legs was beneficial, and he was able to walk occasionally without assistance.

Autonomic function tests were performed after weaning from mechanical ventilation.⁴ A catheter was inserted into the left radial artery, and vital signs were monitored. Head up tilting to 60° resulted in a blood pressure fall from 134/99 to 51/48 mm Hg. The basal plasma noradrenaline concentration was normal. A rise of plasma vasopressin in response to hypotension was absent, suggesting involvement of the afferent baroreflex pathway. There was no overshoot with Valsalva's manoeuvre, which suggested insufficient baroreflex function. The absence of a blood pressure rise to the cold pressor test suggested involvement of the efferent sympathetic system. A noradrenaline infusion test disclosed sympathetic supersensitivity. No β -1 supersensitivity in response to an isoprenaline infusion test was seen.⁴ Increase of his heart rate from 90 to 109 per minute in response to an atropine test showed that the vagal efferents were not completely involved. The results of the remaining autonomic tests were normal.

The control of blood pressure after postural change is mediated by the baroreflex system. Failure of this reflex function can be due to a lesion anywhere in this reflex pathway. Impulses from the baroreceptors, originating from the carotid sinus and aortic arch, travel via the glossopharyngeal and vagal nerves. Most of these baroreceptor afferents terminate in the nucleus tractus solitarius, the major nuclear relay of the baroreflex.^{1,2,3} In addition, the nucleus tractus solitarius not only regulates baroreceptor pathways but is also involved in the central regulation of respiration and swallowing.²⁵ The glossopharyngeal and vagal nerves also convey the sensory impulses from the pharynx, larynx, and the respiratory system to the nucleus tractus solitarius, which contains specific centres for respiration and swallowing.²⁵ Our patient presented with severe orthostatic hypotension, dysphagia, lingual atrophy, and temporary failure of automatic respiration, but had no pyramidal signs, sensory impairment, cerebellar ataxia, or a neurogenic bladder. Although we cannot discuss the relation of a non-metastatic autonomic neuropathy, neither spinal nor peripheral nerve lesions were found. Investigations of the somatic and autonomic functions suggested a medullary lesion. Severe orthostatic hypotension, the absence of overshoot of Valsalva's manoeuvre, a negative response to the cold water test, and a positive response to the atropine test are consistent with an incomplete failure of the baroreflex arc. Although it is difficult to determine the definite lesion responsible for the failure of the baroreflex arc, a tumour located in the dorsal medulla may cause impairment of the nucleus tractus solitarius, the dorsal vagal nucleus, and the hypoglossal nucleus, which are located in close proximity in the dorsal medulla.²⁵

In conclusion, a localised lesion of the dorsal medulla as reported in this case may result in severe orthostatic hypotension, bulbar palsy, and failure of automatic respiration in the absence of pyramidal or sensorimotor signs in the limbs.

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Tardive dystonia after neuroleptic treatment of Tourette's syndrome

We report a patient with Tourette's syndrome who developed tardive dystonia manifest by a task specific, action induced oromandibular dystonia after 15 years of treatment with haloperidol.

A 28 year old man with Tourette's syndrome since the age of seven had been treated with haloperidol (2-4 mg daily) with good effect since the age of 13. Motor and vocal tics had included eye blinking, facial grimacing, shoulder shrugging, head and neck movements, humming and squeaking noises, and occasional snapping-shut jaw movements. Obsessive-compulsive features included repetitive touching and counting behaviours. At the age of 28, he developed severe dystonic movements of the jaw, mouth, and tongue for the first time, which were activated by speaking. Immediately on beginning to speak he displayed forceful dystonic jaw opening and buccolingual movements associated with a pronounced dysarthria. He could prevent these by speaking with a finger or pencil clenched between his teeth. The mouth movements were absent at rest and were not activated by eating or non-verbal jaw movements. There were also mild choreic movements of the hands and fingers. After stopping haloperidol there was transient exacerbation of jaw movements which lasted for several weeks followed by persistent speech activated jaw opening oromandibular dystonia, which remained unchanged for the next 10 months. Eye blinking and cervical tics exacerbated when haloperidol treatment was stopped, and were treated with clonazepam with partial benefit. Benzotropine and tetra-benazine were unhelpful for the oromandibular dystonia but beginning 10 months after onset there was slow improvement followed by complete resolution of the jaw dystonia, which has now been absent for 18 months.

Tardive dyskinesia and tardive dystonia have only rarely been reported in patients with Tourette's syndrome after chronic neuroleptic treatment.^{1,2} Our patient developed an action induced oromandibular dystonia after 15 years of treatment with haloperidol. Diagnosis of tardive dystonia occurring on a

background of Tourette's syndrome may be difficult. In this case, the patient's dystonia differed from dystonic tics sometimes associated with Tourette's syndrome in being highly localised, action induced, repetitive, patterned, not suppressible, and unaccompanied by an urge to move.³ His severe dysarthria was also more consistent with oromandibular dystonia than a dystonic jaw tic. Because cranial and cervical dystonia have been reported in a few patients with tic disorders not exposed to neuroleptic drugs,^{4,5} the possibility of a coincident primary dystonia unrelated to neuroleptic drugs also deserves consideration. The history of prolonged neuroleptic exposure, exacerbation of dystonia after stopping haloperidol, and disappearance of dystonia over 12 months after stopping haloperidol are clinical features much more indicative of tardive dystonia induced by neuroleptic drugs than spontaneous dystonia.

Although tardive dyskinesia has been uncommon in patients with Tourette's syndrome, vigilance for the appearance of new involuntary movements, especially when they appear dyskinetic or dystonic rather than tic-like, is appropriate in the management of Tourette's syndrome with neuroleptic drugs.

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Should patients with central core disease be screened for malignant hyperthermia?

Malignant hyperthermia is a potentially fatal condition of hypermetabolism in skeletal muscle triggered by certain anaesthetic agents. Although neuromuscular disorders may predispose to anaesthetic complications in their own right, only central core disease and malignant hyperthermia myopathy are associated with the characteristic in vitro muscle responses diagnostic for susceptibility to malignant hyperthermia.¹ Central core disease is characterised by weakness, wasting, and orthopaedic complications. Muscle fibres show rounded areas of reduced oxidative staining, known as cores. Malignant hyperthermia myopathy is a non-specific histological myopathy, sometimes with cores, occurring in clinically asymptomatic patients, susceptible to malignant hyperthermia. Most susceptible patients show normal muscle histology. A few show central core disease or malignant hyperthermia myopathy. Conversely, many patients with central core disease are susceptible to malignant hyperthermia. Indeed an assumption has grown that all patients with central core disease are susceptible to malignant hyperther-

mia and do not require screening.² Our study shows that this assumption is wrong and patients with central core disease should be screened for malignant hyperthermia so that they are not denied potentially valuable anaesthesia.

We studied clinical data, in vitro contracture test data, and histological data in 19 members from six families (table). In three families (I, V, and VI), presentation was with a myopathy diagnosed histologically as central core disease and screening for malignant hyperthermia was prompted on this basis. In the other three families (II, III, and IV), presentation was with a malignant hyperthermia reaction and on screening, histological diagnoses of central core disease were made. Screening for malignant hyperthermia was performed according to the European Malignant Hyperthermia Group protocol,³ except for those patients screened before its introduction. The in vitro contracture test was interpreted as susceptible to malignant hyperthermia when reacting abnormally to both halothane and caffeine used separately, negative for malignant hyperthermia when reacting normally to both agents, and equivocal for malignant hyperthermia when reacting abnormally to only one agent. Clinically all equivocal patients are regarded as being susceptible to malignant hyperthermia under anaesthesia. Before the European Malignant Hyperthermia Group protocol the in vitro contracture test was performed in a similar but not identical manner, patients being classified as positive or negative for malignant hyperthermia. The positive patients would include both the susceptible and the equivocal classification. Separate muscle samples were taken for histological examination. These samples were frozen in isopentane cooled in liquid nitrogen. Frozen sections were cut at 10 μ thickness and stained with haematoxylin and eosin, NADHTR, myosin ATPase, periodic acid Schiff's, oil red O, and Gomori stains with standard methods.

In family I a 37 year old woman (case 1; proband) diagnosed both clinically and histologically as having central core disease underwent a further biopsy to screen for susceptibility to malignant hyperthermia. Her mother (patient 2), daughter (case 3), and son (case 4) were also screened. In family II

an 11 year old with scoliosis had a suspected malignant hyperthermia reaction during general anaesthesia for a fractured arm (case 1). She, her sister (patient), and father (case 3) were screened for malignant hyperthermia. The original proband in family III was a woman aged 17 who died of probable malignant hyperthermia during an anaesthetic. The sister of the proband (case 1), a maternal uncle (case 2), and his daughter (case 3) and son (case 4) were screened. Several years later the third cousin (case 5) to the original proband had a malignant hyperthermia reaction. She and her two daughters (cases 6 and 7) were screened. The proband in family IV was a 23 year old man (case 1). He had had several general anaesthetics since infancy for congenital dislocation of the hip. On two occasions he developed muscle rigidity after suxamethonium, the final occasion also being associated with cyanosis and a core temperature of 43°C prompting his referral for malignant hyperthermia screening. His sister (case 2) was also screened. In family V the proband (case 1) was clinically and histologically diagnosed as having central core disease. She and her mother (case 2) were screened for malignant hyperthermia. The proband (case 1) in family VI was screened for malignant hyperthermia because of known central core disease.

The table gives the results. Not all patients with central core disease were susceptible to malignant hyperthermia even within the same family. In family I, the proband had central core disease and was susceptible to malignant hyperthermia. Her daughter also had central core disease but was negative for malignant hyperthermia. In family V, the proband was susceptible, whereas her mother was negative. Although the mother's symptoms were mild, she had classic central core disease histologically. In family VI, only the proband was biopsied. She had congenital dislocation of the hip, scoliosis, and weakness and wasting of both legs, with a classic histological picture of central core disease, but was negative for malignant hyperthermia. The study indicates that patients with central core disease should be screened for malignant hyperthermia. They should not be assumed to be susceptible. A significant number are negative

for malignant hyperthermia and if they are assumed to be susceptible this will unnecessarily deny them potentially valuable anaesthesia. It is important to know the reliability of the in vitro contracture test results in this study. A collaborative study from all European centres has yet to be published. In this unit, no clinically fulminant patient with malignant hyperthermia has tested negative and a review of 402 probands shows a good correlation of the in vitro contracture test result with the severity of the clinical reaction.⁴ This is supported by the finding of 100% sensitivity and 78% specificity using the essentially similar North American protocol.⁵

The data indicate that whereas central core disease and malignant hyperthermia may be related conditions, they are not the same. A similar genetic locus, chromosome 19q13.1, has been implicated in both. At least for malignant hyperthermia this is thought to involve mutation of the ryanodine receptor. Eight mutations so far have been identified but less than 50% of malignant hyperthermia families worldwide are linked to chromosome 19, malignant hyperthermia showing considerable heterogeneity. It is possible that a single gene is mutated in central core disease and malignant hyperthermia, but the protein product has more than one function. Perhaps the location of the mutation and the genetic background of the individual dictate whether one or both functions are lost. Alternatively, the genes for malignant hyperthermia and central core disease may be separate. One of the issues raised by this study is the definition of malignant hyperthermia myopathy. On seeing cores in the biopsy of a patient with a symptomatic myopathy, the pathologist will rightly diagnose central core disease. However, on seeing cores in the biopsy of a patient undergoing screening for malignant hyperthermia, should a diagnosis of central core disease or malignant hyperthermia myopathy be made? We think that recourse should be made to the clinical information. If the patient is symptomatic and susceptible to malignant hyperthermia a diagnosis of central core disease is appropriate. However, if asymptomatic and susceptible to malignant hyperthermia, malignant hyperthermia myopathy is probably better. Malignant hyperthermia myopathy should not be diagnosed in patients negative for malignant hyperthermia, because the name implies malignant hyperthermia susceptibility. Hyperthermia patients negative for malignant hyperthermia with cores may be diagnosed as having central core disease, even when clinically only mildly myopathic. Central core disease is known to have a broad range of clinical expression. The mother of the proband in family V had only mild proximal weakness in both legs, which may have gone underdiagnosed had it not been for her daughter's central core disease. Histologically, this mildly affected mother had classic central core disease. She was negative for malignant hyperthermia and a diagnosis of central core disease was applicable. Arguably, the affected members in family III had malignant hyperthermia myopathy, as they were susceptible to malignant hyperthermia and despite their central cores, they were only clinically mildly affected. Some of the members in this family complained of slight weakness and calf hypertrophy and had raised resting creatine kinase (2106 IU in case 2). A notable histological feature in this family, compared with

Clinical, in vitro contracture test, and histopathological data

Case	Myopathic symptoms	In vitro contracture test results	Percentage of fibres with central cores	Percentage of type 1 fibres
I				
1	Severe	Susceptible	58	98
2	Mild	Negative	2	90
3	Severe	Negative	54	95
4	Absent	Negative	0	35
II				
1	Severe	Susceptible	49	96
2	Absent	Negative	0	46
3	Severe	Susceptible	25	100
III				
1	Absent	Negative	0	25
2	Mild	Susceptible	8	42
3	Mild	Equivocal	2	27
4	Mild	Equivocal	1	53
5	Absent	Susceptible	2	51
6	Absent	Susceptible	1	65
7	Absent	Negative	0	37
IV				
1	Severe	Susceptible	36	100
2	Absent	Negative	0	58
V				
1	Severe	Susceptible	15	96
2	Mild	Negative	96	99
VI				
1	Severe	Negative	17	100

the others, was normal percentages of type I fibres, rather than the very high levels (90% or more seen in the other families).

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MATTERS ARISING

Multiple sclerosis in the north Cambridgeshire districts of East Anglia

The north Cambridge survey is a welcome addition to the United Kingdom series of prevalence studies.¹ We agree that a multi-centre prevalence study would add to the epidemiological knowledge of multiple sclerosis. However, we cannot agree with the inclusion of "suspect cases" in their prevalence figures. As we have pointed out in a previous paper, the measurement of multiple sclerosis can be distorted by using ill defined criteria for measuring the disease.² We contend that the Poser criteria alone (which do not contain a suspect category) should be used in measuring the prevalence of multiple sclerosis. For this reason, we used only the Poser criteria in our survey of west Sussex, and deliberately did not include a suspect category.² As Poser himself says, "for the purposes of prevalence studies only the categories of clinically definite and clinically probable should be used; possible multiple sclerosis should never be included."³

Our concern is that a "suspect" category, which seemed to have been defined differently in the south Wales,⁴ Cambridge, and Southampton surveys,⁵ can lead to confusion in interpreting and comparing prevalence figures. This is because there are no clear criteria of what constitute so called "suspect" cases, and workers are free to use their own criteria. As Robertson says, the inclusion of a suspect category "introduces noise, and generally obfuscates the overall picture."⁴ We agree with this, and argue that

any cases that do not fall into the Poser criteria should be excluded from prevalence figures. To do so would introduce some clarity into what we are striving to measure. In our view, future prevalence surveys should use the Poser criteria and not include "suspect" cases.

The Cambridge team suggest that the very presence of a latitudinal gradient within the United Kingdom has only recently been questioned.¹ It is, in fact, a decade ago that Williams and McKernan made the comment "we find no convincing evidence of a latitudinal effect in the United Kingdom".⁷ A mortality study of multiple sclerosis in the United Kingdom found no gradient south of the Scottish border and discussed the possibility that the high, but diminishing, Scottish rates were artefactual.⁸ The most serious challenge to the latitudinal hypothesis appeared in a letter in the *BMJ* in which a convincing argument was presented to show that the hypothesis was inconsistent with United Kingdom data.⁹

So the challenge to Limburg's hypothesis is not recent.¹⁰ What is recent is that most researchers in the field are at last coming to realise the weakness of the data on which the hypothesis was based.

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NOTICE

Announcement from the British Neuropsychiatry Association: 1996 summer meeting

The 1996 Summer meeting will be held on 14-16 July at Robinson College,

Cambridge. It will include topics on neuro-development, language, and the presentation of short scientific papers and single case videos by members. The Association's AGM will be held on 16 July.

For further details of these meetings please contact: Sue Garratt, Administrative Assistant, BNPA, 17 Clocktower Mews, London N1 7BB. Telephone/Fax: 0171 226 5949.

For details of membership of the BNPA, which is open to medical practitioners in psychiatry, neurology, and related clinical neurosciences, please contact: Dr Jonathan Bird, Secretary BNPA, Burden Neurological Hospital, Stoke Lane, Stapleton, Bristol, BS16 1QT. Telephone: 01179 701212 ext 2925/2929 or Sue Garratt at the address given above.

CORRECTION

H M L Jansen, J van der Naalt, A H Van Zomeren, A M J Paans, L Veenma-van der Duin, J M Hew, J Pruim, J M Minderhoud, J Korff

Cobalt-55 positron emission tomography in traumatic brain injury: a pilot study. *J Neurol Neurosurg Psychiatry* 1996; 60:221-4.

In the table, p223, CT localisation of patient B is Left frontal

NA [no abnormalities]

The first sentence, left hand column p223, should read—Both Co-PET and CT showed abnormalities that were not in accordance with EEG findings

BOOK REVIEWS

All titles reviewed here are available from the BMJ Bookshop, PO Box 295, London WC1H 9TE. Prices include postage in the United Kingdom and for members of the British Forces Overseas, but overseas customers should add £2 per item for postage and packing. Payment can be made by cheque in sterling drawn on a United Kingdom bank, or by credit card (Mastercard, Visa or American Express) stating card number, expiry date, and your full name.

Treatment of Cerebral Palsy and Motor Delay. By SOPHIE LEVITT. (Pp 341; price £19.99). Published by Blackwell Science. 1995. ISBN 0-632-03878-X.

The third edition of Sophie Levitt's excellent book will be of interest and indeed is essential reading for anyone involved in the management of the cerebral palsies, including parents. A major theme throughout the book is the importance of collaboration with parents and the detailed section on practical procedures is written with parents as well as therapists in mind. Forwards to the second