

Matters arising

Sir: In a recent study of elderly subjects (*J Neurol Neurosurg Psychiatry* 1983; 46:410-3) Aziz, Leeming and Blair found a significantly lower mean plasma total biopterin in 18 patients with senile dementia of Alzheimer type than in 35 hospital patients (15 confused, 20 without confusion), 13 healthy controls and 17 schizophrenic patients. They suggest that the differences are due to reduced biopterin synthesis in the patients with Alzheimer's disease, a conclusion which, if correct, could be of considerable importance to the direction of future studies of the disease. Before accepting this explanation other possible explanations for their findings must be considered and investigated.

This group of workers have themselves shown that plasma total biopterin values are closely and positively related to plasma phenylalanine concentrations¹ and to renal function.² Plasma phenylalanine rises and falls with changes of phenylalanine intake and liver function. It is possible that differences between the groups in plasma phenylalanine and/or renal function could account for the differences in plasma biopterins recorded by Aziz *et al.* A few controls with impaired renal or liver function, and patients with dementia on a particularly low protein intake, could account for their findings. The way to deal with this difficulty is to measure plasma phenylalanine and creatinine at the same time as plasma total biopterin. This might also reveal that patients with Alzheimer's disease have increased plasma phenylalanines as well as low biopterins thus adding further weight to the authors' conclusions.

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References

- ¹ Leeming RJ, Blair JA, Green A, Raine DN. Biopterin derivatives in normal and phenylketonuric patients after oral loads of L-phenylalanine, L-tyrosine and L-tryptophan. *Arch Dis Childh* 1976;51:771-7.
- ² Leeming RJ, Blair JA. The effects of pathological and normal pathological and normal physiological processes on biopterin derivative levels in man. *Clin Chim Acta* 1980;108:103-11.

Blair and Leeming reply:

Dr Smith draws attention to the changes in plasma total biopterins which correlate closely with changes in plasma phenylalanine concentrations.¹ She suggests that the lower mean plasma total biopterins in the eighteen patients with senile dementia could be due to reduced plasma phenylalanine levels or renal changes. We have previously reported that in senile dementia patients (six) with significantly lower fasting plasma biopterins than controls (five) (1.15 ± 0.14 (SE) versus $1.78 \pm 0.07 \mu\text{g l}^{-1}$; $p < 0.02$) the plasma phenylalanine fasting levels in the demented are significantly higher than in the controls (0.099 ± 0.003 (SE) versus $0.051 \pm 0.004 \text{ mmol l}^{-1}$; $p < 0.001$) as is the P/T ratio ($1.9 \text{ v } 0.96$).^{2,3} An oral dose of 7 g of phenylalanine to these six demented patients produced significantly higher levels of plasma phenylalanine at 1, 2 or 3 hours following the dose than in control subjects and total plasma biopterin levels were similar in the demented patients to controls at 1 and 2, 3 and 4 hours following the phenylalanine dose.² These observations are consistent with the slow metabolism of phenylalanine due to reduced synthesis of tetrahydrobiopterin. Decreased renal clearance, a likely occurrence in the elderly, causes a significant increase in the plasma total biopterins.⁴ Clearly the reduced total plasma biopterin in senile dementia is not caused by low phenylalanine levels nor by renal insufficiency. Reference 2⁴ quoted by Dr Smith has no comment on renal function.

Another report has shown the plasma biopterin levels but not plasma neopterin levels are significantly reduced in Alzheimer's disease.⁵ This again suggests that a decrease in biopterin synthesis is found in Alzheimer's disease and the reduced levels are not due to altered kidney or liver function.

Direct measurement on necropsy human temporal lobe samples has now shown that tetrahydrobiopterin synthesis is significantly reduced in Alzheimer disease patients compared to controls.⁶

References

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- ² Leeming RJ, Blair JA. Serum Crithidia levels

in disease. *Biochem Med* 1980;23:122-5.

³ Leeming RJ, Blair JA, Melikian V, O'Gorman DJ. Biopterin derivatives in human body fluids and tissues. *J Clin Pathol* 1976;29:444-51.

⁴ Leeming RJ, Blair JA. The effects of pathological and normal processes on biopterin derivative levels in man. *Clin Chim Acta* 1980;108:103-11.

⁵ Young JH, Kelly B, Clayton BE. Reduced levels of biopterin and dihydropteridine reductase in Alzheimer type dementia. *Clin Exp Gerontol* 1984; 4(4), 389-402.

⁶ Barford PA, Blair JA, Eggar C, Morar C, Whitburn S. Tetrahydrobiopterin metabolism in the temporal lobe of patients dying with senile dementia of the Alzheimer type. *J Neurol Neurosurg Psychiatry* 1984;in press.

Focal Paroxysmal Kinesigenic Choreoathetosis

Sir: I was interested to read Plant's report¹ of three patients in whom unilateral movements of paroxysmal kinesigenic choreoathetosis were focally induced by movement of the ipsilateral, but not the contralateral limbs. I have recently seen a 40-year-old woman with unilateral paroxysmal involuntary movements that could be precipitated by voluntary movement of either limb. This patient gave an 18 year history of periodic right-sided involuntary movements made up of finger clenching, wrist and elbow flexion with adduction of the arm drawing the fist across the chest. Occasionally the right side of the face would pull at the same time. There was no associated sensory aura. The movements would last less than a minute and when not experiencing the dyskinesia she had no neurological complaints. Initially these movements occurred only once every two months, always when lying down in bed at night. For the past four years they have occurred up to ten times per day and are frequently precipitated by use of the right limb. Family history was negative.

On examination with the arms outstretched there was a slight dystonic flexion of the fifth finger on the right side and on performing rapid alternating movements of the right hand the right foot took on a dorsiflexed and inverted posture which could not be precipitated by movement of the left hand. Carrying out fine finger movements of the right hand frequently precipitated a tremulous movement in the hand which would then progress to a clenching of the fingers and the full tonic posturing of the limb as described above. Each episode would last between 10 and