by their schizophrenic symptoms. However, except for frontal or temporal hypoperfusion on SPECT, they found no characteristic structural imaging abnormalities and, in accordance with Harrison,² concluded that dementia in elderly schizophrenic patients shows no evidence of any known neurodegenerative disorder and, therefore, requires novel neuropathological explanation. Several recent postmortem studies on such patients showed no excess of Alzheimer's disease or other organic dementing syndromes. This is in line with a personal retrospective study of 99 consecutive necropsy cases of schizophrenic patients aged over 55 (mean age 69.5 (SD 8.25) years) with mean duration of illness of 35.15 (SD 10.1) years, 56% with clinical signs of moderate to severe dementia, where we found a total incidence of definite and probable Alzheimer's disease (using CERAD criteria and Braak staging) of 7.1%, or of 8.7% for those over the age of 65 years. In addition, there was one case each with multi-infarct encephalopathy and Parkinson's disease pathology, and 11 brains showed a lacunary state in the basal ganglia.³ Brain weight in demented elderly schizophrenic patients was significantly lower (mean 1119.5 (SD 106.1) g) than in non-demented ones (mean 1216.3 (SD 36.2) g; $p < 0.001$). These data are in line with previous studies showing that cognitive decline in chronic schizophrenic patients seems best related to loss in brain weight, decrease in brain length, and increased ventricular size.^{4,5} However, demented patients in our cohort were significantly older (mean age 73.36 (SD 6.85) v 64.02 (SD 6.54) years; $p < 0.001$), and had a significantly longer duration of illness (mean 41.1 v 28.9 years; $p < 0.001$), suggesting a progressive cognitive decline with both age and duration of the disorder. This, at least in part, could be explained by recent studies demonstrating reduction of synaptophysin (a synaptic plasma membrane protein) immunoreactivity in the prefrontal cortex⁶ and significant negative correlations between age and concentrations of synaptic plasma membrane proteins and syntax in mRNA in the temporal cortex of schizophrenic patients⁷ reflecting abnormalities in synaptic connectivity; this may cause functional impairment of the limbic circuitry that is thought to be central in the integration of behaviour and cognition.³ These findings are consistent with the hypothesis that changes in synaptic function in both prefrontal or limbic circuits in patients with chronic schizophrenia may contribute to the pathophysiology including cognitive dysfunctions in this disorder.^{3,7,8} However, future prospective clinicopathological and molecular genetic studies using validated methods are necessary to elucidate the bases of cognitive impairment and dementia in chronic schizophrenic patients.

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- De Vries PJ, Honer WG, Kemp PM, *et al.* Dementia as a complication of schizophrenia. *J Neurol Neurosurg Psychiatry* 2001;70:588-96.
- Harrison PJ. The neuropathology of schizophrenia. A critical review of the data and their interpretation. *Brain* 1999;122:593-624.
- Jellinger KA, Gabriel E. No increased incidence of Alzheimer's disease in elderly schizophrenics. *Acta Neuropathol* 1999;97:165-9.
- Bruton CJ, Crow TJ, Frith CD, *et al.* Schizophrenia and the brain: a prospective cliniconeuropathological study. *Psychol Med* 1990;20:285-304.

- Johnstone EC, Bruton CJ, Crow TJ, *et al.* Clinical correlates of postmortem brain changes in schizophrenia: decreased brain weight and length correlate with indices of early impairment. *J Neurol Neurosurg Psychiatry* 1994;57:474-9.
- Glantz LA, Lewis DA. Reduction of synaptophysin immunoreactivity in the prefrontal cortex of subjects with schizophrenia. Regional and diagnostic specificity. *Arch Gen Psychiatry* 1997;54:943-52.
- Sokolov BP, Tcherepanov AA, Haroutunian V, *et al.* Levels of mRNAs encoding synaptic vesicle and synaptic plasma membrane proteins in the temporal cortex of elderly schizophrenic patients. *Biol Psychiatry* 2000;48:184-96.
- Arnold SE. Cognition and neuropathology in schizophrenia. *Acta Psychiatr Scand Suppl* 1999;395:41-50.

The calcified intracorporeal vacuole: an aid to the pathological diagnosis of solitary cerebral cysticercus granulomas

I read with interest the paper by Chacko *et al* reporting the significance of calcified intracorporeal vacuole: an aid to the pathological diagnosis of solitary cysticercus granulomas.¹ I appreciate the efforts of the authors for once again proving that the aetiology for single small enhancing CT lesions is neurocysticercosis. The investigators are right in stating that in 26 patients there was no evidence of tuberculosis or fungal pathology. The presence of histiocytes and eosinophils favour a parasitic aetiology. It would be of interest to know the radiological correlation of oval calcified bodies that were detected in six patients. Did they have type A or type B lesions? The authors, in their earlier study, had concluded that neither the duration of seizures nor the type of lesion on CT was predictive of the presence of the parasite in the granuloma.² I am keen to know the seizure control of these patients with oval calcified bodies, as the authors have stated that a small proportion of study patients had intractable epilepsy. Single small enhancing CT lesions are reported to be the cause of the seizure in 26% of Indian patients who present with partial seizures. Cysticercus granulomas and tuberculomas are the two common differential diagnoses that are considered in a patient with seizures and solitary enhancing lesion on CT.³ The authors have demonstrated very well the aetiology, diagnosis, and management of single small enhancing CT lesions in their previous studies.³⁻⁴ This study adds one more feather to their cap in confirming the aetiology of such lesions. It is heartening to see that general practitioners, physicians, and even neurologists in this part of the country treat these patients with antituberculous drugs. Educating general practitioners and general physicians about the nature and aetiology of these lesions will definitely improve the management of patients.

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- Chacko G, Rajshsekhar V, Chandy MJ, *et al.* The calcified intracorporeal vacuole: an aid to the pathological diagnosis of solitary cerebral cysticercus granulomas. *J Neurol Neurosurg Psychiatry* 2000;69:525-7.
- Rajshsekhar V, Chacko G, Haran RP, *et al.* Clinicoradiological and pathological correlations in patients with solitary cysticercus granuloma and epilepsy: Focus on presence of the parasite and edema formation. *J Neurol Neurosurg Psychiatry* 1995;59:284-6.
- Rajshsekhar V, Chandy MJ. Validation of diagnostic criteria for solitary cerebral cysticercus

granuloma in patients presenting with seizures. *Acta Neurol Scand* 1997;96:76-81.

- Rajshsekhar V. Etiology and management of single small CT lesions in patients with seizures: understanding a controversy. *Acta Neurol Scand* 1991;84:465-70.

Chacko replies:

All six patients with oval calcified bodies had type A lesions, of which two were ring lesions and four were discs.

Follow up of 6 months to 3 years is available for four of these patients and they are all seizure free, with three of them still on antiepileptic medication.

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Change in oxcarbazepine (Trileptal®) formulation is associated with more side effects and higher blood concentrations

In an *editorial*, Marson and Chadwick review some of the evidence for the effectiveness and tolerability of new drug treatments for epilepsy.¹ They discuss the role of randomised clinical trials for providing data that satisfy the requirements of the licensing bodies but that do not reflect day to day clinical practice. With oxcarbazepine (Trileptal®) we recently experienced another complicating factor, a change in formulation, which may influence interpretation of results of clinical trials.

Oxcarbazepine had recently been licensed in the United Kingdom and the United States but was already registered in The Netherlands in 1991. In our epilepsy centre we have had extensive clinical experience with oxcarbazepine since 1986.² In 2001 we noticed new symptoms such as diplopia, dizziness, dysarthria, and ataxia in patients on a stable drug regimen, including oxcarbazepine. These symptoms had a fluctuating course during the day. In the autumn of 2000 the manufacturer Novartis substituted the formulation of oxcarbazepine in The Netherlands for the formulation which had been licensed in the United Kingdom and the United States. Taking into consideration this change in formulation we hypothesise that these new symptoms could be side effects of oxcarbazepine, probably caused by higher blood concentrations of the active compound in relation to this new formulation.

Oxcarbazepine is a 10-keto analogue of carbamazepine (CBZ) with similar anticonvulsant efficacy, but with a different pharmacokinetic profile and possibly a better tolerability.^{3,4} It is rapidly reduced to a 10-monohydroxy derivative (MHD) with an elimination half life of 1.3-3.8 hours. Oxcarbazepine acts as a prodrug of MHD, the clinically relevant metabolite of oxcarbazepine; MHD is cleared with a half life of 8.8-24.5 hours.

We evaluated steady state oxcarbazepine and MHD serum concentrations obtained before and after change of the oxcarbazepine formulation from four patients with presumed side effects. The mean (range) MHD concentrations increased from 27.0 (25.4-32.7) $\mu\text{g/ml}$ to 38.4 (37.5-39.6) $\mu\text{g/ml}$. Routinely, we do not measure oxcarbazepine concentrations, because they are usually very low or not detectable. As we still had all serum samples from these four