Title: REDUCED CSF URIDINE IN HEAD INJURY PATIENTS

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Introduction. Harkness and Lund have previously shown that in perinatal CSF the purine metabolites xanthine and hypoxanthine are elevated in infants who later evidence abnormal CNS function (1). We recently began a study of xanthine and hypoxanthine in neurosurgical patients with traumatic brain damage who required ventriculostomy for monitoring of intracerebral pressure. As part of this management, ventricular CSF is removed to help decrease intracerebral pressure, in addition to pharmacological manipulations of systemic perfusion pressure, mannitol, steroids, and other routine clinical care.

Methods. CSF was obtained from ventriculostomy sites of head injury patients or neonatal subjects undergoing shunt revision. Patients scheduled for lumbar subarachnoid blockade for surgical procedures served as controls. CSF was mixed with a solution of EHNA (an adenosine deaminase inhibitor) dipyridamole (to block adenosine uptake into cellular elements) and indomethacin (2) and stored at $4^{o}C$ until analysis within several days. Analysis was via high pressure liquid chromatography (20 mM NH_4PO_4, pH 6.6 with 1% CH_3CN on C_{18} reversed phase column-U.V. detector at 2500A). Values are expressed as nmoles/ml of original CSF. Recovery was 85-90%.

Results. It quickly became evident that the high pressure liquid chromatography elution profile of head injury patients was missing a large characteristic peak present in normal lumbar fluid. This compound was tentatively identified a uridine based on its chromatographic characteristics and peak co-elution with ^{3}H uridine. For this reason the concentrations of this normally occurring pyrimidine in CSF were also measured in head injury as well as neonatal and normal subjects. As seen in the table, CSF uridine in head injury patients was only 12% that of normal subjects. Xanthine values were also significantly elevated ($p < .05$). Patients with elective shunt revision had uridine present at concentrations only 62% of normal adult lumbar fluid. The uridine concentration was not a function of red cell contamination in the CSF samples. A significant, though weak, positive correlation between xanthine and CSF lactate was also noted.

Discussion. In separate experiments, we have demonstrated that uridine will block the development of wild-running seizures provoked in rats by inferior collicular stimulation. Since uridine is an endogenous compound with anticonvulsant activity similar to that of GABA, and since it is reduced in head injury patients, the deficiency of CSF and possibly CNS uridine may contribute to post-traumatic cerebral excitation. Uridine also serves as the only transport vehicle for pyrimidines into the CNS, where it is utilized in many basic cell repair processes. It is presently unknown if the low uridine concentrations reflect decreased transport of the base into brain or increased utilization in brain. Supplementation with uridine should be evaluated as a means to amerliorate electrical and structural damage following head injury and cerebral ischemia.

References.

1. Harkness RA and Lund RJ: J. Clin. Pathol. 36:1-8, 1983.

2. Gehrke CW, Kuo KC, Davis GE, and Suits RD: J. Chromatog 150:455-476, 1978.

Source	Uridine	Hypoxanthine	Xanthine
Head Injury Adults (7)	0.49** ±0.23	3.88 ±0.55	5.99* ±0.79
Hydrocephalic Infants (3)	2.57 ±0.82	6.45 ±1.95	10.7 ±3.3
Subarachnoid Block (32)	4.13 ±0.34	3.31 ±0.26	3.21 ±0.27

All values are Mean ± SEM of individual patient means expressed as nMoles/ml CSF ( ) = No. of patients.
* $p < .05$ ** $p < 0.01$ relative to subarachnoid block subjects.