do not persist for more than three weeks.⁴ Likewise, there was no evidence of haemosiderin deposition in the stalk which might be expected after haemorrhage. Stalk enlargement could have been an effect of untreated diabetes insipidus, in which the first case might have expected resolution of the abnormality with treatment. However, the swelling persisted for three months despite adequate treatment of the diabetes insipidus. It is possible that unrecognised injury or infection with ensuing inflammation resulted in the swelling observed initially. It is known that insults to the stalk can lead to reorganisation and proximal enlargement.⁵ We may have observed the resolution of such changes.

We conclude that pituitary stalk enlargement may occur in idiopathic cranial diabetes insipidus, persist for months, and eventually disappear. Serial imaging with CT or MRI will exclude progressive infiltrative or neoplastic causes.

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Ropinirole (SK and F 101468) in the treatment of Parkinson's disease

Ropinirole (4-[2-(dipropylamino)ethyl]-1,3-dihydro-2H-indol-2-one), a selective D₂ agonist has been shown to have anti-Parkinsonian effects at doses between 0.6 mg twice a day and 2 mg twice a day in an open inpatient study.¹ We report the results of a further outpatient open study in fourteen patients with idiopathic Parkinson's disease.

Participating in the study were seven patients with presumed Parkinson's disease (mean age 56.5 years, disease duration 2.5 years and mean Hoehn and Yahr Stage II) and seven patients with disabling levodopa-induced on-off oscillations (median age 66 years, disease duration 10.0 years and duration of levodopa treatment 4.0 years, daily levodopa dose 750 mg, median duration of disabling oscillations 1.0 years, mean Hoehn and Yahr stage when "off" III and when "on" II). Four of the patients treated with levodopa had severe interdose chorea and one patient had biphasic dyskinesias. Three patients were also receiving anticholinergic medication, three were taking L-deprenyl (selegiline); none of the patients had a history of psychiatric disorder or evidence of hepatic, renal or cardiovascular dysfunction.

Both groups were initially treated with 0.6 mg of ropinirole twice daily for one week. The dose was increased to 1 mg twice daily for the second week and by further weekly increments of 1 mg twice daily to a maximum of 7 mg twice a day over an eight week period. If adverse reactions developed, patients continued on the previously tolerated dose for another week or a dose increase of less than 1 mg twice a day was made; if gastrointestinal side-effects or symptomatic orthostatic hypotension re-occurred, despite modification of ropinirole dosing, domperidone 20 mg twice daily was given, in some cases, for the remaining trial period. If interdose dyskinesias increased in the oscillating patients levodopa was concomitantly reduced. After each dose increment observations of lying and standing pulse and blood pressure were made at baseline and then hourly for the following four hours.

Motor assessments were carried out on the day of dose increase before and two hours after dosing, using the Modified Webster scale² and tapping and walking tests.³ Assessments of motor fluctuations were carried out using self-scoring diaries to record a percentage daily "on" time and severity of dyskinesias.

Of the previously untreated patients two showed improvement comparable with that seen with oral levodopa at doses of 12 mg and 6 mg a day respectively. The first patient had a Webster score which reduced from 14 to 10, a 44% increase in the number of finger taps and a 40% decrease in walking time. The second patient had a 43% increase in numbers of finger taps, but could not increase the dose further because of nausea despite domperidone. Two of the de novo patients dropped out before the treatment period was finished, one because of incapacitating somnolence at 4 mg daily and one following symptomatic orthostatic hypotension after a single dose of 1 mg. Three patients had no response to the drug at daily doses of 10, 12 and 14 mg respectively. However, two of these patients subsequently failed to respond to apomorphine or chronic levodopa treatment raising the possibility of a diagnosis other than idiopathic Parkinson's disease.

Four of the seven patients with levodopa-induced on-off oscillations showed a worthwhile clinical response with a reduction of mean "off" hours per day from 3.9 (1.9-6.5) to 1.3 (0.4-2.3). The average dose needed to obtain an optimal response was 5.8 mg per day (3.2-8 mg), but beneficial effects began at 2.3 mg daily (1.2-4.0). The duration and intensity of interdose dyskinesias increased in three patients, but diminished to even below baseline level by a mean reduction of 15% of the total daily levodopa dose in two patients. Two patients treated with up to 10 mg a day in addition to their unchanged levodopa dose did not improve. In one, the mean "off" hours remained unaffected, while the other experienced prolonged episodes of disabling biphasic dyskinesias. One patient developed intolerable drowsiness and somnolence at 2 mg a day and discontinued the study and two had nausea and symptomatic orthostatic hypotension controlled by domperidone. Laboratory tests and urine analyses remained normal throughout the eight week period.

We conclude that ropinirole has anti-Parkinsonian effect and that the optimum dose range for most patients may be 4-8 mg a day. Adverse reactions are similar to those seen with other dopamine receptor agonists and can be reduced by the use of domperidone

and possibly more gradual dose increments than occurred in this trial. We would recommend in future that oral levodopa and subcutaneous apomorphine tests are carried out on previously untreated patients with Parkinson's syndrome⁴ before the assessment of a new dopaminergic agonist, to exclude as far as possible patients with multi-system degeneration unresponsive to this group of drugs.

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Cardiovascular autonomic function tests—are three Valsalva's and six deep breaths necessary or will singles do?

In the assessment of autonomic neuropathy, two widely used tests of cardiovascular autonomic function assess the heart rate response to three consecutive Valsalva manoeuvres and to six consecutive deep breaths.¹ We aimed to see whether the response to a single Valsalva manoeuvre was significantly different from that from the average of three and whether the response to a single deep breath was significantly different from that from the average of six deep breaths.

The study group consisted of 36 diabetic patients, 25 male and 11 female, 15 insulin treated, mean age 54 years (range 30-82), mean duration of diabetes 17.4 years (range 3 months-51 years). All had symptoms which may have been due to diabetic neuropathy.

They underwent heart rate monitoring using a computer-assisted system for the collection and analysis of heart rate data for cardiovascular autonomic function tests (RR Medical Electronics, Leeds, UK). A Valsalva manoeuvre was performed by the patient blowing into the tube of a sphygmomanometer and sustaining a pressure of 40 mm Hg for 15 seconds while the R-R interval was recorded, the result being expressed as the Valsalva ratio: the longest R-R interval during the 45 seconds after the manoeuvre divided by the shortest R-R interval during the manoeuvre. All the patients performed the manoeuvre properly and, as far as could be ascertained, achieved an intrathoracic pressure which was adequately raised. Heart rate variability during deep breathing was calculated by the patient resting quietly and breathing deeply in for over five seconds and

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 Ewing² 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.

Sixteen of 17 patients with a mean-of-three-derived Valsalva ratio less than 1.21 (abnormal according to previous criteria² had a single Valsalva ratio less than 1.21. Seventeen of 19 patients with a mean-of-three-derived Valsalva ratio greater than 1.21 had 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 criteria¹) 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 criteria¹) 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 (89%). 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 components of variance 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 (5.70 (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 (14.38 (0.68) minutes, $p < 0.0001$).

In this study a 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 abnormal 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 say, in a particular case 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 even though falling 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 traditional three Valsalva manoeuvres and six deep breaths when performing cardio-

vascular 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.³ A battery of five tests has been proposed by Ewing and Clarke¹ 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 coworkers⁴ may be preferable.⁵ Several potential advantages for the tests in the latter battery, compared with those in the battery of Ewing,¹ have been suggested⁵—that they are easier and quicker to perform, more comfortable for the patient, 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.

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Benign relapsing meningo-myelitis

Myelitis and encephalomyelitis are relatively common both as monophasic or relapsing diseases. Investigation of an infectious 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 meningo-myelitis. Aetiological investigations were negative and we found only one report on three similar cases in the literature.¹

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 to be 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 (40°C) and the cerebrospinal fluid showed $142 \times 10^6/l$ cells (mainly lymphocytes), 0.70 g/l 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, rifampicin 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 assisted ventilation for eight days. The CSF showed $94 \times 10^6/l$ cells (mainly lymphocytes), 3.91 mmol/l glucose and 0.60 g/l protein. After a month he recovered almost completely and at four months the neurological examination was entirely normal. During this admission he was treated with sulphamethoxazole 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 aggressive. Over the next few days a flaccid and areflexic tetraparesis again developed. There was no evidence of a sensory loss level but proprioception was impaired and urinary retention was present. The cerebrospinal fluid contained 64×10^6 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. In the serum: red and white cell blood counts, haematocrit, erythrocyte sedimentation rate, electrolytes, urea nitrogen, creatinine, glucose, liver and kidney function tests, protein electrophoresis and immunoelectrophoresis; rheumatoid factor, antinuclear antibodies and LE-cell tests, serum complement and immune complex levels; VDRL and FTA-ABS tests, Wright (Brucella serology, agglutination test) Rose Bengal Plate test, Widal and Weil-Felix reactions, Paul-Bunnell test, serological tests for hepatitis B surface antigen and antibody and for human immunodeficiency viral antibodies (HIV1 and HIV2), CMV IgG and IgM complement fixation titre, complement fixation titres for other viruses (herpesvirus, adenovirus, parainfluenzae 1 and 3, measles, mumps, respiratory syncytial) in acute and convalescent periods, indirect immunofluorescent test for Lyme disease (Institut Pasteur, Paris) and serological tests for toxoplasmosis antibodies.

In the CSF there were normal or negative results for: microscopical examination of stained specimens (Gram) and cultures for acid-fast bacilli, bacteria and fungi, antigens to cryptococcus, complement fixation titres for virus in acute and convalescent periods,