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Letters

Tetrahydrobiopterin metabolism in senile dementia of Alzheimer type

Sir: The rate controlling co-factor in the synthesis of the neurotransmitters dopamine and noradrenaline is 5, 6, 7, 8,-tetrahydrobiopterin (BH_4)[1]. Disturbances in BH_4 metabolism have been detected in various disease states showing neurological disfunction.[1] Recently, significantly reduced serum biopterin levels were reported for subjects diagnosed in life as senile dementia of Alzheimer type[2] using a microbiological assay technique. We now report the use of HPLC[3] to investigate the BH_4 metabolism in subjects diagnosed post-mortem as suffering from dementia.

At post-mortem examination, samples of cerebro-spinal fluid (CSF) were obtained from demented subjects characterised as suffering from Alzheimer's disease or cerebrovascular disease, as well as from a group of age-matched controls. All subjects had been prospectively assessed for the presence or absence of dementia. Analysis of these samples was carried out using HPLC with a fluorescence detector, and the total biopterin estimated by acid/iodine oxidation prior to HPLC separation.[4] (see table).

Table *Concentrations of neopterin and biopterin in cerebrospinal fluid*

	Age range (years)	*Total neopterin in μg/l (mean ± SD)*	*Total biopterin in μg/l (mean ± SD)*	*Neopterin/biopterin ratio (mean ± SD)*
Senile dementia of Alzheimer type (8)	51-89	20·4±13·0	19·6±11·0	1·1 ± 0·7
Cerebrovascular disease (3)	81-89	14·7± 4·2	5·5± 2·2	3·1±2·0
Control (7)	78-91	42·2±34·5	49·9±22·3	0·9±0·7

Using the Wilcoxon sum of ranks test, the values for total biopterin (biopterin + BH_2 + BH_4) were significantly lower ($p < 2\%$) in patients with senile dementia of Alzheimer type and cerebrovascular disease than in controls, although the neopterin levels were not significantly different. Other subjects suffering from neurological disorders also were investigated. Pick's disease patients showed reduced biopterin concentrations (13·5 and 22·0 μg/l) with neopterin concentrations of 37·0 and 60 μg/l respectively. One Huntingdon's chorea patient showed reduced levels of biopterin (16·0 μg/l) and neopterin (19 μg/l). A single cerebrovascular disease subject with no symptoms of dementia showed a reduced concentration of biopterin (15·0 μg/l) and a neopterin concentration of 44 μg/l.

The lower neopterin levels in patients with cerebrovascular disease and senile dementia of Alzheimer type suggest a dilution effect, possibly due to loss of brain tissue, which could account for the lower total biopterin concentrations. Alternatively, the low biopterin concentrations could be due, at least in part, to an impairment of tetrahydrobiopterin metabolism. This is in agreement with other results[4] which show a reduced BH_4 level in the CSF of a group of pre-senile dementia subjects.

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Meningitis and disseminated cutaneous zoster complicating herpes zoster infection

Sir: Herpes zoster or shingles is commonly seen as a painful and unpleasant condition affecting a single dermatome. Rarely, however, more serious neurological complications may develop including meningo-encephalitis, encephalomyelitis, cranial nerve palsies and peripheral neuropathy.[1 2] It is less well known that herpes zoster infection can present as aseptic meningitis.

A 24-year-old computer operator from Guyana presented with a two day history of bifrontal headache aggravated by coughing and straining at stool, neck stiffness, photophobia and left-sided sharp chest pain which was worse with inspiration. On the day of admission he developed nausea and profuse sweating. He had lived in Britain since the age of eight years and had contracted chickenpox when aged ten. One year previously he had been vaccinated against smallpox. On examination he was unwell but not obtunded. His temperature was 38·5°C. He had marked neck stiffness with positive Kernig's and Brudzinski's signs and mild photophobia. The rest of the examination was completely normal. Initial investigations revealed Hb 13·5 g/dl, WBC 7·2 × 10^9/l (neutrophils 49%, lymphocytes 40%, monocytes 10%) and his blood film showed "reactive lymphocytes". A biochemical profile including liver function tests, chest radiograph and ECG were normal. A lumbar puncture yielded clear CSF under normal pressure. Microscopy showed 410 WBC/mm^3 (95% lymphocytes). Gram and acid-fast stains were negative. The CSF protein was 1·08 g/l and CSF glucose 4·0 mmol/l (blood glucose 5·3 mmol/l). Subsequent culture for viruses and bacteria was sterile. He improved considerably within 24 hours, but two days after admission a vesicular eruption suddenly appeared over the left posterolateral chest wall in the region of T5 dermatome at the site of his original chest pain. Over the next three days additional disseminated vesicles developed on the arms, legs and trunk. Characteristic herpes viruses were seen when the vesicular fluid was examined by electron microscopy. An additional series of investigations was performed: EEG was normal; no viruses were isolated from CSF, throat or stool culture; serum varicella-zoster complement fixation test titres (VZ CFT) were <1/8 on admission, 1/64 after one week, 1/512 after two months and although cross-reacting herpes simplex antibody was detected there was no significant rise in titre; CSF VZ CFT titre was 1/8 after one week when the