Letters

carinic action, is a commonly prescribed eyedrop for middle aged and elderly patients.

In dementia of the Alzheimer type, deterioration of intellectual function and behavioural changes have been linked to the neurochemical deficiency and morphological lesions involving the cholinergic system. Diminished activity of choline acetyltransferase is believed to result in acetylcholine deficiency while the loss of cholinergic neurons in the nucleus basalis of Meynert is thought to decrease cholinergic input into different cortical and subcortical regions.⁷⁻²¹ If we relate these hypotheses to our cases, we can speculate that a chronic low level of muscarinic receptor stimulation occurs in dementia of the Alzheimer type. In such a situation, pilocarpine could induce muscarinic receptor hyperactivity or supersensitivity in some patients with dementia of the Alzheimer type and give rise to mental status changes. This proposed mechanism will have to be verified by future appropriately designed clinical and animal studies.

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Matters arising

Age-specific incidence rates for motor neuron disease

Sir: The recent paper by Li, Swash and Alberman¹ states that they are not aware of previous estimates of age-specific rates in motor neuron disease. We originally reported in 1980^{2,3} that age-specific incidence rates for motor neuron disease rise with increasing age. We presently have a paper in press which updates our previous study and confirms this finding.⁴ Although the authors report theirs is the first age-specific incidence figure in motor neuron disease, they have been reported prior to our 1980 paper.⁵

The use of hospital admissions as the source of cases implies that the diagnosis of motor neuron disease will always be made and recorded. This may be true for younger patients; however, elderly patients, particularly those in nursing homes, are less likely to be hospitalised and are more likely to have multiple disease involvements, such as cardiovascular, and pulmonary, which may obscure the diagnosis of motor neuron disease. A greater proportion of overlooked diagnoses of motor neuron disease is likely among elderly patients.

In our experience as well as that of Li et al, the rise in incidence was not apparent in women aged over 80 years. The numbers are small and the possibility exists that motor neuron disease is more commonly overlooked in elderly women. Thus, the significance of this finding is not now obvious and deserves further study.

We agree that the findings of Li et al are important and support our observation that the age-specific incidence rates of motor neuron disease increase with advancing age.

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Li *et al* reply

We were interested to see Drs Kurland and Mulder's comments on age specific incidence rates in motor neuron disease, and note that our findings are in agreement with theirs. Clearly, this implies a common causative factor operating in these widely separated environments and it would be interesting to compare cohort data for these different populations. We agree with Kurland and Mulder that the diagnosis of motor neuron disease is probably often overlooked in elderly patients, thus resulting in an under-estimate of incidence rates in older populations. This is a common limitation of epidemiological data taken from retrospective surveys of case-notes, but in our work we have tried to exclude this factor as far as possible by utilising data from two separate Health Authorities, both with relatively well-organised neurological services. Similar trends were found in the two sets of data.

Cryptococcal meningitis and cerebral toxoplasmosis in a patient with acquired immunodeficiency syndrome.

Sir: We were very interested in the *short report* of Bahls and Sumi¹ about the documented simultaneous infection of the central nervous system with *Toxoplasma gondii* and *Cryptococcus neoformans* in an AIDS patient. We have also observed such an association on the same underlying disease.

A 26 year old homosexual man was admitted with fever, cough and meningitis. Transbronchial biopsy, blood and CSF cultures showed *Cryptococcus neoformans*. CD4/CD8 lymphocytes ratio was under 0.2. Serum sample was LAV/HTLV III antibody positive by two different techniques (ELISA, Western blott). Despite amphotericin B and 5-fluorocytosine in combination, seizures

and confusion with right hemiparesis appeared. The cranial computed tomographic scan revealed three ring-enhancing mass lesions. Echoguided neurosurgical puncture of the left parietal mass lesion allowed brain biopsy which showed *Cryptococcus neoformans* (PAS stain). The patient died 4 weeks later. Toxoplasmosis serological and CSF tests were non-diagnostic. Brain culture from mice after intraperitoneal inoculation were positive for *Toxoplasma gondii*.

This new case emphasises the possibility of an infectious agent hiding another. Brain biopsy is indicated in such patients because of the lack of correlation between clinical presentation, CT scan appearance of mass lesions in the central nervous system, isolation of an infectious agent anywhere and the specific diagnosis of mass lesions.² In this case, however, despite a brain biopsy in an affected area, it was not very useful, because routine haematoxylin and eosin stain was negative for *T. gondii*, and culture from laboratory animal was necessarily slow. The immunohistological staining with peroxidase anti-peroxidase stain method-fast and specific diagnosis procedure for *T. gondii*³ must be recommended, particularly in immunodeficient patients needing a rapid and specific diagnosis, critical to the directing of appropriate and urgent therapy for a potentially curable condition.

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Cryptococcal meningitis and cerebral toxoplasmosis in AIDS: another case report.

Sir: We read with interest the *Short report* of Bahls and Sumi¹ on the association of cryptococcal meningitis and cerebral toxoplasmosis in a patient with Acquired Immune Deficiency Syndrome (AIDS) and we would like to document a further case.

A 34 year old homosexual male was admitted with a 4 months history of slight fever, cough with occasional haemoptysis and weight loss. Three months later he developed a headache. One day before admission the patient became less alert. Neurological examination showed a comatose patient with nuchal rigidity and left facial paralysis. The diagnosis of AIDS and cryptococcal meningitis was made by clinical and laboratory evaluation and was treated with amphotericin B and 5-fluorocytosine. After 2 months he developed progressive hemiparesis and CT scan showed multiple, ring-enhancing, low-density lesions. Slightly increased serologic titres against *Toxoplasma gondii* were detected and therapy with pyrimethamine and sulfonamides was consequently started. In the next week the patient quickly improved, the CT lesions disappeared and he soon became asymptomatic. Unfortunately, after one and a half months, therapy was discontinued because severe pancytopenia had developed, and he progressively experienced again right limb weakness and aphasia. Later, he died of pneumonitis from *Pneumocystis carinii*. Pathological findings in the central nervous system revealed cryptococcal meningo-encephalitis, multiple necrotising abscesses for *Toxoplasma gondii* and medulla and spinal cord infection by cytomegalovirus.

In our opinion, taking into account that cryptococcus and toxoplasma are both common causes of infection in patients with AIDS,²⁻⁵ their association may frequently occur. Consequently, we suggest the immediate onset of therapy with pyrimethamine and sulfadiazines if the diagnosis of toxoplasmosis is suspected⁵ in patients with cryptococcal meningitis and AIDS. Brain biopsy should be reserved for cases with poor response to treatment because its use is limited by its potential morbidity and the presence of false-negative results.

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