from naltrexone, and thus further studies were not deemed feasible. In light of the recent report by Hyman et al. in which no beneficial effects of naltrexone were observed, our findings using higher doses and longer treatment periods than Hyman et al. are of importance in interpreting their negative findings.

The 10 patients (4 women, 6 men; age range 67-73 yrs) with probable Alzheimer’s disease (according to NINCDS-ADRDA criteria) had a mean duration of symptoms of three years and scored between 2:5 and 13 on the Blessed Dementia Rating scale. The trial was conducted in an open dose-finding manner (two weeks each of 50, 150 and 300 mg of naltrexone daily). No patients were on any other psychoactive medications in the one month preceding, or during, the trial. Psychometric testing was carried out at the initial visit and then biweekly. Parallel 10 word versions of the Rey auditory verbal learning test (RAVLT), Wechsler Memory Scale paired associates, tests of verbal fluency and digit span were given. A 30 minute delayed recall of the RAVLT words was also given.

The mean total number of words produced on the RAVLT increased significantly with the 150 mg and 300 mg doses (overall ANOVA F (3,27) = 3.71, p = 0.02). There was a mean increase in the number of words recalled of approximately 25% from baseline to testing after the 150 mg or 300 mg dose. There were no changes in digit span, paired associates or verbal fluency. Six patients showed no change in their RAVLT performance, but four patients showed substantial changes between baseline and testing after the 150 mg dose, with little additional improvement at 300 mg (table). None of these patients showed improvement on word recall at 30 minutes, however. Three patients developed transient 10-20 fold elevations of aspartate transaminase during the trial, at the 150 or 300 mg dosages, though in one patient the enzyme levels were increasing (though still normal) after the 50 mg dose.

Because improvements did not occur in verbal fluency or digit span, we believe that the increase in total words recalled on the RAVLT by some of the patients may be indicative of a beneficial effect of chronic naltrexone administration (with doses of 150 mg or higher for at least four weeks) on some aspects of episodic memory in patients with probable Alzheimer’s disease. The fact that this was an open trial limits the interpretation of this finding, but does point to the need for development and testing of other oral narcotic antagonists. The failure of Hyman et al. to find improved performance in patients while on naltrexone may reflect the use of a double-blind crossover format which would be more likely to avoid spurious effects. On the other hand, our findings suggest that higher doses and longer administration periods may be necessary for cognitive effects to occur. In addition, naltrexone may act by inducing opiate receptor proliferation, so that there may be a carry-over effect of naltrexone that would falsely elevate performance on the placebo portion of a crossover study. Thus, the negative finding of Hyman et al. must not be taken as definitive. Manipulation of the opioid system may yet prove fruitful in the treatment of Alzheimer’s disease since it may modulate both cholinergic and noradrenergic function, both of which may be abnormal in the disease.

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Reversible muscle spasms in hyperthyroidism

SIR: A patient with hyperthyroidism presented with severe generalised muscle spasms. The rapid disappearance on antithyrotic treatment and the relapse on thyroxine replacement therapy suggested a causal relationship.

A 39-year-old woman suffered from bouts of stiffness when walking, which increased in frequency and severity during the 2 week period prior to examination. When going downstairs, she had a feeling of being pulled backwards, because the muscles of her neck, trunk and extremities became stiff. Furthermore, she felt “overwrought, restless and distressed”, was emotionally unstable and perspired heavily. These symptoms gradually increased and every attempt to sit down, get up or walk, and every emotion gave rise to the same “muscle spasms”, as she called them, whereby her head was pulled backwards, and her trunk, arms and legs were stretched. This caused her to fall backwards several times. Her sleep was not disturbed by spasms.
On examination, we saw a very nervous, profusely perspiring, emotionally labile woman, who demonstrated a retrocollis with stretching of her back and extremities on being spoken to, or when asked to execute simple motor activities. She could not sit up because of the stiffness and when in a supine position, she could be lifted as a board from her bed to the examination table. Because of severe contractions of the sternocleidomastoid muscle, it was difficult to palpate the thyroid gland. Her pulse rate was 120/min. There was a mild tremor of the hands. Motor power was difficult to judge because of generalised hypertonia. Tendon reflexes were brisk, the right plantar response was extensor, the left was equi- nocal. Laboratory studies revealed hypothyroidism: T4 167 nmol/l (normal values 60–150 nmol/l); free T4 43 pmol/l (normal 8–0–25.0 pmol/l); free T4 index 184 (normal 59–154). Following administration of iodium containing contrast medium for CT, the hyperthyroidism was aggravated (T4 259 nmol/l, free T4 84 pmol/l). Thyroid stimulating immunoglobulin and antibodies against thyroid mitochondria and parietal cells were present; antibodies against thyroglobulin were absent. Other causes of a pyramidal syndrome were ruled out (normal vitamin B12, skull CT, diameter of cervical vertebral canal and craniocervical junction, Queckenstedt’s tests and cerebrospinal fluid), as was myopathy (normal EMG, the paravertebral muscles, however, showed continuous but normal activity, and normal muscle biopsy).

The patient was treated with 3 x 20 mg thiamazole, 3 x 40 mg propranolol chloride, and 3 x 10 mg oxazepam. Five weeks later she was biochemically euthyroid. At that time she was calm, her pulse rate was normal, the hypertonia had decreased and so had the spasms. She could sit and walk again and rise from a chair. It was still difficult for her to rise from a supine position because of some remaining axial spasms. The plantar reflexes had become flexor. After two months, she was given 50 µg thyroxine to inhibit the production of TSH. At the same time propranolol and oxazepam were stopped. A few days later she had a relapse of the muscle spasms, the hypertonia and the nervous complaints, but to a milder degree than on admission. The thyroxine was stopped. A week later she had improved to the state prior to the relapse. Two months later the muscle spasms had completely disappeared and no neurological signs were found, except for a mild “clumsy” gait.

The clinical picture shows aspects that are compatible with both dystonia and stiff-man syndrome. Voluntary movements and emotional stress caused the spasms to occur, which is known in either condition.1 2 The absence of spasms during sleep does not differentiate between the two, however; the fact that the spasms were not painful is very uncommon in stiff-man syndrome.2 Heavy perspiration and distress can be seen both in stiff-man syndrome2 and in a state of hyperthyroidism. Extensor plantar response have been described in both.3 4 Choreathetosis is known to occur in hyperthyroidism.4 5 Fahn6 mentioned torticolis spastica and Nutt et al7 the occurrence of Meige syndrome in hyperthyroidism, which both can be regarded as focal dystonia. Neither muscle spasms nor generalised dystonia or stiff-man syndrome have ever been clearly associated with hyperthyroidism.2 8 In our patient the decreasing T4 level was accompanied by disappearance of the muscle spasms and other signs. Administration of a small amount of thyroxine caused them to return. After stopping the thyroxine they again vanished. This suggests a direct or indirect causal relationship between thyroxine (the active T3) and the clinical symptoms.

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Kearns-Sayre syndrome, hypoparathyroidism, and basal ganglia calcification

Sir: Hypoparathyroidism has been rarely described in patients with the Kearns-Sayre syndrome. We describe a young boy who was treated for hypoparathyroidism from the age of 2 years, and had the first features of the Kearns-Sayre syndrome at the age of 6. CT scanning of the brain at the age of 11 years showed no evidence of intracranial calcification which is found in up to 50% of cases of this syndrome and is almost invariably found in idiopathic hypoparathyroidism.2

A West Indian boy presented at the age of 2 years with a 6 day history of diarrhoea and vomiting. He had always been a jittery rather irritable child, tending to shake in all four limbs when handled since birth, and one month prior to presentation had had a febrile fit. Developmental milestones had been normal. He had walked at 10 months and spoke at 11 months. He was found to be hypocalcaemic (1.48 mmol/l), hyperphosphataemic (2.42 mmol/l) and had a low parathormone level (0.18 ng/l). A diagnosis of primary hypoparathyroidism was made and he was commenced on calcium supplements and vitamin D (calciferol 50,000 units daily) with ascorbic acid (500 mg/day).

Over the next 4 years he had a number of upper respiratory tract infections, one episode of oral candidiasis, and one of otitis media. He continued to be irritable, at times had bad temper with occasional short lasting generalised shaking episodes without loss of consciousness. Throughout this period his serum calcium and phosphate levels were normal. An EEG demonstrated an excess of slow forms with episodic slow activity. These episodes were controlled with phenytoin 50 mg twice a day. Testicular descent was not complete until the age of six and he was enuretic until the age of 8 years.

At the age of 6 years it was first noticed he had drooping of the eyelids. Over the next two years he developed difficulty with walking due to unsteadiness and had frequent falls. From the age of 8 he developed a progressive proximal muscle weakness. At the age of 11 bilateral fascia lata slings were inserted to correct the bilateral paresis.

On examination at the age of 11 he had atypical bilateral diffuse pigmented changes in both fundi with normal choroid and retinal vessels. There was marked limitation of abduction of both eyes, bilateral paresis and facial weakness, and a myopathic facies. He had a proximal muscle weakness with normal upper but brisk lower limb reflexes and