

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