$51.2 \pm 1.4 \mu\text{m}^3$, which was also significantly less ($p < 0.001$) than that of $69.1 \pm 1.3 \mu\text{m}^3$ measured in the controls. Reductions in nerve cell number and nucleolar volume of 67% and 26% respectively, are similar to these decreases in Alzheimer type dementia and Down's syndrome and may be presumed, therefore, to lead to substantial depletion of brain noradrenaline in this condition also.

It therefore seems that loss of noradrenergic activity is found in all those dementias characterised by a neurofibrillary degeneration of nerve cells even though senile plaques may not always be present. The alterations in protein synthesis that lead to formation of paired helical filaments have been related to the presence of toxic substances, particularly aluminium,⁹ within the brain, which may accumulate from an altered permeability of the microvasculature, stemming from loss of modulation by noradrenergic fibres¹⁰. Changes in cholinergic activity, similar to those in Alzheimer type dementia,¹¹ and Down's syndrome,¹² occur in scrapie,¹³ a slow virus disease affecting sheep and goats, in which amyloid plaques, similar to senile plaques, but not neurofibrillary changes, are present in the brain.¹⁴ This suggests that alterations in the cholinergic rather than noradrenergic neurotransmitter system may be fundamental to plaque formation in ATD and Down's syndrome, a conclusion strengthened by the close quantitative relationship¹⁵ that occurs between reductions in choline acetyl transferase activity and frequency of senile plaques in cases of Alzheimer type dementia.

DMA MANN

PO YATES

J HAWKES

Department of Pathology,
The University,
Manchester M13 9PT, UK

References

- Mann DMA, Lincoln J, Yates PO, Stamp JE, Toper S. Changes in the monoamine containing neurones of the human CNS in senile dementia. *Br J Psychiat* 1980;**136**:533-41.
- Tomlinson BE, Irving D, Blessed G. Cell loss in the locus caeruleus in senile dementia of Alzheimer type. *J Neurol Sci* 1981;**49**:419-28.
- Bondareff W, Mountjoy CQ, Roth M. Selective loss of neurones of origin of adrenergic projection to cerebral cortex (nucleus locus caeruleus) in senile dementia. *Lancet* 1981;**i**:783-4.
- Adolfsson R, Gottfries CG, Roos BE, Winblad B. Changes in brain catecholamines in patients with dementia of Alzheimer type. *Br J Psychiat* 1979;**135**:216-23.
- Yates CM, Ritchie IM, Simpson J, Maloney AFJ, Gordon A. Noradrenaline in Alzheimer-type dementia and Down's syndrome. *Lancet* 1981;**ii**:39-40.
- Cross AJ, Crow TJ, Perry EK, Perry RH, Blessed G, Tomlinson BE. Reduced dopamine- β -hydroxylase activity in Alzheimer's disease. *Br Med J* 1981;**1**:93-4.
- Perry EK, Tomlinson BE, Blessed G, Perry RH, Cross AJ, Crow TJ. Noradrenergic and cholinergic systems in senile dementia of Alzheimer type. *Lancet* 1981;**ii**:149.
- Mann DMA, Lincoln J, Yates PO, Brennan CM. Monoamine metabolism in Down's syndrome. *Lancet* 1980;**ii**:1365-6.
- Crapper DR, Quittkat S, Krishnan SS, Dalton AJ, De Boni U. Intraneuronal aluminium content in Alzheimer's disease, dialysis encephalopathy and experimental aluminium encephalopathy. *Acta Neuropathol (Berl)* 1980;**50**:19-24.
- Raichle ME, Hartman BK, Eichling JO, Sharpe LG. Central noradrenergic regulation of cerebral bloodflow and vascular permeability. *Proc Nat Acad Sci USA* 1975;**72**:3726-30.
- Perry EK, Gibson PH, Blessed G, Perry RH, Tomlinson BE. Neurotransmitter enzyme abnormalities in senile dementia. *J Neurol Sci* 1977;**34**:247-65.
- Yates CM, Simpson J, Maloney AFJ, Gordon A, Reid AH. Alzheimer-like cholinergic deficiency in Down's syndrome. *Lancet* 1980;**ii**:979.
- McDermott JR, Fraser H, Dickinson AG. Reduced choline acetyl transferase activity in scrapie mouse brain. *Lancet* 1978;**ii**:318-9.
- Bruce ME, Fraser H. Amyloid plaques in the brains of mice infected with scrapie. *Neuropath Appl Neurobiol* 1975;**1**:189-202.
- Perry EK, Tomlinson BE, Blessed G, Bergmann K, Gibson PH, Perry RH. Correlation of cholinergic abnormalities with senile plaques and mental test scores in senile dementia. *Br Med J* 1978;**2**:1457-9.

Progressive spastic paraplegia due to persistent echo virus encephalomyelitis in a child with X-linked hypogammaglobulinaemia

Sir: We wish to describe a boy who presented with signs of a progressive spastic paraplegia and was found to suffer from hypogammaglobulinaemia and chronic encephalitis due to Echo virus type 29. Intact T cell function was indicated by the lymphocytic infiltrates in the CNS and by lymph nodes depleted of lymphocytes and with absent reactive follicles in the vestigial germinal centres. Although there was no family history in our patient, his age, sex and

persistent encephalitis suggest the X-linked form of hypogammaglobulinaemia. The particular points of interest in this case are absence of frequent infections and preservation of normal intelligence.

A 16-months-old boy was admitted with increased tone in his limbs and brisk tendon reflexes. He had lost his motor skills from the age of 12 months when he was noticed to cease walking and after the age of 14 months he was no longer able to sit without support. He was born to healthy unrelated parents at term following a normal pregnancy. Birth weight was 3290 g. The neonatal period was normal. His early developmental milestones were normal; he sat unsupported at 6 months, pulled to stand at 9 months and walked holding on at 10 months. He began to speak at 12 months and progress of his mental development continued unimpaired. Except for a febrile illness with erythematous rash and vomiting at the age of 3 months he did not have any other illnesses.

Investigations at the age of 16 months were normal for blood count (leucocytes $9.6 \times 10^9/l$, neutrophils 41%, lymphocytes 57%, monocytes 2%), liver function, urate, blood and urine amino and organic acids, blood lactate and pyruvate and lysosomal enzymes. Computed tomography of the brain and myelography showed no abnormality. The CSF contained $0.010 \times 10^6/l$ white blood cells with 80% lymphocytes, 0.1 g/l protein and normal glucose. Enterovirus was isolated from the CSF.

The child had another febrile illness with a rash at 17 months and died at 20 months from fulminant *Pseudomonas aeruginosa* septicaemia with purulent cholecystitis. At necropsy apart from cholecystitis the most important finding was in the CNS. The brain was normal in size and outward appearance but slight opacity of the meninges was noted. On coronal sectioning the only abnormality was slight enlargement of the lateral ventricles. Histological examination revealed slight to moderate lymphocytic infiltration of the cerebral and spinal meninges. Perivascular lymphocytic cuffs (fig A) were present in all regions of the cerebrum, brain stem, cerebellum and spinal cord. The infiltration was extensive but the individual cuffs were thin. In addition a moderate degree of microglial proliferation with nodule formation (fig B) was seen in the optic nerves, hypothalamus, thalamus, brain stem, cerebellum and spinal cord. Neuronal degeneration was less obvious in the cerebral and cerebellar hemispheres but more pronounced in the brain stem, where in addition to the colliculi nuclei pontis and

inferior olives the 6th, 8th, and 10th cranial nerves were affected. All levels of the spinal cord were involved with neuronal degeneration in the anterior horns; Clark's column was similarly damaged. The crossed pyramidal tracts showed gross axonal degeneration. The spinal roots appeared normal.

The findings of a low grade encephalitis and the *Pseudomonas* sepsis unusual for the age led to the immunological investigation of a stored deep-frozen specimen of serum. The results were IgG < 2 IU, IgA < 2 IU, IgM 18 IU. The enterovirus isolated from the CSF at 16 months was found to be an Echo virus type 29.

Patients with immunoglobulin deficiency usually recover uneventfully from virus infections. However enteroviruses may occasionally cause persistent encephalitis in children with X-linked hypogammaglobulinaemia.¹⁻³ Intact B-cell function seems to be essential especially for the termination of CNS echovirus infections.^{1,2} This suggests, that antibody-dependent, cell-mediated cytotoxicity which was demonstrated on target cells infected with herpes and mumps virus⁴ might also have a role in the elimination of Echo virus. In addition Echo virus is known to inhibit lymphocytic transformation.⁵ This effect upon

cellular immunity and the high rate of spontaneous mutations among RNA viruses,⁶ are some other factors which acting together may conceivably cause an infection to become chronic. Wilfert¹ and Medici⁷ suggest that hypogammaglobulinaemic patients with the HLA type B7 are predisposed to develop persistent encephalitis. Treatments with gammaglobulin,^{1,2,7} specific antibody containing plasma¹ and with intraperitoneally implanted thymus⁷ have not been successful. No treatment was attempted in our patient, because the warning signs and symptoms of an immunodeficiency were not present in early life, and thus, the diagnosis was not reached during life time. It is of particular interest to note that progressive spastic paraplegia was the only sign of the CNS infection.

This case supports the view that intact B-cell function is essential for the eradication of Echo virus infection of the central nervous system.

JEGGER
SLINGAM
MAGDA ERDOHAZI
J WILSON PhD

*The Hospital for Sick Children,
Great Ormond Street,
London WC1N 3JH, UK*

References

- ¹ Wilfert CM, Buckley RH, Mohanakumar T, *et al*. Persistent and fatal central-nervous-system Echo virus infections in patients with agammaglobulinemia. *N Engl J Med* 1977;**296**:1485-9.
- ² Webster ADB, Tripp JH, Hayward AR, *et al*. Echovirus encephalitis and myositis in primary immunoglobulin deficiency. *Arch Dis Child* 1978;**53**:33-7.
- ³ Davis LE, Bodian D, Price D, Butler JJ, Vickers JH. Chronic progressive poliomyelitis secondary to vaccination of an immunodeficient child. *N Engl J Med* 1977;**297**:241-5.
- ⁴ Roitt IM, Shen L, Greenberg AH. Antibody-dependent-cell-mediated cytotoxicity. In: Beers RF and Bassett EG, eds *The role of immunological factors in infectious, allergic and autoimmune processes*. New York: Raven Press 1976.
- ⁵ Willems FTC, Melnick JL, Rawls WE. Viral inhibition of the phytohemagglutinin response of human lymphocytes and application to viral hepatitis. *Proc Soc Exp Biol Med* 1969;**130**:652-61.
- ⁶ Johnson RT, Lazzarini RA, Waksman BH. Mechanisms of virus persistence. *Ann Neurol* 1981;**9**:616-7.
- ⁷ Medici MA, Kagan BM, Gatti RA. Chronic progressive panencephalitis in hypogammaglobulinemia. *J Pediatr* 1978;**93**:73-5.

Transient unilateral mydriasis with basilar aneurysm

Sir: Third nerve palsy is a valuable localising sign of a posterior communicating aneurysm and is characteristically accompanied by dilatation of the pupil. Third nerve compression in basilar artery aneurysm is less common. We report a patient with transient unilateral pupillary dilatation without external ophthalmoplegia associated with sacular basilar aneurysm. This sign in basilar aneurysm, has not to our knowledge, previously been reported.

Following a generalised convulsion with no aura or focal features a 31-year-old decorator complained of severe headache and vomiting. Both plantar responses were extensor. After about 24 hours the abnormal signs had resolved, but his headache persisted in diminishing intensity for the subsequent week. Two weeks later, a few minutes after sexual intercourse, he had a further seizure lasting several minutes, following which he vomited and again complained of severe generalised headache and photophobia. About 10 hours later his left pupil became dilated, remained unreactive to light for about an hour and then returned to normal. No mydriatics had been instilled and there was no associated change in his level of consciousness or headache, no diplopia and no alteration in pulse rate or blood pressure. Examination revealed neck stiffness, positive Kernig's sign and mild bilateral papilloedema. A computed tomographic scan showed moderate dilatation of lateral and third ventricles and a small amount of blood in the occipital horns of both lateral ventricles. Bilateral carotid and vertebral angiography showed a large bilobed aneurysm at the bifurcation of the basilar artery projecting to the left. No other aneurysms were seen. At operation (HAC) through a right pterional approach, a bilobed aneurysm, pointing to the left, was identified at the basilar bifurcation. It was directly related to the left third nerve. There was minimal thrombus around the aneurysm but most of the blood clot was within the third ventricle into which the aneurysm had ruptured. A straight Heifetz clip was applied. After operation he returned to his pre-operative clinical state. Three weeks later a ventriculo-peritoneal shunt was inserted for persistent ventricular dilatation and further progress was uneventful.

The cause of the transient pupillary dilatation in this patient may have been

Fig (A) Photomicrograph of frontal cortex showing sparse mononuclear exudate in the meninges and in the molecular layer. H&E $\times 60$
(B) Photomicrograph of inferior olive with neuronal degeneration and microglial proliferation. H&E $\times 60$