LETTERS TO
THE EDITOR

Coexisting vertical and horizontal one and a half syndromes

Supranuclear ocular movements comprise chiefly vertical and horizontal movements; horizontal movements are controlled by the subcortical centres located mainly at the pontine level and vertical movements at the level of the rostral midbrain.\(^{1,2}\) The classic one and a half syndrome is produced by a unilateral pontine tegmental lesion that includes the paramedian pontine reticular formation and medial longitudinal fasciculus on the same side, and has been considered an important ocular sign in neurological diagnosis.\(^{3,4}\) Vertical, as distinct from horizontal, one and a half syndrome, has also been documented recently.\(^{1,2,5,6}\) We report on a patient with concurrent vertical and horizontal one and a half syndromes.

A 57 year old man was admitted to hospital with a sudden onset of dysarthria and loss of consciousness while playing golf. He had a history of aortic regurgitation and heart failure 8 years previously, and underwent aortic valve replacement 5 years previously, when he started to take oral antiplatelet and anticoagulant drugs. On admission, he was comatose, and his blood pressure was 140/76 mm Hg. He also had atrial fibrillation, Cheyne-Stokes respiration, bilateral miosis, and a positive Babinski's sign. Brain CT showed lesions suspected of being infarcts in the right medial thalamus and the left upper cerebellum. According to neurological findings on day 4 after onset of disease, he was in a state of hypersomnia. While awake, his head tilted slightly to the left, the right eye was slightly deviated upward, the left eye slightly downward, and there was bilateral miosis. For horizontal ocular movements, only the right eye could abduct with monocular horizontal nystagmus. Also, there was bilateral conjugated leftward palsy, indicating horizontal left one and a half syndrome. On the other hand, for vertical ocular movement, only the left eye could gaze downward. Also, difficulty in downward gaze of the right eye and bilateral conjugated upward palsy, indicating vertical one and a half syndrome, were noted (figure A). Doll's eye test (oculocephalic reflex) was weak but positive, and the eyes were unable to converge. There was also ataxic dysarthria, cerebellar ataxia of the left limbs and trunk, right sided hemisensory disturbance, and bilaterally positive Babinski's sign. Brain MRI showed infarcts in the right medial thalamus, left dorsal portion of the upper midbrain, and left upper cerebellum (figure B). On magnetic resonance angiography performed at the same time, partial obstruction of the left posterior cerebral artery was noted at its origin. Cardiogenic cerebral embolism was suspected in the pathogenesis of the serial episode in this patient.

At 7 days the patient still tended to become unconscious, accompanied by Cheyne-Stokes respiration, when talking to a familiar person. About 1 month later he talked about occurrences at the onset and began to show an interest in his surroundings. At 2 months, adduction of the left eye, bilateral leftward gaze, downward gaze of the right eye, and bilateral upward gaze showed moderate improvement. The gait disturbance persisted and he is still in a wheelchair.

Classic horizontal one and a half syndrome is commonly caused by a vascular accident...
occurring in the lower pons involving the paramedian pontine reticular formation and the medial longitudinal fasciculus. In the present patient one and a half syndrome, however, was thought to be due to two concurrent lesions of distinct nerve tracts in the upper left medulla—that is, descending fibres from the frontal eye fields of the cerebral cortex after decussation at the midbrain level and medial longitudinal fasciculus fibres ascending on the opposite side.

Attention has recently focused on the rostral interstitial nucleus of the medial longitudinal fasciculus, interstitial nucleus of Cajal, and posterior commissure, all located in the tegmentum of the mesencephalon, as the brain stem centres for vertical eye movement. Vertical one and a half syndrome consists of a bilateral conjugate upgaze palsy and a unilateral downward palsy, or a bilateral conjugate downward palsy and a monocular upgaze palsy. It has been reported that the fibres involved in upward gaze from the posterior commissure may explain bilateral upgaze palsy, and the fibres involved in downward gaze may be affected on one side before their decussation in contralateral lesion, or after their decussation in ipsilateral lesion. A patient was also reported with bilateral downgaze palsy and bilateral lesions of the rostral interstitial nucleus of the medial longitudinal fasciculus. Furthermore, it was reported that a unilateral lesion of the interstitial nucleus of Cajal resulted in tilting of the head towards the opposite side. Therefore, it can be assumed that the leftward tilting of the head seen in the patient under study was caused by a lesion of the right interstitial nucleus of Cajal. The patient’s disease thus seems to be a rare case of the coexistence of two distinct syndromes, vertical and horizontal one and a half syndromes, although the lesions responsible for these syndromes are different. Even though the exact anatomical and physiological mechanism underlying vertical gaze still remains obscure in many respects, vertical one and a half syndrome is considered to be one of the important neurological signs suggestive of a lesion affecting the rostral medulla. The particular pathogenetic mechanism of this interesting syndrome will be elucidated through future elaborate comparative studies of clinical manifestations and diagnostic imaging.

This work was supported by the Research Grant for Longevity Sciences (11C-05) from the Ministry of Health and Welfare.

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Malignant catatonia secondary to sporicidal encephalitis lethargica

Catatonia is a neuropsychiatric syndrome characterised by a combination of psychosomatic withdrawal and various movement disorders. Kahalbakh first described this syndrome in 1868 when he noted this condition of “profound mental symptoms, Kaposi limitted catatonia to a subtype of dementia praecox, later redefined by Bleuler in 1906 as catatonic schizophrenia. Since then, it has become increasingly apparent that the catatonic syndrome is a continuous spectrum of illness that can exist in a wide range of clinical presentations, from primarily affective disorders as well as secondary to various underlying medical conditions, leading the DSM-IV to broaden its categorisation of catatonia to include these other entities. In the early 1900s, a condition known variously as epidemic encephalitis, encephalitis lethargica, or Von Economo’s disease was described, affecting more than 65 000 patients from 1919 to 1929. Case descriptions highlight this time as striking similarities to our modern definitions of catatonia. Throughout recent years, isolated cases of encephalitis lethargica have been reported in association with features of sporicidal encephalitis lethargica and discussion manage of this entity in the context of catatonia.

The patient was a 22 year old previously psychologically and neurologically healthy woman who was transferred to the Barrow Neurological Institute after a 4 week stay in hospital for progressive immobility, mutism, posturing, and tremor. Initial evaluation had shown a CSF lymphocytosis, increased liver transaminases, and an EEG with bifrontal slowing. Further investigation as to aetiology of her meningoecephalitis was negative including brain MRI, brain biopsy, vasculitic disorders as well as kinetic form into a more parkinsonian picture with progression into a mute, immobile state punctuated by occasional dyskinesias. The pathological substrate for catatonia is largely unknown. When it is produced by an anatomical derangement, abnormalities are most often seen in the thalamus, subthalamic nuclei and substantia nigra. In patients dying from encephalitis lethargica, severe destructive changes were seen in the substantia nigra and, to a lesser extent, in the subthalamic nuclei and other basal ganglia structures. Our patient had a normal brain MRI and FDG-PET suggesting asymmetric thalamic hypometabolism which resolved with ECT, suggesting at least functional impairment in these anatomical areas.

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J Neurol Neurosurg Psychiatry 2000;69:401–409

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J Neurol Neurosurg Psychiatry, first published as 10.1136/jnnp.69.3.401 on 1 September 2000. Downloaded from http://jnnp.bmj.com/ on September 16, 2023 by guest. Protected by copyright.
Evaluation for the aetiology of catatonia is outlined in our report. Treatment is aimed at addressing any underlying medical conditions that may be producing the syndrome and once this is done, directly treating the catatonia itself. Historically, this has been varied, but recent studies suggest excellent efficacy for both high dose intravenous benzodiazepines and ECT. Our patient began responding within 24 hours of her first ECT and although spontaneous recovery remains a possibility, we think that her improvement is due to ECT. Data regarding outcome in epidemic encephalitis lethargica reports a mortality up to 35% with an additional 50% experiencing neuropsychological and psychiatric sequelae. Post-encephalitic parkinsonism could be seen as far out as 20 years in patients who seemed to have recovered from the acute infection. Recovery in our patient has been complete without evidence for a progressive or relapsing neurological or psychiatric disorder, although follow up has been limited to 1 year.

In conclusion, catatonia may be produced by various both neurological and psychiatric. Without a history of previous psychiatric impairment, aggressive investigation should be pursued for treatable medical conditions. Catatonia due to medical conditions may be successfully treated with therapies typically reserved for psychiatric indications.

The clinical syndrome of encephalitis lethargica, although no longer epidemic in nature, is still sporadically seen and the underlying inflammatory cause is, as yet, unknown.

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**Downbeat nystagmus from heat stroke**

Downbeat nystagmus is an ocular motility disturbance with structural lesions of the cerebellum and vestibulocerebellum, it can also occur in the setting of tonic insults and metabolic abnormalities. Heat stroke is the most severe form of heat related illness, and is associated with multisystem organ failure. Heat stroke is infrequently associated with a cerebellar syndrome. We describe a patient in which downbeat nystagmus was associated with a midline cerebellar syndrome in a patient with heat stroke, suggesting that the vermal cerebellum and vestibulocerebellum may be particularly susceptible to thermal injury.

A previously healthy 22 year old man without relevant medical history collapsed while on a 4 mile run during military basic training. Initial core body temperature was 39°C. He was incoherent and combative. Laboratory data showed increased creatine kinase, increased liver function tests, and prolonged coagulation variables. Measures to lower body temperature were initiated and he was transferred to our institution.

On arrival, core body temperature was 37°C. He was able to follow commands. His sodium concentration was 135, potassium 3.2, calcium 7.5, magnesium 1.6, alanine transaminase (ALT) 2739, aspartate transaminase (AST) 2112, white blood count 4.2, haemoglobin 12.5, platelet count 43 000, international normalised ratio (INR) 2.9, and ammonia 33. Serological tests for HIV and RPR were negative. An ECG and chest radiograph were unremarkable.

Over the next 3 days, his patient’s liver enzymatic activity improved. He received several transfusions to correct his thomboctoype mia and hypocogulability. Three days after admission, the patient’s family noted that his speech was slurred. The patient complained of blurred vision when reading or looking down.

Neuro-opthalmological examination 5 days after the onset of his visual symptoms showed near visual acuity of J16 in primary gaze (second order), and J1 in up gaze. Kinetic perimetry was full in both eyes. Pupils, external examination, anterior segments, and fundi were within normal limits. Motility examination showed full ductions and versions. Vertical and horizontal saccades were hypometric. Vertical and horizontal smooth pursuit were abnormal (vertical more than horizontal), showing low pursuit gain. There was impaired suppression of the vestibulo-ocular reflex. Downbeat nystagmus was present in primary gaze, worsening in down-gaze, and gaze down and laterally. This was poorly suppressed by fixation. His neurological examination showed cerebellar ataxia (truncal more than appendicular), and dysarthria.

A high quality MRI of the brain with and without contrast and with diffusion weighted MRI also supports this theory that cerebellar damage in heat stroke is caused by direct thermal injury, our patient’s magnesium concentration was only slightly below normal for our laboratory. Furthermore, the syndrome persisted even after correction of his serum magnesium into the normal range. It may be that in the setting of an already compromised cerebellum, even borderline hypomagnesaemia may promote or accentuate downbeat nystagmus.

Our case provides clinical findings which are compatible with experimental data supporting localisation of downbeat nystagmus to the vestibulocerebellar region. It provides further evidence that magnesiaemia be particularly susceptible to thermal injury. The normal diffusion weighted MRI also supports the theory that cerebellar damage in heat stroke is caused by direct thermal injury, rather than a hypoxic-ischaemic insult.

The work was supported in part by a departmental grant (Ophthalmology) from Research to Prevent Blindness, New York, NY. This study was an enhancement of Health CORE grant P30-EY0 6360. NJN is a recipient of a Research to Prevent Blindness Lew R Wasserman Merit Award.

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Clinical characteristics of published cases of cerebellar syndrome from heat stroke

<table>
<thead>
<tr>
<th>Patient</th>
<th>Year</th>
<th>Age(s) (°C)</th>
<th>Temperature</th>
<th>Cause of fever</th>
<th>Clinical syndrome</th>
<th>M or U</th>
<th>NMS</th>
<th>Recovery</th>
<th>Initial imaging</th>
<th>Follow up imaging</th>
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<tbody>
<tr>
<td>1</td>
<td>1970</td>
<td>47M 42.2</td>
<td>Confined in heated cell</td>
<td>Hypotonia, intention tremor, ataxia, dystartria</td>
<td>NMS = neuroleptic malignant syndrome; CBLR = cerebellar; NL = normal.</td>
<td>Unknown</td>
<td>None</td>
<td>CBLR atrophy</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>2</td>
<td>1987</td>
<td>50F 43.2</td>
<td>Exertion in heat</td>
<td>NMS, dystartria, hypotonia</td>
<td>CT NL</td>
<td>Nearly complete 5 months</td>
<td>CBLR atrophy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>1983</td>
<td>50F 42.5</td>
<td>NMS</td>
<td>Latex ataxia, dystartria</td>
<td>CT NL</td>
<td>None</td>
<td>CBLR atrophy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>1995</td>
<td>39M 41.6</td>
<td>NMS</td>
<td>Gait ataxia</td>
<td>CT NL</td>
<td>Complete 1 year</td>
<td>None</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>1996</td>
<td>44F 42.1</td>
<td>Exertion in heat</td>
<td>Dysartria</td>
<td>CT NL</td>
<td>Complete 2 weeks</td>
<td>CBLR atrophy</td>
<td></td>
<td></td>
<td></td>
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<td>6</td>
<td>1996</td>
<td>39F 41.1</td>
<td>Heat stroke</td>
<td>Gait ataxia</td>
<td>MRI NL</td>
<td>Complete 7 days</td>
<td>Not done</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>1996</td>
<td>55M 40.9</td>
<td>Pneumonia</td>
<td>Gait ataxia</td>
<td>MRI NL</td>
<td>Complete 3 days</td>
<td>Not done</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>8</td>
<td>1996</td>
<td>48F 40.7</td>
<td>Pneumonia</td>
<td>Gait ataxia</td>
<td>MRI NL</td>
<td>Complete 5 days</td>
<td>Not done</td>
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<tr>
<td>9</td>
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<td>47M 40.7</td>
<td>Pneumonia</td>
<td>Gait ataxia</td>
<td>MRI NL</td>
<td>Complete 6 days</td>
<td>Not done</td>
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<tr>
<td>10</td>
<td>1996</td>
<td>60M 40.8</td>
<td>Erythrasma</td>
<td>Gait ataxia</td>
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<td>None</td>
<td>MRI at 10 weeks</td>
<td>CBLR atrophy</td>
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<td></td>
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<tr>
<td>11</td>
<td>1997</td>
<td>45M 42</td>
<td>Exertion in heat</td>
<td>NMS, dystartria, hypotonia</td>
<td>CT NL</td>
<td>None</td>
<td>CBLR atrophy</td>
<td></td>
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Apolipoprotein E ε2 may be a risk factor for sporadic frontotemporal dementia

Frontotemporal dementia (FTD) is the second most common form of presenile dementia, after early onset Alzheimer’s disease. Up to half of cases of FTD are thought to be familial, probably with an autosomal dominant mode of inheritance, some with mutations on chromosome 17. The genetics of sporadic FTD have been less studied, although several groups have examined the potential association of FTD with apolipoprotein E (APOE) ε4, with inconclusive results.

We studied 11 patients with sporadic FTD (excluding patients with first degree relatives with dementia) in the cohort of the Oxford project to investigate memory and aging (OPTIMA). Nine of the 11 were histopathologically confirmed and the remaining two fulfilled the consensus criteria of Neary et al. (three of the nine had also been clinically diagnosed by these criteria and all three were confirmed at necropsy); only one of the nine confirmed cases was Pick-type. Apolipoprotein E genotyping was performed, blind to diagnosis, by polymerase chain reaction methods for the 11 patients with FTD (mean age at death or last examination: 65.7 years; six women) and for 136 elderly controls (mean age: 77.5 years; 77 women), without cognitive impairment and with CAMCOP scores greater than 80, from the OPTIMA cohort. An older control group was used to minmise the chance inclusion of future cases of FTD. APOE allele frequencies did not vary with age in the controls. Controls and patients were Caucasians from the Oxford region. Genotyping results are shown in the table.

Allele frequencies of APOE in cases of FTD versus controls, respectively, were: 0.32 versus 0.06 for APOE ε2, 0.64 versus 0.78 for APOE ε3, and 0.05 versus 0.16 for APOE ε4: The one Pick-type case was an APOE ε2/ε3 heterozygote. We did not have enough cases of FTD to distinguish between allele frequencies of predominantly frontal and mainly temporal cases. Control frequencies were similar to those widely reported for Caucasians. All control and FTD genotypes were in Hardy-Weinberg equilibrium for both APOE alleles.

We examined eight previous reports with APOE genotypes of cases of FTD and controls. This showed that seven of the eight had APOE ε3 odds ratios of FTD less than 1, as in our study, consistent with a protective association, whereas results for APOE ε2 and for APOE ε4 were highly varied. Frequencies of APOE ε2 in FTD ranged from zero to a significant excess noted by Gustafson et al. We suggest that these contrasting results are due to differences in diagnostic and exclusion criteria. Not all reports specified their diagnostic criteria and four of the eight were based solely on clinical diagnosis of FTD, which admits the possible inclusion of concomitant or misdiagnosed Alzheimer’s disease, especially if NINCDS-ADRDA criteria were used. Including cases of Alzheimer’s disease would be expected to raise the APOE ε4 frequency and to lower that of APOE ε2. Perhaps more importantly, only two studies of the eight excluded or separated familial cases.

Our suggestions, that APOE ε2 may be a risk factor for sporadic FTD and APOE ε3 might be protective, need to be investigated in a larger, probably familial, study. The diagnostic and exclusion criteria should be used. We propose the inclusion only of histopathologically confirmed cases of or of those fulfilling the consensus criteria of Neary et al. (list 1 or 2, FTD or progressive non-fluent aphasia strictly applied, and the exclusion of cases with first degree relatives with dementia, or with signs of parkinsonism at an early stage, or of corticobasal degeneration.

If it is indeed shown that APOE ε2, although protective against late onset Alzheimer’s disease, is a risk factor for sporadic FTD, this will provide a new insight into mechanisms of risk and protection related to APOE in both diseases.

Since submitting this letter, we have read an important and relevant report by the Manchester group, easily the largest and most comprehensive study to date on APOE frequencies in FTD and related disorders. The group examined 35 controls and 163 patients, including 58 with FTD without family history, and found no association of any APOE allele with FTD. Their APOE ε2 allele frequencies were 0.06 in controls, similar to ours, and 0.09 in non-familial cases of FTD. When pooling their data with ours, however, we obtained APOE ε2 frequencies of 0.12 in sporadic FTD (n=69) and 0.06 in controls (n=171). This gave an odds ratio of sporadic FTD for that allele of 2.15 (95% CI 1.4–2.2, p=0.04).

We especially thank all patients and volunteers, members of OPTIMA, the Department of Neuropathology, Radcliffe Infirmary, Dr M John, Dr S Fernando, C Johnston, D Warden and S Litchfield. This work was supported by Bristol-Myers Squibb.

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Bilateral visual improvement after unilateral optic canal decompression and cranial vault expansion in a patient with osteopetrosis, narrowed optic canals, and increased intracranial pressure

Osteopetrosis (Albers-Schönberg disease, marble bones) is a relatively rare disease that is caused by increased skeletal mass and bone density. It results from a defect in the development or function of osteoclasts with consequent impairment of bone resorption. The defect may be intrinsic to the osteoclast lineage or the mesenchymal cells that support the development and activation of the osteoclasts. Osteopetrosis is inheritable, and four clinical forms have been distinguished: autosomal-recessive malignant, autosomal-dominant benign, mild autosomal-recessive, and autosomal-recessive osteopetrosis with renal tubular acidosis. Of the four, the first two are the most prevalent. The disease is characterised clinically by multiple fractures, abnormally shaped bone, and anaemia. Its neurological manifestations include cerebrovascular complications, peripheral nerve palsies, papilloedema, and blindness from optic nerve atrophy. Optic nerve atrophy is common and can result from the chronic effects of papilloedema or compression by a narrowed optic canal. Optic neuropathy associated with papilloedema can be prevented by aggressive management of intracranial pressure (ICP), whereas that associated with narrowing of the optic canal is usually treated by neurosurgical decompression.

A 19-year-old man, diagnosed with autosomal-recessive osteopetrosis at about 5 months of age, presented in March 1997 with a dramatic decline in vision. He previously had had an acuity of 20/30 in his right eye, 20/50 in his left eye, and full visual fields for most of his life. A brain CT in 1986 showed no optic canal narrowing. In 1994, he developed increased ICP and underwent a left optic nerve sheath fenestration and placement of a lumbo-peritoneal shunt (LPS). His vision remained normal until August of 1996 when he began to experience declining vision. He was referred to the Johns Hopkins Hospital in March of 1997.

Visual acuity with correction was 20/200 in each eye. Near vision was 20/400 in each eye. Visual fields were limited in each eye to a tiny paracentral area of about 5 degrees. Colour vision was markedly impaired, with the patient being unable to identify any of the figures on the Hardy-Rand-Rittler (ERR) pseudochromatic plates. Pupils were equal and reactive to light, and there was a left relative afferent papillary defect of 0.3 log units when measured using a neutral density filter. Extraocular movements were normal. Ophthalmoscopy disclosed bilaterally pale optic discs.

Non-contrast CT of the head showed marked diffuse thickening of the calvarium with a ground glass appearance. The bony dysplasia involved the skull base, and there was narrowing of both optic canals, the petrous carotid canals, the internal auditory canals, and the cochlear and vestibular apparatus (figure A). There was also ossification of the mastoid and frontal sinuses. The CT also showed evidence of increased ICP, including a dilated third ventricle. An indium radionuclide study showed that the LPS catheter was patent, but ultrasonography demonstrated bilateral enlargement of the retrobulbar optic nerves and a positive 30 degree test, consistent with increased ICP, and a lumbar puncture disclosed an opening pressure of 450 mm Hg, with normal CSF contents.

Consideration was given to treating the patient with acetazolamide, but because of the severity of visual loss associated with pale optic discs, and because it was unclear if his decreased visual function was caused by compression of the optic nerves by the narrowed optic canals or increased ICP, it was decided to perform bilateral non-simultaneous optic canal decompressions combined with a cranial vault expansion. A bicornal incision was made, a full thickness scalp flap was turned down to the level of the superior orbital rims bilaterally, and a large bifrontal bone flap was removed. The roof of the right optic canal was then removed along its entire length using a high speed drill and curettes. The bone flap, which was 3 cm thick, was thinned to about 1 cm and replaced, producing a significant cranial expansion.

Four days after surgery, the patient's visual acuity had improved to 20/30 bilaterally, he could correctly identify figures on seven of 10 HRR plates with the right eye and six of 10 colour plates with the left eye, and his visual fields were markedly expanded, almost to normal. A postoperative CT confirmed complete unroofing of the right optic canal (figure B).

Osteopetrosis related visual loss is often ascribed to optic nerve compression secondary to the narrowing of the optic foramina. However, optic nerve dysfunction can also result from the effects of increased ICP. Because our patient's unilateral optic canal decompression resulted in bilateral improvement in visual acuity and visual fields, it is reasonable to conclude that increased ICP and not narrowing of the optic canals was the cause of his visual deterioration. Thus, the cranial vault expansion that was performed in addition to the unilateral optic canal decompression was responsible for the rapid and dramatic improvement in the patient's visual function.

This case provides an important lesson on the evaluation of any patient with optic neuropathy that is presumed to be secondary to narrowing of optic canals in the setting of one of the craniosenoses. Although direct compression may indeed be primarily responsible for visual deterioration in patients with osteopetrosis and related conditions, increased ICP, related to either thickening of the skull or secondary occlusion of one of the cerebral venous sinuses, should always be considered a potential aetiology, and aggressively treated when identified or suspected.
The London handicap scale

Jenkinson et al. show that London handicap scale scores are about the same if items are weight equally rather than using the published scale weights. We reached much the same conclusion using the data from which the scale weights were derived.

Handicap is defined as disadvantage in role performance due to impairments or disabilities, which implies valuation of the extent to which role performance is affected. Value—from the viewpoint of health services research—is quantified as the "utility" of a state of health. The scale weights were derived by asking various population samples to value different combinations of problems, described using the handicap dimensions and items from the handicap scale. These were analysed to determine the contribution of each of the component parts of the description.

The fact that equal weighting gives roughly the same scores as the empirically derived weights is probably because the items were carefully chosen on the basis of clinical experience to be approximately equally spaced across the range of possible severity. Does it matter if different weighting methods lead to much the same results? Weighting processes are inexact, but they empirically derived or equal weighting, but the second approach simply increases the level of approximation. The 95% confidence intervals around the agreement between estimated and approximated values are derived or equal weighting, but the second approach simply increases the level of approximation. The 95% confidence intervals derived or equal weighting, but the second approach simply increases the level of approximation. The 95% confidence intervals derived or equal weighting, but the second approach simply increases the level of approximation. The 95% confidence intervals derived or equal weighting, but the second approach simply increases the level of approximation. The 95% confidence intervals derived or equal weighting, but the second approach simply increases the level of approximation. The 95% confidence intervals derived or equal weighting, but the second approach simply increases the level of approximation.
In the study of Stocchetti et al villages without a neurosurgeon have a total area. In the study of Stocchetti et al villages without a neurosurgeon have a

(3) When applying Cavalieri's principle it becomes mathematically possible to calculate the coefficient of error of the individual lesion mass volume. It declines in direct proportion to the total number of CT planes and to the total number of grid intersection points. Generally, a coefficient of error of less than 0.05 is obtained if the number of CT planes used is 10 or more, and the number of grid intersection points is 50 or more. 0.05 is obtained if the number of CT planes (I=normal, II=diffuse injury, III=diffuse injury with swelling, IV=diffuse injury with shift, V=operated mass lesion, and VI=non-operated mass lesion). Intracranial mass lesions are rarely measured, it is reassuring that some centres have documented expertise in such measurement. We do not think, however, that our data, and the conclusions drawn from them, are potentially misleading, and we will try to clarify our arguments.

As indicated in the paper, we compared two pragmatic methods and a computer based method. There are, of course, limitations to each method, and tracing on the computer screen can be tricky, however, a careful tracing is feasible in expert hands and we think that the resulting calculation still gives a very acceptable reference point. If this reference method is to be questioned, an appropriate, preferably superior, method should be identified. We cannot think of any pragmatic method that would be the best choice. Regarding the other points that aroused the concern of Vos et al, we agree on many and will try to clarify them.

(1) Randomness is an important prerequisite; it was not mentioned in the paper but the grid was placed on the CT slices at each reader's convenience and choice. Whether this was random or not is debatable, but it seems to ensure an adequate guarantee against systematic error.

(2) Our data did not obscure the beauties of the Cavalieri method of direct estimation, performed better than the Ellipsoid method, particularly for irregularly shaped lesions. We agree that the method performs even better with bigger lesions reconstructed using thin slices. As one of our goals was to describe feasibility, however, the comments of Vos et al further stress that the best can be obtained from the Cavalieri method at the price of more time and work, as we verified and reported in the paper. Counting more than 50 points in more than 10 slices adds to the precision, but seriously increases the burden of measurements.

(3) We did not base our comparison only on mean data. We stress the concern of Vos et al on the analysis of mean data to the extent that we have used another method, based on that of Bland and Altman. This method compares every single lesion, obtained with each method, against the corresponding reference value. The results of this detailed comparison are illustrated in figs 1 and 2 of our paper. Numerical data, summarising the analysis according to Bland and Altman, are reported in the text and table. Both in the results section and in the discussion we stated that the mean data were not able to describe the discrepancies found in single cases.

(4) Accordingly, we assessed interobserver variability by ANOVA of individual measurements, and not of the mean data. In other words, we asked whether the measurement of any specific lesion by one examiner was significantly different from the other examiners' results. The ANOVA on the readings by the three examiners using the Ellipsoid method gave a p value of 0.86, and the same analysis applied to the Cavalieri direct estimator gave a p value of 0.81; we therefore concluded that this analysis excluded significant differences. It cannot be said that our interobserver variability was not omitted, but was in fact logically considered, and we must apologise if the text was not clear.

(5) We agree with the final paragraph of Vos et al on the structure of the Marshall classification, in which volume is one part of the grading. That was correctly indicated in our paper. From our experience in multicentre, international clinical trials, we are less optimistic about the proper use of the TCDB CT classification, but that is another point in favour of improving the methods for CT readings.

In conclusion we have applied a methodology that seems solid enough to substantiate our conclusion and, we hope, to fulfil the requirements of careful and competent readers.

NINO STOCCHETTI AND ANGELO COLombo

This two volume book is unique in providing a comprehensive overview of all the aspects of basic neuroscience relevant to the neurosurgeon. As such it can be regarded as an essential source of information for neurosurgical trainees around the world. The authors state in the foreword to this edition that their ambition was to "reflect in as up to date fashion as possible the expanding knowledge so essential both to trainees and established neurosurgeons alike if they are to base their clinical practice on a proper scientific basis." They can be congratulated on fulfilling their objective with such a well presented and beautifully illustrated new edition. Although clearly intended for a neurosurgical readership, there are sections that are likely to prove valuable for practitioners in other disciplines, particularly neurologists, oncologists, and orthopaedic surgeons involved in spinal surgery.

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BOOK REVIEWS


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clincial neurosurgeon. There are now and increased sections covering genetics, embrodology, biomechanics, and measurement, bringing the total of chapters to 83 in 11 sections. An additional feature distinguishing it from the blue second edition is the handsome red cover, perhaps unconsciously reflecting changes in the political climate! Each chapter is very clearly laid out with an introductory outline, well structured headings, a summary, relevant references, and a list of further reading. The manuscript is well proportioned, confining experts to present their knowledge in a concise manner in quite short chapters. This means that the reader can quickly assimilate the aspects of importance. The devotion of a section to biomechanics appears justified. The field has expanded rapidly and is a field that contains concepts with which the neurosurgeon should, at the very least, be familiar. Knowledge of how the spine responds to forces after injury and following fixation is a prerequisite to planning treatment. This has been well described, with plenty of good illustrations and radiographic images.

The chapters in the new section “Measure- ment and the Neurosurgeon” are welcome. They have been written in a fresh, understandable style that is kind to the reader and have been specifically targeted to the neurosurgeon. The wealth of information contained in this section is generous. Much useful information is to be found there, but also to those who might find themselves on the other side of the table.

**RUPERT KETT-WHITE**


Information is a vital tool for patients wishing to gain more control over their lives. Different sources of information will suit different patients, and this book is a useful addition to the range of available resources. Its strength comes from the authors immense clinical experience. Its weakness is that it is too hospital centred. A formidable fist of potential investigations is described (including PET). Idiopathic Parkinson’s disease is described as a diagnosis of exclusion. which will certainly alarm the neuroradiologists in my health dis- trict.

Patients are given invaluable forewarning of conditions in a late 20th century British hospital: “Don’t expect to be seen at the time specified on the appointment letter...” “You may see a different doctor each time”; “The neurologist may know very little about the individual’s circumstances and about him or her as a person”. Some advice about how to complain would have been invaluable. Readers are advised that “You may be presented to a large number of doctors in the course of a clinical presentation” but there is no mention of multidisciplinary case conferences, how to deal with a therapist, or hospital discharge planning.

The limited information about community care arrangements is dated, making no men- tion of care management, or of the statutory right of carers to have their own needs separately assessed. There is an invaluable and fairly comprehensive list of non-statutory resources, although much more could have been said about management of difficulties in car mobility. Oddly, wheelchairs are not in the index and get scant attention in the text. There are two unusually helpful sections on sexual dysfunction, but not enough on the management of sleep disorders. Levodopa does increase alertness in some patients, but not in others, and in my experience improved night time mobility can sometimes improve sleep. Books of this type can never suit everyone and can never be comprehensive, but there is plenty of useful and accessible informa- tion in this one. I commend it to patients and families and especially to neurologists.

**CHRISTOPHER WARD**


The express aim of the editor of this book was to create “a master reference file on the field of neuroimaging”. This may sound somewhat enigmatic, particularly as, in Europe at least, we recognise two ways of using imaging: to look at the nervous system: neuroradiology, a clinical specialty practiced by organ special- ised radiologists familiar with a wide range of techniques, closely related to the clinical neuro- rosciences to which this journal is devoted— neurology, neurosurgery and psychiatry—and neuroimaging, usually the domain of physi- cists, psychologists, or neuroscientists expert in the application of a single technique, the impact of which on routine clinical practice has, it can be argued, often been neglected. A failure to distinguish clearly between the two markedly upsets the balance of this book.

The text is divided into four sections: history and technology (16 chapters); brain (11); head, neck, and spine (13, of which only four deal with the spine); and paediatrics (10). In each the space devoted to some sub- jects seems inversely proportional to their clinical impact. Thus, in section I, the physical- basis of CT and MRI merits 24 pages, with 15 references, whereas functional MRI occupies 22 pages, supported by no fewer than 154 references. Functional MRI is in vogue, but come on, what about a sense of proportion? If that were not enough, two chapters on radionuclide studies (PET and SPECT respectively) have 60 pages of text between them, with 1011 references; one could be forgiven for wondering if the author had simply downloaded his Reference Manager!!! I can only suppose the reason magnetic spins were taken up 22 pages, with 117 references, must be that it is one of the editor’s hobby horses.

To put things in perspective, a chapter of about 50 pages on cerebral angiography devotes 46 pages in depth to tech- nique, etc (of which two, on arch aortogra- phy, include the provocative statement that “the aortic arch angiogram should be evalu- ated before any vertebral arteries are cannula- ted”), 10 lines to indications, including the questionable statement (in the age of MRI) that intra-arterial injection should be used to detect arterial dissection. I failed to find a description of spinal angiography or its indications. Spinal arteriovenous malforma- tions or fistulae do not appear in the index. It would be tedious to go through the rest of the two volumes in the same way, but cer- tain things stand out. Children’s brain tumours, admittedly photogenic but usually not a source of significant problems, occupy 80 pages (plus 651 references), while that most difficult and complex field, paediatric metabolic and endocrine disease, in which a source of definitive information, helpfully presented, would have been invaluable for the jobbing neurologist, paedia- trician, or neuroradiologist, is given rather superficial treatment in 23 pages, with 97 references. In several chapters, too many cita- tions are of other radiology textbooks rather than of authoritative source material.

The chapter on degenerative disease of the spine, written by musculoskeletal specialists who seem to deal principally with orthopaed- ic surgeons or rheumatologists, is out of place in a book on neuroimaging (however defined). It deals largely with plain films, and does not address the issues germane to neurological practice; furthermore, like a number of the contributions in this work, it is a discussion of postoperative appearances and surgical instrumentation, essential knowledge for today’s clinicians. Chapter 50, on hydro- cephalus and cerebrospinal fluid dynamics, should carry a hazard warning that it presents views so personal as to be not only idiosyn- cratic but potentially misleading. Conversely, the chapter on the orbit and visual system, sensibly concentrating on the use of CT for the former, is admirable, apart from the cap- tions to figure 77: the lesion described as a dermoid is almost certainly a dermolipoma.

Some 73 North American authors, few—as yet—major international figures, contributed to the 52 chapters, more than a dozen of which are the result of collaboration between at least three people. As this might lead one to expect, the literary and intellectual level, including the critical evaluation of the literature central to review-type chapters, is very variable. How- ever, the illustrations are almost uniformly excellent and the 75 page index, included in both volumes, if also somewhat idiosyn- cratic and voluminous, is generous. Much useful information is to be found between these hard covers, although for me the book fails to live up to the promise of the rather facetious foreword. Does it deserve a place on that already perilously overburdened departmental bookshelf? Neuroimagers will, I imagine, identify rival texts as more suited to their specially focused needs; trained neurora- diologists will indeed find much valuable reference material, but also some worrisome deficiencies and debatable notions. **IVAN MOSELEY**


This is a multiauthor reference book with contributions from epidemiologists, neurora- diologists, neurologists, and cardiologists. It succeeds in being both comprehensive and concise, making it a valuable book to have available to “dip into”. However, it is quite a long haul to read from start to finish.
There are chapters of practical use to physicians in both community and hospital based, who are involved in vascular risk factor management and specifically the primary and secondary prevention of stroke. For example, the chapter on "when to anticoagulate and at what dose" is particularly useful. Topics such as lipid lowering, antiplatelet strategies, and the management of carotid disease are covered well with pragmatic advice based on the available evidence. Where there are gaps in the evidence is also clearly stated.

There is a helpful section on haematological disorders and stroke risk with detailed information on the congenital and acquired thrombophilias and advice on routine screening for these problems. A chapter devoted to the aetiology of "young stroke" is particularly welcome. At the cellular level there is a fascinating chapter on the molecular mechanisms affecting the development of symptomatic carotid plaques—obviously fertile ground for further research.

Contained within each chapter are helpful tables usually summarising results from available randomised controlled trials and there are some clear schematic diagrams to illustrate relevant pathophysiological and biochemical pathways. In summary this book would be an excellent addition to any hospital or community service involved in this very important subject. It will be of value to general practitioners, physicians, cardiologists, neurologists, and trainees.

LIZ WARBURTON


This is an incredibly enjoyable book, which provides a fascinating insight into the history of neuroscience. It was devised by the late A Earl Walker and has been put together as a tribute to his industrious efforts to trace the history of neuroscience from ancient to modern times, and it serves as a fine tribute to him. The book builds through 11 chapters from prehistoric times through Galen and Vesalius to the founders of modern day neurology from the later part of the 19th century. The book contains endless fascinating insights into multiple aspects of neuroscience and although the illustrations are a little disappointing in parts there are some rare pictures, such as one of James Parkinson himself.

The book opens with a series of chapters which lay out the historical perspective of neuroscience, following which chapters detailing specific conditions are presented. Thus in the chapter on peripheral nerves we discover that Rollo in 1797 first described diabetic neuropathy, whereas Bonnius in 1642 first described heri-bori. Those chapters on regional neurology then pass on to the final chapters of the book that deal with the evolution of neurosurgery, which details in particular the first descriptions of various brain tumours. The book concludes with a chapter on the modern age of neuroscience and a magnificent list of references. If these were not enough, we are then treated to three appendices on art and neurology, medical fees, and a glossary of neurological syndromes. All most illuminating, although the account on art and neurology is not as exhaustive as it could be, given the fascinating speculations that are rife in this area. For example, what was the problem with Monet giving rise to his visual failure in later life and what, if anything, is the neurological abnormality shown in Dürer’s drawing of praying hands. This book is, though, a treasure trove of fascinating facts—for example, it was news to me that Galen was the first to describe the corpus callosum while the quadrigeminal bodies had to wait until Willis before they were acknowledged. This attention to detail and the ingenuity of these earlier investigators is inspiring, although many of these early investigators may have run into problems with local ethics committees or the Home Office inspector—for example, Galen cut the spinal cord at a time when it was not observed on the modern state of the animal. Indeed the industry of some of these early investigators is to be greatly admired. For example, Raymond de Vieussens de Montpellier dissected 500 fixed brains in his bid to clarify some of the finer points of neuroanatomy.

A book such as this is always going to struggle to define its audience, not least because historical biographies are irrelevant to the high tech age of molecular genetics and functional imaging. If we can see the acetylcholine receptor at the resolution of a few Angstroms, why bother with the gross techniques of years gone by. However, there is much to admire and learn about through a knowledge of the pioneering days of neuroscience, and the elucidation of anatomical structures along with clinical conditions. It teaches much about diligence and thoughtful investigation as well as ingenuity in the face of seemingly intractable problems and scientific dogma. It is a book that is, therefore, not solely relegated to that of source material for quiz questions but reminds us of how our specialty took shape. It documents the influences that have made neurology and neurosurgery what it is today and the inspiration that has fallen on individuals over the ages and through whom we have made giant leaps in our understanding of how the brain works in health and disease. As you might have guessed by now, I loved this book and strongly recommend it to others.

ROGER BARKER


This book undertakes an extensive review of the fast moving field of cell death, an area of neurobiology that is currently the centre of intensive investigation both at the level of mechanisms and disease pathogenesis. The book divides into four sections that move from cellular and molecular mechanisms to animal models and human disease with possible therapeutic interventions bringing up the rear. It is thus a book that will interest both neuroscientists and neurologists alike, albeit a rather select group in each case.

The chapters are generally well written although a little sparse on illustrations, which can make some of the chapters quite daunting and intimidating. For example, the chapter on Parkinson’s disease has only one figure in 12 pages of text, which tends to put all but the most dedicated reader off. In this chapter there is also evidence of some delay from the time of writing to publication as there is no real mention of the recent genetic advances in familial Parkinson’s disease which should be in there given that the book was published in 1999. This is a pity given that this is currently a burgeoning field and the possible contribution of these genetic defects (for example, α-synuclein and parkin) in understanding the pathogenesis of idiopathic Parkinson’s disease is a major research interest at the present time. However other chapters are more up to date; for example, the chapter on Huntington’s disease discusses intranuclear inclusions even though their significance is still currently not known—do they represent a precursor to cell death or a marker of cellular neuroprotection?

Overall though the book is well presented both in terms of the topics selected and their discussion with a generally high quality of figures, including a series of rather beautiful colour plates in the middle of the book. It is therefore a book that will be a useful addition to the libraries of neurologists with an interest in neurodegenerative disorders, although other neurological conditions associated with neuronal death are touched on (for example, viral encephalitis, HIV-1 infection, trauma, and schizophrenia) which may widen its appeal. However this book will probably only ultimately interest those seeking greater neuroscientific understanding of neuronal cell loss and as such will bypass most neurologists.