then out for over five seconds whilst recording the R-R interval. The maximum and minimum R-R intervals were converted to heart rates, with the difference between them being the heart rate variability.

Three Valsalva manoeuvres were performed consecutively for each patient as described by Ewing and the Valsalva ratio was calculated for each. The Valsalva ratio from the first manoeuvre was compared with the mean-of-three. Heart rate variability was obtained from a mean-of-six deep breaths and from a single deep breath performed in random order.

In 17 patients with a mean-of-three-derived Valsalva ratio less than 1:21 (abnormal according to previous criteria) there was a single Valsalva ratio less than 1:21. Seventeen patients had a mean-of-six-derived Valsalva ratio greater than 1:21 and a single Valsalva ratio greater than 1:21. Twenty three of 24 patients with a mean-of-six-derived heart rate variability less than, or equal to, 10 beats per minute (abnormal according to previous criteria) also had a single breath-derived heart rate variability less than, or equal to, 10 beats per minute. Nine of 10 patients with mean-of-six-derived heart rate variability greater than 10 beats per minute (normal or borderline according to previous criteria) also had a single breath-derived heart rate variability greater than 10 beats per minute.

Thus a single Valsalva ratio finds the same result as a mean-of-three-derived Valsalva ratio with a sensitivity of 16/17 (94%) and a specificity of 17/19 (86%). Similarly, a single breath-derived heart rate variability gave the same result as a mean-of-six-derived heart rate variability with a sensitivity of 23/24 (96%) and a specificity of 9/12 (75%). The Valsalva data were further analysed by estimating the component of the three Valsalva ratio readings from each patient. In keeping with the hypothesis that one Valsalva manoeuvre is sufficient, within-subject variance (0.11) was extremely small in comparison to between-subject variance (4.17).

The mean (SEM) time taken to do a single Valsalva ratio and a single breath heart rate variability (570 (0.74) minutes) was significantly less than that to do three Valsalva ratios and derive the heart rate variability from a mean of six breaths (1438 (0.68) minutes, p < 0.0001).

It is proposed that any single Valsalva ratio and a single breath-derived heart rate variability gave similar results to those derived from multiple procedures and took far less time to perform. There were only a small number of cases where there were discrepancies with the classification of a patient as normal or not. As there is no gold standard for the presence or absence of autonomic neuropathy in a particular patient it is not possible to rule out a possibility of discrepancy, whether the multiple tests were right, or vice versa. As it turned out, in most of these cases of discrepancy, the actual numerical values were similar, differing little on different sides of the lower limit of normal used.

Many patients find the Valsalva manoeuvre uncomfortable and performing three consecutively is considerably more of an ordeal for the patient than performing just one. The single deep breath is an extremely quick and simple test. There would seem to be no benefit to be gained from continuing to use the test, thus three single manoeuvres and six deep breaths when performing cardiovascular autonomic function tests. Use of the shortened tests should enable more patients to be studied more quickly and easily, without loss of accuracy of testing, as long as the test is performed properly.

In the assessment of autonomic neuropathy a battery of tests is considered preferable to relying on just one. A battery of five tests has been proposed by Ewing and Clarke and these are well established and much used around the world for clinical and research purposes. Nevertheless, it has recently been proposed that a battery based on O'Brien and coworkers may be preferable. Several potential advantages for the tests in the latter battery, compared with those in the battery of Ewing, have been suggested—that they are easier and quicker to perform, more comfortable for the patients, and more accurate. In that they use age-related normal ranges based on a large group of normal subjects, and they generate less artifacts. As this “O'Brien battery” uses only one deep breath and one Valsalva manoeuvre, the findings of our study add further weight to the arguments in favour of its general adoption as the cardiovascular battery of choice in the assessment of autonomic neuropathy.

KT MORTIARY
REJ RYDER
CA HARDSTY
Diabetes Research Unit,
Clinical Sciences Centre,
Northern General Hospital,
Sheffield S7 5AU, UK


Benign relapsing meningomyelitis

Myelitis and encephalomyelitis are relatively common both as monophasic and relapsing diseases. Investigation of an infective cause is essential at the first presentation particularly if the cerebrospinal fluid has inflammatory features. Multiple sclerosis would be the most common diagnosis in those cases with a relapsing course.

We describe a young man who presented at 10, 13 and 16 years with three stereotyped attacks of meningomyelitis. Aetiological investigations were negative and we found only one report on three similar cases in the literature.

The boy was born in 1972, lived in Paris and returned to Portugal when he was eight. He currently lives in a small village working as a shoemaker.

In December 1983 he presented with fever, vomiting and headache which was followed by drowsiness and an inability to walk. When first seen two weeks later he appeared very sleepy but cooperative. Neurological examination revealed a flaccid paraparesis, sensory loss from the T8 level, urinary retention and almost absent tendon reflexes with extensor plantar responses. He was febrile (40C) and the cerebrospinal fluid contained 101010 1 cells (mainly lymphocytes), 0.70 g/1 protein and 2.75 mmol/l glucose. Four days later he was paraplegic with a higher sensory level (T4) and some respiratory distress. He was treated with dexamethasone and to cover the possibility of tuberculosis infection isoniazid, rifampycin and streptomycin was started. After two weeks there was gradual recovery of motor, bladder and sensory functions which was complete by four months.

In December 1985 he developed a second episode. After a short period of fever and myalgia he developed a flaccid and areflexic paraparesis with a sensory loss below T8, urinary retention and bilateral extensor plantar responses. Three days later he progressed to a tetraplegia with increasing respiratory difficulty and he required intubation for eight days. The CSF showed 94 x109 1 cells (mainly lymphocytes), 3.91 mmol/l glucose and 0.06 g/l protein. After a month he recovered almost completely and at four years had no neurological problems and was entirely normal. During this admission he was treated with sulphasalazine and trimethoprim for an intercurrent urinary tract infection.

His third episode occurred in December 1988 when he presented with pyrexia, headache and drowsiness. When aroused he was confused and agressive. Over the next few days a flaccid and areflexic tetraparesis again developed. There was no evidence of a sensory level but proiceproprone was impaired and urinary retention was present. The cerebrospinal fluid contained 64 x109 1 cells/l (lymphocytes), 2.74 mmol/l glucose and 0.92 g/l protein. During recovery a spastic paraparesis emerged and a cerebellar syndrome with nystagmus, scanning speech, and bilateral dysmetria was noted. A few months later the neurological examination was again normal. During this admission he was treated with dexamethasone and ceftriaxone to cover the possibility of Lyme disease.

During the three admissions the following investigations were normal or negative: aches and pains in the serum: red and white cell blood counts, haemocrit, erythrocyte sedimentation rate, electrolytes, urea nitrogen, creatinine, glucose, liver and kidney function tests, complement titres, rheumatoid factor, antinuclear antibodies and LE-cell tests, serum complement and immune complex levels; VDRL tests; and FTA-ABS tests, Wright (Brucella serology, agglutination test) Rose Bengal Plate test, Widal and Weil-Felix reactions, Paul-Bunnel test, serological tests for hepatitis B surface antigen and antibody and syphilis, mycoplasmal and human immunodeficiency (HIV1 and HIV2), CMV IgG and IgM complement fixation titre, complement fixation titres for other viruses (herpesvirus, adenosivirus, parainfluenzae 1 and 3, measles, mumps, respiratory syncytial virus) and convalescent periods, indirect immunofluorescent test for Lyme disease (Institut Pasteur, Paris) and serological tests for toxoplasma and fungi.

In the CSF there were normal or negative results for: microscopical examination of stained specimens (Gram) and cultures for aerobes, anaerobes, Brucella, fungi, acid-fast bacilli, bacteria and viruses such as enterovirus, coxsackie, rubella, echovirus, mumps, parainfluenzae, echovirus, varicella, herpes simplex, hepatitis B antigen and Epstein-Barr virus. Automated screening methods for cryptococcus, complement fixation titres for virus in acute and convalescent periods,
indirect immunofluorescent test for Lyme disease (Institut Pasteur, Paris), Rose Bengal Plate test, immunoelctrophoresis and IgG secretion index. After the last episode electro-physiological studies (motor conduction velocity and F wave latency in the legs, brainstem auditory evoked responses, visual evoked responses) and a cerebral and whole spinal cord MRI scans were all normal.

Our patient had recurrent meningomyelitis and latterly encephalitis, in which each episode was preceded by fever and myalgia and developing severe neurological deficits requiring, on one occasion, mechanical ventilation. In spite of the severity of the motor and sensory dysfunction there was never complete recovery. The initial CSF inflammatory profile was the only abnormality found. All the other repeated investigations were normal or negative. We can only find one similar report in the literature.1


Creutzfeld-Jacob disease following cadaveric dura mater graft

There have been three previous reports of Creutzfeld-Jacob disease (CJD) following repair of dural defects by surgical grafting of commercially prepared, lyophilised cadaveric dura mater, one each from USA,1 New Zealand2 and Italy.3 We have recently seen the first case of CJD in the United Kingdom presumed to have been transmitted by cadaveric dura mater graft.

In October 1985 a 26 year old man had a foramen magnum decompression and cervical laminectomy for syringomyelia and cervical cord compression. During the procedure a dural graft was stitched from the level of the third cervical vertebra to the occiput. Post-operatively he had a spastic gait and an ataxic left arm with spinothalamic sensory loss, but he remained independent and worked as a builder. In August 1989, at the age of 30, he became increasingly withdrawn: he had difficulty recognising people, and his speech, comprehension and balance became impaired. On admission to hospital in September 1989 he was alert but severely dysphasic and dysarthric. He had a spastic tetraparesis and ataxia of all four limbs. He was unable to feed himself or walk unaided. Haematological and biochemical investigation and enhanced CT brain scan were normal. The cerebrospinal fluid was acellular with protein 0-9g/l and normal glucose. He deteriorated and became drowsy and more severely atactic, and developed frequent myoclonic jerks. The electroencephalogram evolved into a pattern of intermittent repetitive triangular wave complexes on a background of generalised irregular slow-frequency activity characteristic of CJD. He died in December 1989, four months after the onset of symptoms.

Histological examination of the brain showed widespread spongiform degeneration with gliosis and neuronal loss involving the neocortex, striatum and cerebellum.

This patient’s illness began 46 months after insertion of the dural graft, compared with intervals of 19, 31, and 44 months for the other three reported cases who were 28, 25 and 27 years old respectively. All four patients are considerably younger than the mean age of 63 years for sporadic cases occurring in the UK in whom no aetiological factors have been identified.4 They had all received the same type of lyophilised human cadaveric dura mater material, manufactured by B Braun Melsungen AG, Germany, and all the grafts were inserted within a 20 month period between May 1985 and November 1986. The transmissible agent thought to be responsible for CJD is resistant to inactivation by boiling, 10% formaldehyde and ultraviolet or ionizing radiation, but it can be inactivated by autoclaving at 134°C for 18 minutes, or by immersion in 1 molar NaOH for one hour. The latter treatment has been incorporated into the manufacture of “Lyodura” since 1987.5 Since its introduction in 1969, over half a million packages of “Lyodura” have been used but only four cases of CJD in this group of patients have been reported to date: the risk of CJD related to “Lyodura” therefore seems low.

The implications arising from these cases are clear: autologous graft material should be used where possible. Appropriate standards should be applied in selection and preparation of donor material and physicians should be alert to this relationship in patients with a previous history of neurosurgery who develop a demenitising illness.

H WILLSON AN GALE JE MCLAUGHLIN
Departments of Neurology and Histopathology, Royal Free Hospital, London, UK


MATTERS ARISING

Ticlopidine, a new anti-thrombotic drug

In your editorial! Charles Warlow answers the question: “Ticlopidine, a new anti-thrombotic drug: but is it better than aspirin for long term use?”. The editorial gives a lot of important information. However, I like to make some comments:

1) Professor Warlow says that there has been no large trial of aspirin alone in major ischaemic stroke. In one of the large secon-
Benign relapsing meningo-myelitis.

L M Monteiro and M Correia

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