over the age of 65 are lacking. Nevertheless, as syphilis may remain latent for over 30 years, syphilis serology should be checked at any age and positive results further investigated by examination of the cerebrospinal fluid (CSF) (Weatherall *et al*, 1985). Negative CSF serology excludes active neurosyphilis, whereas a positive result should lead to treatment and follow-up CSF examination (Adams & Victor, 1985).

Until a study in this age group finds evidence to the contrary, we believe that syphilis screening remains an essential investigation.

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References

ADAMS, R. D. & VICTOR, M. (1985) *Principles of Neurology* (3rd edn). New York: McGraw-Hill Book Company.

WEATHERALL, D. J., LEDINGHAM, J. G. G. & WARRELL, D. A. (1985) *Oxford Textbook of Medicine*. Oxford: Oxford University Press.

Lipopigment in the CNS

SIR: Dowson (*Journal*, July 1989, **155**, 1–11) highlights the uncertainty surrounding the origin and significance of lipopigment in the central nervous system (CNS). Most authors would share the view that lipofuscin is not itself a causal factor in ageing, but rather a by-product, indicating that destructive oxidative processes have taken place (Sohal & Wolfe, 1986). Lipopigment itself may originate from several possible sources, but there is strong evidence to suggest that free-radical damage is an important factor. Damage to biological molecules produces malonaldehyde and other substances, inducing polymerisation of amine-containing molecules. The conjugated Schiff bases thus formed have similar emission spectra to those of chloroform extracts of purified lipofuscin, suggesting a common biochemical link (Tappel, 1975).

Dowson also suggests that chronic neuroleptic administration may protect against ageing, extrapolating from the effects of chlorpromazine on intracellular pigment in rat neurons. It has been suggested that phenothiazines, being heterocyclic compounds incorporating ring nitrogen and sulphur atoms, may act as free-radical scavengers. However, the 'cross-over effect' has also been noted, for instance with promethazine, which may be protective towards membranes at one concentration but deleterious at another (Slater, 1972). There is, indeed, growing evidence to suggest that neuroleptics may themselves induce free-radical damage in the CNS. This has been proposed as one mechanism by which tardive dyskinesia may be produced. Metabolites of phenothiazines, particularly the ortho-dihydroxylated derivatives, have been shown *in vitro* to generate toxic free-radical species (Heikkila & Cohen, 1975). Pall *et al* (1987) demonstrated increased products of free-radical damage in the cerebrospinal fluid of patients taking phenothiazines. In a trial of the antioxidant alpha-tocopherol, a marked reduction in the symptoms of tardive dyskinesia was described (Lohr *et al*, 1988).

The situation is clearly highly complex, as psychotropic drugs and their metabolites may exhibit different properties at various sites. Despite the difficulties of studying esoteric biochemical reactions in the CNS, the results may have considerable therapeutic implications. This line of inquiry therefore merits further research.

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References

HEIKKILA, R. E. & COHEN, G. (1975) Reactivity of various phenothiazine derivatives with oxygen and oxygen radicals. *Biochemical Pharmacology*, **24**, 363–368.

LOHR, J. B., CADET, J. L., LOHR, M. A., *et al* (1988) Vitamin E in the treatment of tardive dyskinesia: the possible involvement of free radical mechanisms. *Schizophrenia Bulletin*, **14**, 291–296.

PALL, H. S., WILLIAMS, A. C., BLAKE, D. R., *et al* (1987) Evidence of enhanced lipid peroxidation in the cerebrospinal fluid of patients taking phenothiazines. *Lancet*, *ii*, 596–599.

SLATER, T. F. (1972) Free radical scavengers. In *Free Radical Mechanisms in Tissue Injury*, pp. 48–61. London: Pion Limited.

SOHAL, R. S. & WOLFE, L. S. (1986) Lipofuscin: characteristics and significance. *Progress in Brain Research*, **70**, 171–183.

TAPPEL, A. L. (1975) Lipid peroxidation and fluorescent molecular damage to membranes. In *Pathobiology of Cell Membranes*, Vol. 1 (eds B. F. Trump & A. V. Arstila), pp. 145–170. New York: Academic Press.

Tardive dystonia

SIR: Cooper *et al* (*Journal*, July 1989, **155**, 113–115) reported tardive dystonia in a schizophrenic patient in his 20s which was worsened by anticholinergic drug treatment. This case is atypical. In a report by Kang *et al* (1986), 57% of patients with tardive dystonia were improved with anticholinergic drugs. Of the other patients with tardive dystonia reported in

the literature, there is no mention of exacerbation by anticholinergic agents.

The phenomenon of "delayed-onset dystonia" has been reported by Burke *et al* (1980): eight cases of persistent dystonia appeared years after non-progressive cerebral insults, including perinatal anoxia, trauma, and cerebral infarction. There was no history of neuroleptic treatment. It is interesting to note that the patient reported by Cooper *et al* had a history of prematurity, two perinatal anoxic episodes, epilepsy, and a focus of left temporal spike waves on the EEG.

The brain damage may have acted as a predisposing factor for the development of tardive dystonia in this patient. Another possibility is the occurrence of delayed-onset dystonia in a patient on neuroleptic treatment. One of the diagnostic criteria for tardive dystonia is exclusion of secondary causes of dystonia (Burke *et al*, 1982). Delayed-onset dystonia is one which may easily have been overlooked.

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References

BURKE, R. E., FAHN, S. & GOLD, A. P. (1980) Delayed-onset dystonia in patient with "static" encephalopathy. *Journal of Neurology, Neurosurgery and Psychiatry*, **43**, 789–797.

——, ——, JANKOVIC, J., *et al* (1982) Tardive dystonia: late-onset and persistent dystonia caused by antipsychotic drugs. *Neurology*, **32**, 1335–1346.

KANG, V. J., BURKE, R. E. & FAHN, S. (1986) Natural history and treatment of tardive dystonia. *Neurology*, **36** (suppl. 1), 121.

Nicotine and dementia

SIR: The results reported by Sahakian *et al* (*Journal*, June 1989, **154**, 797–800) on the effects of nicotine in patients with dementia of the Alzheimer type are interesting and clearly warrant further evaluation. We would however like to raise some methodological concerns.

Firstly, the inclusion of cigarette smokers is questionable. There is evidence that prolonged or repeated exposure to nicotine can cause a desensitisation blockade of the receptors (Wonnacott, 1987) and that, as a result, subjects who smoke regularly may be less sensitive to the effects of subcutaneous nicotine. In addition, the density of nicotinic receptors in the brain has been shown to be increased in brain tissue taken from habitual smokers (Benwell *et al*, 1988). Although the possible psychopharmacological consequences of the change in receptor density remains to be established, it seems reasonable to suggest that patients who are also regular smokers may not respond to systemic nicotine in the same way or to the same degree as non-smokers. Therefore, the apparent lack of response to the drug in some of the tests (e.g. the short-term memory test) may simply reflect the heterogeneity of the patient population used.

Secondly, there is wide intrasubject variability in performance on cognitive tests in demented patients. Since the effects of subcutaneous nicotine are of rapid onset it is feasible to test the patients before and after administration of drug or placebo at each session. Positive results with this experimental design would be of greater significance.

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References

BENWELL, M. E. M., BALFOUR, D. J. K. & ANDERSON, J. M. (1988) Evidence that smoking increases the density of nicotine binding sites in the brain. *Journal of Neurochemistry*, **50**, 1243–1247.

WONNACOTT, S. (1987) Brain nicotine binding sites. *Human Toxicology*, **6**, 343–353.

Depression-dependent exacerbation of TD

SIR: I read with interest the case "Depression-dependent exacerbation of tardive dyskinesia" reported by Sachdev (*Journal*, August 1989, **155**, 253–255). The case is presented well, but I would like to draw readers' attention to previous literature on this topic.

Yassa *et al* (1983), investigating patients with affective disorder, found a prevalence of tardive dyskinesia (TD) of 41%, with affected patients being older than those without TD. Yassa *et al* (1987) went on to investigate patients being started on antidepressants. Of 50 patients, three developed TD, two improving on withdrawal of the drugs. They quote a number of authors who have reported both the presence of TD in patients on antidepressants (15 cases) and others describing affective disorder as an exacerbating risk factor for TD in other disorders.

I would support Sachdev in the assertion that current biochemical theories are contradicted by these cases and that new explanations will have to be found. I would add that the model would have to take account of possible predisposing factors (age, sex, previous neuroleptic use, organic damage,