umschriebenen Grosshirnrinden-Atrophie ("Picksche Krankheit"). *Zeitschrift fur die Gesamte Neurology und Psychiatrie*, **101**, 470–511.

PICK, A. (1892) Ueber die Beziehungen der senilen Hirnatrophie zur Aphasie. *Pragur Medicinische Wochenschrift*, **17**, 165–167.

——— (1901) Senile Hirnatrophie als Grundlage von Herderscheinungen. *Wiener Klinische Wochenschrift*, **14**, 403–404.

——— (1904) Zur Symptomatologie der linksseitigen Schlafenlappenatrophie. *Monatsschrift fur Psychiatrie und Neurologie*, **16**, 378–388.

——— (1906) Uber einen weiteren Symptomenkomplex im Rahmen der Dementia senilis, bedingt durch umschriebene, starkere Hirnatrophie (gemischte Apraxie). *Monatsschrift fur Psychiatrie und Neurologie*, **19**, 97–108.

POECK, K. & LUZZATTI, C. (1988) Slowly progressive aphasia in three patients: the problem of accompanying neuropsychological deficit. *Brain*, **111**, 151–168.

SAM, M., GUTMANN, L., SCHOCHET, S. S., *et al* (1991) Pick's disease: a case resembling amyotrophic lateral sclerosis. *Neurology*, **41**, 1831–1833.

SANDSON, T. A., DAFFNER, K. R., CARVALHO, P. A., *et al* (1991) Frontal lobe dysfunction following infarction of the left-sided medial thalamus. *Archives of Neurology*, **48**, 1300–1303.

SNOWDEN, J. S., NEARY, D., MANN, D. M. A., *et al* (1992) Progressive language disorder due to lobar atrophy. *Annals of Neurology*, **31**, 174–183.

STRUB, R. L. (1989) Frontal lobe syndrome in a patient with bilateral globus pallidus lesions. *Archives of Neurology*, **46**, 1024–1027.

TESTA, H. J., SNOWDEN, J. S., NEARY, D., *et al* (1988) The use of [99mTc]-HM-PAO in the diagnosis of primary degenerative dementia. *Journal of Cerebral Blood Flow and Metabolism*, **8**, S123–S126.

VERITY, M. A. & WECHSLER, A. F. (1987) Progressive subcortical gliosis of Neumann: a clinicopathological study of two cases with review. *Archives of Gerontology and Geriatrics*, **6**, 245–261.

WECHSLER, A. F. (1977) Presenile dementia presenting as aphasia. *Journal of Neurology, Neurosurgery and Psychiatry*, **40**, 303–305.

———, VERITY, M. A., ROSENSCHEIN, S., *et al* (1982) Pick's disease: a clinical, computed tomographic, and histologic study with Golgi impregnation observations. *Archives of Neurology*, **39**, 287–290.

*Bob Baldwin, BSc, MRCP, MRCPsych, *Consultant Psychiatrist, York House, Manchester Royal Infirmary, Oxford Road, Manchester M13 9BX*; Hans Förstl, MD, PhD, *Psychiatrische Klinik, Zentralinstitut fur Seelische, Gesundheit, 6800 Mannheim, 1–J5, Postfach 122120, Germany*

*Correspondence