Letters

The cytopathogenic agent in CSF: evidence for a relationship with enolase levels

Sir: We have previously described a cytopathic effect induced *in vitro* by some cerebrospinal fluid (CSF) samples¹ which has been observed with CSF from patients with a variety of neurological and psychiatric conditions.² Despite early suggestions that a virus-like agent may have been involved in the production of the cytopathic effect we later demonstrated that the effect could be observed in the presence of inhibitors of protein synthesis. This was inconsistent with the effect being due to an active viral infection.³ Recently Mered *et al*⁴ reported a failure to detect any evidence for viruses present in the CSF of schizophrenics. Although their negative virological findings do not necessarily conflict with our results we were surprised at their failure to report the development of a cytopathic effect in any of their tests.

A coded series of 91 CSF samples was retested according to the method described previously.³ In spite of a storage time of up to five years in some cases, 72 of the samples gave identical results, a concordance ($p < 0.001$) which shows that we are dealing with a reproducible phenomenon. In a recent report⁵ the retesting of 53 CSFs in a different laboratory also produced a highly significant relationship between the initial findings and the retest ($p < 0.01$).

As the cytopathic effect was noted in CSFs from a wide variety of neuropsychiatric and degenerative conditions, including schizophrenia, dementia and Huntington's chorea, we were interested in the question of what could be common to these conditions. As cellular degeneration is either known or has been postulated to occur in all of these conditions, we measured enolase levels as a general marker of pathological change in the CNS which could be measured in CSF. Levels of enolase enzymes are elevated in cases of human herpes encephalitis, Huntington's chorea⁶ and anoxic conditions of the CNS.⁷ The increase in enolase levels has been attri-

buted to the leakage of proteins due to cell damage,⁸ alpha enolase being released by non-neuronal (including glial) cells and gamma enolase being a neuronal specific isoenzyme.

We measured both alpha and gamma enolase levels by radioimmunoassay⁹ in a coded series of CSF samples from psychiatric patients diagnosed as either schizophrenic or affective, and compared cytopathic effect-positive samples with cytopathic effect-negatives using Student's *t* test. A significant ($p < 0.02$) relationship was observed between cytopathic effect status and increased alpha enolase concentrations. The increase in gamma enolase levels observed in the cytopathic effect-positives was not significant (table).

We conclude that, although the cause has not yet been identified, the cytopathic effect is a reproducible phenomenon, and is associated with elevated CSF alpha enolase levels. This may reflect cell damage in the CNS or blood brain barrier of some psychiatric patients, although it remains to be determined whether the *in vitro* cytopathogenic component is a cause or a product of such damage.

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References

- ¹ Tyrrell DAJ, Crow TJ, Parry RP, Johnstone EC, Ferrier IN. Possible virus in schizophrenia and some neurological disorders. *Lancet* 1979;i:839-41.
- ² Crow TJ, Johnstone EC, Owens DGC, *et al*. Characteristics of patients with schizo-

phrenia or neurological disorder and virus-like agent in cerebrospinal fluid. *Lancet* 1979;i:842-4.

- ³ Taylor GR, Crow TJ, Ferrier IN, Johnstone EC, Parry RP, Tyrrell DAJ. Virus-like agent in CSF in schizophrenia and some neurological disorders. *Lancet* 1982;ii:1166-7.

- ⁴ Mered B, Albrecht P, Torrey EF, Weinberger DR, Potkin SG, Winfrey CJ. Failure to isolate virus from CSF of schizophrenics. *Lancet* 1983;ii:919.

- ⁵ Tyrrell DAJ, Parry R, Davies H, Bloxham C, Crow TJ. Further studies of the cytopathic effect in tissue cultures inoculated with CSF from patients with schizophrenia and other nervous system diseases. *Br J Exp Pathol* 1983;64:445-50.

- ⁶ Royds JA, Davies-Jones GAB, Lewtas NA, Timperley WR, Taylor CB. Enolase isoenzymes in the cerebrospinal fluid of patients with diseases of the nervous system. *J Neurol Neurosurg Psychiatry* 1983;46:1031-6.

- ⁷ Scarna H, Dalafosse B, Steinberg R, *et al*. Neurone-specific enolase as a marker of neuronal lesions during various comas in man. *Neurochem Internat* 1982;4:405-11.

- ⁸ Semba R, Kato K. Increased nervous system specific enolases in rat plasma and cerebrospinal fluid in bilirubin encephalopathy detected by an enzyme immunoassay. *Neurochem* 1982;39:360-5.

Computed tomography and acute carbon monoxide poisoning

Sir: According to Sawada *et al*,¹ low density areas in the globus pallidus in CT scans soon after severe carbon monoxide poisoning suggest a poor outcome. A close correlation between such CT scans and pathological findings has been established.² However, such low-density lesions may appear later involving different pathological mechanisms and with a different prognosis, as shown in the case reported below.

A 22-year-old Caucasian woman presented in Rabat on 25 November 1981 after carbon monoxide poisoning. The initial coma lasted at least four hours. She left the hospital the day after. On 1 December 1981, headache and visual disturbance appeared with distortion of optical images and micropsia. She was transferred to Lille. The patient was aggressive. There was diffuse hypotonia with brisk tendon reflexes in the lower limbs; the plantar responses were flexor. The EEG showed 5 Hz slow waves anteriorly and 2 Hz slow waves in the parietal areas bilaterally. CT scan was normal. Her symptoms disappeared within 72 hours, but there was bradyphrenia and the EEG remained abnormal. A new CT

Table Enolase (ng/ml) in CSF

Cytopathic effect	Present	Absent	
Alpha enolase (SEM)	13.9 (1.3)	10.1 (0.9)	$p < 0.02$
Gamma enolase (SEM)	15.1 (1.4)	12.0 (0.8)	$p < 0.07$
N	11	23	
Mean age (yr)	27.6	33.9	
Age range (yr)	25-59	18-60	