consequence, however, is that the effectiveness of simple interventions can be gauged in a large population.

This case record survey of burns at the Chalfont Centre for Epilepsy is unique in that it included all burns and had an accurate record of the cause in most cases. The seizure charts kept prospectively by staff and residents allowed the frequency of burns per seizure to be calculated. The data are considered to be reasonably accurate as all but the most trivial burns were recorded. Brief, inconspicuous seizures may not have been recorded, particularly simple partial, absence seizures or myoclonic jerks. All complex partial, secondary generalised, and generalised tonic-clonic seizures would, however, have been noted. From the 303 patients there were a total of 34 burns, at least 19 of which were seizure related, and 18 631 seizures were recorded during the 1 year period. Only one required skin grafting but six required over 3 weeks to heal. Therefore only one in every 980 seizures resulted in a burn with one in 3105 resulting in a burn taking longer than three weeks to heal.

Although there were significantly more burns in independent houses, there were also a greater number of seizures per person on average in this group. As most burns were related to seizures, correcting for the number of seizures per person abolished the significance of level of independence on number of burns.

It is of note that almost no burns occurred secondary to showers or heating devices, which is in stark contrast with all previous reports. Five years ago thermostatic regulators were put on to hot water supplies and covers were installed to protect hot water pipes and heating appliances. These changes followed several severe burns in previous years from the above sources.

A further difference between this study and previous, community based studies was that there were very few cooking related burns in this study. This is almost certainly due to the fact that even the most independent residents do relatively little cooking as a canteen is available at lunchtimes and residents are encouraged to use microwave ovens.

Lastly, most burns were caused by hot drinks; either severe burns from large containers of hot water such as kettles or teapots, or milder burns from individual cups. The scope for reducing future morbidity from burns in persons with epilepsy is therefore in this area. The use of microwave ovens to heat individual cups of hot water is one option as these were already in widespread use for food preparation. The use of insulated flasks instead of teapots would prevent surface burns and the exit valve would prevent hot water being spilt. Further, hot water heaters, which are only able to dispense a fixed amount of water, are available and would be an alternative to kettles.

Burns are therefore a relatively rare but potentially serious cause of morbidity in people with epilepsy. The more severe burns are also largely preventable by simple interventions, which do not interfere greatly with a person's independence.

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A quartet of Down's syndrome, Alzheimer's disease, cerebral amyloid angiopathy, and cerebral haemorrhage: interacting genetic risk factors

Since 1993 the ε4 allele of apolipoprotein E (apoE) on chromosome 19 has been recognised as the major genetic risk factor for sporadic Alzheimer's disease. Deposition of amyloid β protein (Aβ protein) in the cerebral cortex is a key feature of Alzheimer's disease and may be of pathogenetic importance. Sporadic cerebral amyloid angiopathy often coexists with Alzheimer's disease and involves the deposition of Aβ protein in leptomeningeal and cortical blood vessels. Both conditions may occur in Down's syndrome, presumably because of the increased expression of β-amyloid precursor protein (APP) associated with trisomy 21, the chromosomal location of the APP gene.

Intracerebral haemorrhage is the principal, though uncommon clinical manifestation of cerebral amyloid angiopathy. Studies have suggested that the apoE ε2 allele and also the ε4 allele may occur more often in patients with cerebral amyloid angiopathy related haemorrhage.[1 2] We report, to our knowledge, only the second case of cerebral amyloid angiopathy related haemorrhage in Down's syndrome and suggest that the patient's neuropathology and clinical manifestations were modulated by interacting influences of the APP and apoE genes.

A 46 year old man with Down's syndrome was found dead in his bed. There were no suspicious circumstances. He had a long history of well controlled absence seizures on 800 mg sodium valproate a day. One month before his death he had had a left lower lobe pneumonia, from which he recovered well with intravenous antibiotic. He was cognitively impaired with some deterioration in behaviour in the last few years of his life, necessitating placement in care. There was no family history of dementia or intracerebral haemorrhage. He took no antiplatelet or anticoagulant medication and was not hypertensive. A necropsy was performed.

The patient had a typical Down's syndrome facies. No head injury was apparent. There was evidence of bronchopneumonia in the left lung. There was no significant coronary atheroma and no evidence of congenital heart disease. Neuropathological examination disclosed a small brain (940 g) with a band of haemorrhage in the subarachnoid space overlying the frontal and parietal lobes of the right cerebral hemisphere. Coronal sections disclosed a large haematoma 7 cm×5.5 cm×5.5 cm lying superficially in the hemisphere beneath the subarachnoid haemorrhage. The middle third of the right cerebral hemisphere was expanded with a 5 mm shift of the midline structures and a supracallosal hernia to the left. There was extensive secondary haemorrhage into the tegmentum of the midbrain and upper pons, as a consequence of brainstem compression due to raised intracranial pressure.

Histological examination of sections of cerebral neocortex stained by silver impregnation (modified Bielschowsky's stain) disclosed numerous non-neuritic plaques and sparse neuritic plaques. There were scanty neurofibrillary tangles. The age related neuritic plaque score and history of dementia gave a "definite" neuropathological diagnosis of Alzheimer's disease according to the criteria of the Consortium to Establish a Registry for Alzheimer's disease (CERAD). In sections from the haematoma wall there was extensive acute ischaemic necrosis in addition to the haemorrhage. Immunostaining for Aβ protein (Dako mouse monoclonal antibody raised to residues 8–17 of Aβ protein) confirmed the presence of multiple plaques within the cortical ribbon and showed severe amyloid deposition in many blood vessels within the cortex and overlying meninges. Some blood vessels had narrowed lumens and others displayed a "double barrel" appearance, typical findings in cerebral amyloid angiopathy associated vasculopathy. There was microscopical evidence of previous haemorrhage in the form of multiple small intracortical glial scars with haemosiderin pigment in macrophages. In the sections examined there was no evidence of fibrinoid necrosis.

The apoE genotype of the patient was ε2/ε4, determined by analysis of DNA extracted from formalin fixed paraffin embedded brain tissue as described previously.[1]

Only once before has a cerebral amyloid angiopathy related haemorrhage been reported in a patient with Down's syndrome and Alzheimer's disease.[3] Indeed an analysis of death certificates listing Down's syndrome as the underlying or a contributing cause of death did not document intracerebral haemorrhage among 793 cases examined from the United States during 1976.[4] This seems surprising as Down's syndrome is associated with both Alzheimer's disease and cerebral amyloid angiopathy, the second predisposing to intracerebral haemorrhage. The studies on our patient may suggest some reasons why the expected quartet of findings is a rare but aetiologically related occurrence.

Patients with Down's syndrome have a shorter life expectancy because of excess mortality from haemopoetic malignancies, congenital heart defects, and respiratory tract infections.[4] Although there is "premature" Alzheimer's disease in Down's syndrome, predisposition to these other conditions can have an early fatal outcome.

Our patient was predisposed to Alzheimer's disease not only because of his extra copy of the APP gene, but also because of his apoE ε4 allele. By the age of 40, virtually all patients with Down's syndrome have neuropathological changes characteristic of Alzheimer's disease. The increased dosage of the APP gene has been shown to produce increased serum concentrations of APP and the two major forms of Aβ protein—Aβ40 and Aβ42. The ε4 allele increases the risk of dementia in patients with Down's syndrome. Indeed the combination of Down's syndrome with the ε4 allele leads to very high deposition of Aβ protein in plaques.[5] Possession of the ε4 allele also predisposes to deposition of Aβ protein in the cerebral leptomeningeal and cortical vasculature. Evidence currently suggests that the ε2 allele, although protective against Alzheimer's disease, pre-

disposes to haemorrhage due to cerebral amyloid angiopathy.[1 2] We previously found more than a threefold overrepresentation of both the ε2 allele and the 2/4 genotype in patients with cerebral amyloid angiopathy related haemorrhage and speculated that whereas ε4 is a risk factor for deposition of Aβ protein in blood vessel walls, ε2 is a risk factor for haemorrhage from amyloid laden blood vessels.[1] Although ε2 and ε4 alleles are neither necessary nor sufficient for cerebral amyloid angiopathy related haemorrhage, these apoE alleles seem to be major susceptibility polymorphisms for cerebral amyloid angiopathy (ε4) and cerebral amyloid angiopathy related haemorrhage (ε2). Because the ε2 allele is only 8% of the apoE alleles in the population, including the subgroup of patients with Down's syndrome, it does not commonly coexist with the more closely related conditions of Alzheimer's disease, cerebral amyloid angiopathy, and Down's syndrome to produce cerebral haemorrhage.

In conclusion, we suggest that in this patient with Down's syndrome, three copies of the APP gene, possession of the apoE ε4 allele, and age (46 years) predisposed to Alzheimer's disease and cerebral amyloid angiopathy whereas the apoE ε2 allele predisposed to haemorrhage from the amyloid laden blood vessels.

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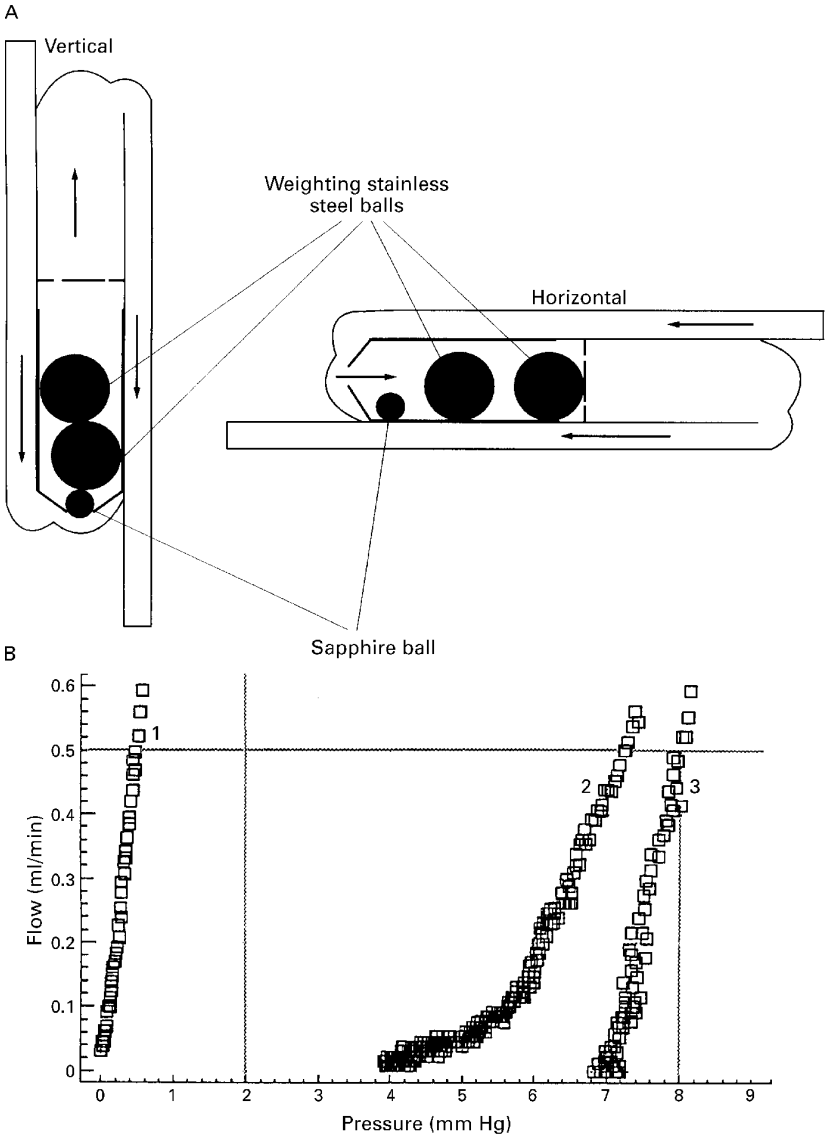
Chhabra hydrocephalus shunt: lessons for gravitational valves

Overdrainage is a significant clinical problem after shunting for hydrocephalus as confirmed by the UK Shunt Registry.[1] Various devices have been developed to reduce the rate of CSF drainage in the upright position which have been assessed by the UK Shunt Evaluation Laboratory.[2] The average price of a shunt varies from £175 to £650 in the United Kingdom. Surprisingly, the prices are higher in the developing countries.[3] However, some local lower cost constructions are available and are reported to function well.[4]



(A) Diagram of the Chhabra shunt. Two weighting balls control the opening pressure, depending on whether the body position is vertical or horizontal. (B) Pressure-flow performance curves of two-ball Chhabra shunts in the horizontal (1) and vertical (2,3) body positions. Curve 2 was recorded when the pressure pulsations of magnitude 7 mm Hg peak to peak and frequency 20/min were superimposed on a slowly changing static pressure. Each point represents 2 minutes average of flow (plotted along y axis) and pressure (x axis).

The Chhabra shunt is a low cost device, developed and manufactured in India, that incorporates a gravitational siphon preventing mechanism. In the vertical position one, two, or three (depending on performance level) stainless steel weighting balls press on a sapphire ball which closes the CSF flow aperture, increasing the shunt's opening pressure (figure (A)). In the horizontal position the opening pressure is theoretically equal to zero mm Hg, as the balls fall away. A similar principle is applied in constructions of other "gravitational" shunts—namely, the Cordis horizontal-vertical LP valve, the newly designed dual-switch Miethke valve (Germany) and the Fuji, another low cost valve (Philippines).

We tested a sample of two Chhabra medium pressure shunts (containing two balls) using a 2 week evaluation protocol.[2] Our main aim was to investigate the impact of posture (horizontal-vertical) on shunt pressure-flow performance. We also investigated how the fluctuations in proximal pressure, simulating the presence of naturally occurring waves of intraventricular pressure, may alter shunt function. Such waves may occur not only due to heart and respiratory function but also due to body movements during walking, jogging, etc.

The figure (B) shows two typical pressure-flow performance curves recorded in the horizontal and the vertical position. They represent two almost straight parallel lines. Their slopes depict the low hydrodynamic resistance of the shunt (1.3 mm Hg/ml/min) This is much lower than the physiological resistance to CSF outflow, which normally lies within the range 6–10 mm Hg/ml/min.[5] The average operating pressure determined for the vertical shunt position was around 7 mm Hg and for the horizontal position it was 0.6 mm Hg. The area between these lines represents the possible operating range in all the intermediate body positions. Therefore, we conclude that the operating pressure of the shunt varies with the body position, as intended.