are highly effective anticonvulsants against seizures induced in animals by a variety of mechanisms including kindling. Adenosine receptor antagonists exert their protective actions indicating tonic adenosinergic control of ictal susceptibility. Animal studies have shown a rapid and substantial release of adenosine and its metabolites inosine and hypoxanthine during experimental seizures. The physiological actions and metabolism of adenosine in the human CNS remain to be fully elucidated. We report that acute increases of adenosine and its metabolites can be detected in lumbar CSF after clinical status epilepticus in humans.

Seven patients with new onset status epilepticus were studied. Five patients (aged 12 to 67) developed go-30 minute status epilepticus with three or more clonic or tonic-clonic seizures occurring in less than one hour without regaining consciousness between seizures. Causes included viral encephalitis, cysticercosis, uraemia, benzodiazepine withdrawal, and drug toxicity. One patient (48 years old) with diabetes and chronic renal failure developed epileptic seizures after ventricular ventilation. Two patients (aged 22 to 53) evaluated for other neurological conditions (demyelinating neuropathy, headaches, cranial neuropathy, multiple sclerosis) were used as controls.

In this study we have quantitated nanomolar concentrations of adenosine in CSF obtained from control patients without seizures in the low nanomolar range whereas concentrations of the adenosine metabolites inosine and hypoxanthine were considerably higher (table). The concentrations of adenosine and its metabolites in lumbar CSF most likely reflect brain interstitial concentrations as the relative concentrations of these compounds in CSF samples are almost identical with those measured in the interstitial fluid from the frontal cortex of animals. The low concentrations of adenosine cannot be attributed to ex vivo degradation as there is no appreciable metabolism of adenosine in CSF.

Five patients evaluated for generalised convulsive status epilepticus underwent diagnostic lumbar punctures 0.1 to 13 hours after admission. No changes in CSF adenosine concentrations were found but inosine and hypoxanthine concentrations were substantially higher than controls (table). The time interval from last seizure to CSF sample seemed to be an important factor with the maximum increase of hypoxanthine (greater than sixfold) seen at one hour. Nevertheless, increases in hypoxanthine concentrations were still evident up to 13 hours. Patient 4 had another diagnostic lumbar puncture 12 days after recovery from her last seizure and all adenosine metabolite concentrations were similar to controls.

This study is the first to document rapid and substantial changes in adenosine metabolites in CSF after status epilepticus in humans. Our findings complement the recent findings of Durand and Spencer who reported profound increases in extracellular fluid adenosine from the hippocampus in four patients with complex partial seizures, using microdialysis probes attached to depth electrodes. Our findings also closely parallel the reported changes in adenosine metabolites in interstitial fluid after experimental seizures in animals. For example, Park et al. found that extracellular adenosine concentrations rose significantly during 10 minutes of bicuculline induced seizures in paralysed, ventilated piglets. Smaller increases in inosine and hypoxanthine were found during the same period. Ten minutes after cessation of seizures, adenosine concentration returned to preictal values whereas inosine and hypoxanthine continued to rise, indicating that adenosine released at the time of seizures is rapidly metabolised. Our findings of similar increases in inosine and hypoxanthine concentrations but not adenosine in patients after generalised status epilepticus can be explained by such rapid metabolism of adenosine in vivo.

The physiological relevance of our findings to the regulation of epileptic phenomena in humans is unknown. Even so, the experimental data in animals indicate that adenosine and its metabolites are important endogenous modulators of seizure initiation and propagation. Whether similar mechanisms are operative in humans remains to be determined.

Bilateral cavernous sinus thrombosis causing Korsakoff's amnesic syndrome

Korsakoff's amnesic syndrome (Korsakoff's psychosis) is a condition in which learning and memory are affected out of proportion to other cognitive functions. It has not been previously reported as a complication of cavernous sinus thrombosis. Our patient developed Korsakoff's amnesic syndrome after bilateral medial temporo-occipital infarcts as a complication of cavernous sinus thrombosis.

A 44 year old man was admitted with fever of 15 days duration, and altered senility of 10 days duration preceded by a day of recurrent vomiting. Three days before admission he developed a painful swelling of his left eye associated with redness and sudden total loss of vision in that eye. He was high grade, intermittent, and associated with sweating. The altered senility was in the form of restlessness, incoherent speech, disorientation, and an inability to recognise his relatives properly. He had had hypertension for four years duration, was on irreversable treatment, and was a past smoker. He had no history of alcohol intake.

On examination he was drowsy, febrile (99°F), and had a blood pressure of...
A detailed mental status examination three weeks after admission showed that attention was mildly abnormal with mild anemia in naming objects and parts of objects; the remaining language functions were essentially normal. He was disoriented for time, place, and person. Immediate and remote memories were mildly impaired with gross recent memory (both verbal and visual new learning abilities) impairment. Momentary confabulations were noted with normal constructional abilities. Abstraction was impaired with partially preserved insight and a grossly normal fund of information. Mild impairment of the frontal lobe (inability to do alternating motor patterns) and occipital dysfunction (prosopagnosia and a colour agnosia) were seen. Parietal lobe tests were normal.

Follow up 15 months after discharge showed a persistent confabulatory amnesic state with total blindness of his left eye. The right eye was normal. Visual evoked potentials were normal on the right side but absent on the left. He was unable to return to work or function independently due to the continued severity of his memory impairment.

An MRI at this time showed bilateral well delineated temporal infarcts, which were hypointense in T1 and hyperintense in T2 images (fig 2). There was evidence of bilateral temporal atrophy with dilation of the temporal horns of the lateral ventricles. The left eyeball was atrophic.

A neuropsychological assessment 18 months after the onset showed that on the Weschler memory scale his raw score was 22 and his Lui weighted score was 64. Overall memory quotient was 69. Functional analysis indicated that disturbances persisted in all the memory functions, with recent and immediate memory the worst.

Korsakoff's amnesic syndrome after cavernous sinus thrombosis has not been reported before. Damage to three relatively discrete neuroanatomical regions has been primarily implicated in the amnesic syndrome—namely, the medial temporal lobes, the medial thalamic nuclei, and the basal forebrain. Mishkin's model proposes that the degree of impairment of recognition memory was a direct function of the amount of conjoint damage to the amygdala and hippocampus irrespective of the specific structure involved. In this case the bilateral temporal-occipital infarcts also resulted in bilateral hippocampal damage together with amygdalar involvement (fig 2), which is consistent with Mishkin's model for amnesia. This finding is consistent with the hippocampal abnormalities in amnesic patients as shown by high resolution MRI.

Clinicopathologically this patient had infarctions bilaterally in the territory drained by the basal vein of Rosenthal (BVR). The BVR receives tributaries from the insula, cerebral peduncles, medial temporal lobe, and veins of the temporal horn. It communicates with the cavernous sinus either through the sphenoparietal sinus or through the superior petrosal sinus, via the lateral mesencephalic vein. In instances of hypoplastic posterior segment of the BVR, the vein drains anteriorly via the lateral mesencephalic vein. In this patient the thrombotic process may have extended to the BVRs by any one of these channels or, alternatively, the BVRs may have had hypoplastic posterior segments. The diencephalic structures, drained by the internal cerebral veins, were spared in this patient as was the basal forebrain, confirmed by MRI.

Levine et al recommend early anticoagulant treatment in cavernous sinus thrombosis to reduce morbidity, but the spontaneous haemorrhagic conversion as seen in our patient suggests that adequate
imaging either with CT or MRI to rule out mesial temporal infarcts should be mandatory before giving anticoagulant treatment.

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Hearing loss as a false localising sign in raised intracranial pressure

Benign intracranial hypertension (BIH) is an idiopathic disorder characterised by headache and visual disturbances with papilloedema (unilateral or bilateral), in which a space occupying lesion or infective processes have been excluded by neuro-imaging, analysis of CSF, and additional ancillary investigations. Recently this Journal has carried a series of reports describing rare associated cranial nerve palsies.1-3 We report a case of left sided raised intracranial hearing loss occurring in conjunction with worsening symptoms of raised intracranial pressure in a patient with established BIH that resolved after lumbar puncture.

In a 24 year old woman presented to the eye casualty department with a week’s history of headache—worse on bending—nausea with intermittent vomiting, and visual blurring. She had been taking oral contraceptives but there was no other relevant drug or medical history. Examination showed obesity (95 kg/155 cm), bilateral papilloedema, and normal visual acuity although testing fields by confrontation showed a small central scotoma affecting the right eye and decreased temporal fields in the left eye. Computed tomography, brain MRI, and MR angiography were performed. The puncture produced clear and colourless CSF with an opening pressure of 36 cm CSF. The CSF constituents were normal, with a protein concentration of less than 0.1 g/l and 2 white cells per cubic mm. The CSF glucose to plasma ratio was normal. The following peripheral blood indices were also normal: full blood count, viscosity, urea and electrolytes, liver function tests, thyroid functions, creatine, protein, venereal disease research laboratory test, and anticholinergic antibody. OKP-Humpfrey field analysis showed pronounced peripheral field constriction. The initial management was withdrawal of the oral contraceptive pill. Diuretic treatment with chlorothalidone was commenced and dietetic referral arranged.

These measures initially resulted in considerable symptomatic improvement. However, several months, the headaches recurred with increasing visual obscurations. These symptoms progressed to daily bilateral obscurations of vision for up to 1 minute despite diuretic treatment. In association with this she had noted increasing impairment of hearing in the left ear, with no associated tinnitus, in the week before readmission. Repeat neurological examination on readmission revealed chronic papilloedema, with peripheral constriction of the fields but normal visual acuity. Neuro-otological examination confirmed clinical hearing loss of 57% in the left ear. The Weber test was bilaterally. Pure tone audiometry showed a mild left sided conductive hearing loss, with an air bone gap ranging between 5 and 20 dB at 250 to 4000 Hz. Tympanometry showed normal middle ear pressure and compliance bilaterally. Repeat lumbar puncture subsequently confirmed raised pressure of 29 cm CSF. On the second day after lumbar puncture the patient noted normalisation of the hearing acuity in the left ear. Repeat audiometry and tympanometry were performed showing resolution of the previously noted mild conductive hearing loss and unchanged tympanometry.

Abducens nerve palsies are described in between 9% and 36% of cases of benign intracranial hypertension as false localising signs. Other cranial nerve palsies occurring with this disorder are rare, but oculomotor, trochlear, trigeminal, and facial nerve lesions have recently been reported.1-3 It has been suggested that potential mechanisms for these occurrences are direct compression of the nerve root by cerebral tissue, traction of the nerve by causal displacement of the brainstem, or vascular disturbance as a consequence of the above.

In this case there was not only a close relation between the worsening symptoms of raised intracranial pressure and the development of left sided hearing loss but also rapid normalisation of hearing acuity on reduction of the raised intracranial pressure, suggesting that the hearing loss may have been a pressure related phenomenon. In the current case however, the audiometric pattern was indicative of a conductive hearing loss. A potential explanation is to infer an increase in the perilymphatic fluid pressure transmitted through the cochlear aqueduct as a result of the rise in CSF pressure. This might dampen the movement of the stapedial footplate and of the round window membrane giving a small conductive hearing loss. The alternative explanation of persistent malleus or incus effusion is unlikely given the normal tympanometry.

Although otological manifestations have been previously reported in raised intracranial pressure of varying aetiologies including benign intracranial hypertension,1,3 hearing loss is not normally considered in the context of false localising signs. It may be under recognised given the typically mild nature of the hearing loss1 and the wide prevalence of hearing loss in the normal population.

In a series of 20 patients with benign intracranial hypertension the commonest otological manifestations were objective pulsatile tinnitus and low frequency hearing loss.1 Both these symptoms improved transiently in all patients after lumbar puncture. In the longer term these patients responded well to weight reduction and treatment with diuretics. Wider awareness of this association will allow such patients to avoid unnecessary investigation and benefit from appropriate explanation and reassurance.

Bromate intoxication with polyneuropathy

Acute bromate intoxication is a rare event in neurological clinics. Previous reports described renal failure and hearing deficit in addition to nausea, vomiting, haemolytic anaemia, depressed consciousness, and seizure.1 We report a woman who attempted suicide by taking a hair permanent wave preparation. This resulted in severe acute bromate intoxication and she developed renal failure, deafness, and toxic polyneuropathy.

The 25 year old woman (body weight 57 kg) took 7-5 g sodium bromate in the suicide attempt in 1992. Nausea, vomiting, and diarrhoea developed rapidly. Stomach lavage and irrigation by activated charcoal were carried out at a local hospital. Tinnitus and dizziness occurred five hours later, followed by deafness. Blood urea nitrogen was 10 mg/dl (normal 7-20 mg/dl) and serum creatinine 1-4 mg/dl (normal 0-5-1-2 mg/dl for women). Oliguria was noted on the second day, with blood urea nitrogen rising to 16 mg/dl and 3 mg/dl respectively. The urine sediment disclosed 3-5 red blood cells per high power field (normal 0-2), and 45–50 white blood cells per high power field (normal <5 per high power field). Proteinuria was present (protein 3-5 mg/dl but without casts). Serum bromide (Br-) concentration was 85 µg/ml (none present in normal subjects). Glucose and ketone bodies were resistant to furosemide. On the third day, serum urea nitrogen reached 48 mg/dl and creatinine 9-3 mg/dl. Because of deteriorating renal function she was referred to the Veterans General Hospital and received three courses of haemodialysis.

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