

Computed tomograph of neck and upper thorax.

was no histological evidence that the 'goitre was benign, though clinically cancer seemed to be unlikely.

To our knowledge our patient is the first reported case of Horner's syndrome where there was histological proof of benign thyroid disease and where the condition resolved after surgery.

We thank Mr H R Matthews of East Birmingham Hospital for permission to report this case.

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(Accepted 19 October 1987)

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## Nifedipine for epilepsy? A pilot study

Theoretical considerations suggest that blockers of calcium channels may have anticonvulsant activity, and this has been confirmed in seizure models *in vitro*<sup>1</sup> and *in vivo*.<sup>2</sup> Results with the sedative flunarizine in humans have been promising.<sup>3</sup> The conventional calcium antagonists verapamil and diltiazem have been found to inhibit the biotransformation of carbamazepine and produce neurotoxicity.<sup>4,5</sup> In this pilot study we assessed the antiepileptic potential of nifedipine, a dihydropyridine derivative.

### Patients, methods, and results

Twelve patients who had intractable epilepsy (four women, eight men; age 20-58 years; duration of epilepsy 2-42 years) agreed to take part in the study, which was approved by the local ethical committee. Ten had complex partial epilepsy with secondary generalisation. One patient experienced only partial seizures and one generalised tonic-clonic fits. The patients were receiving the following treatment: carbamazepine (seven), carbamazepine with sodium valproate or phenobarbitone (two), phenytoin (two), and sodium valproate and phenobarbitone (one). For more than a year all had attended the epilepsy clinic at this hospital, where they routinely completed monthly "seizure frequency" charts.

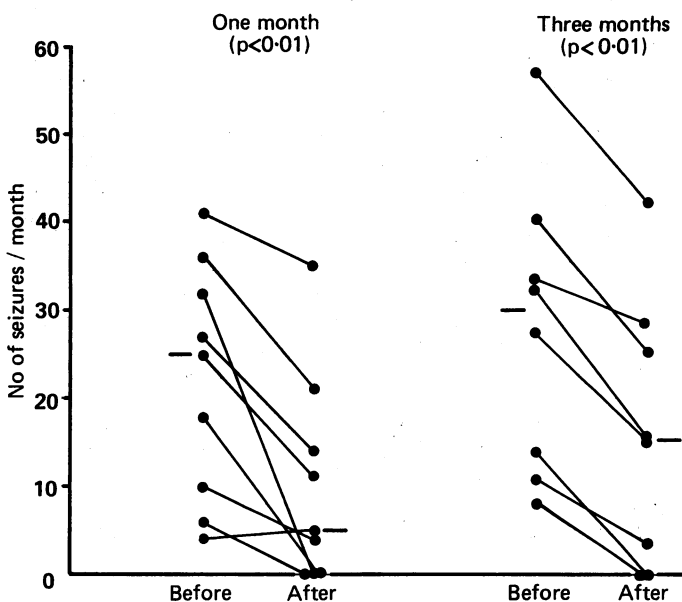
The patients were admitted to this hospital for two weeks. They continued to take anticonvulsant drugs in unchanged dosages, and the concentrations were monitored. Blood for assaying carbamazepine and sodium valproate concentrations was drawn at 0800 ("trough"), 1100 ("peak"), and 1600 for three consecutive days before treatment with nifedipine was started and on days 1, 2, 3,

5, 7, and 10 of nifedipine treatment. The concentrations of phenytoin and phenobarbitone, whose elimination half lives exceed 24 hours, were obtained once daily. The mid-afternoon measurement of all drugs was repeated in the outpatient department after a further two and four months. The patients were treated with nifedipine 20 mg thrice daily in addition to their existing antiepileptic treatment. Their frequency of seizures was charted for three months before and after nifedipine treatment was started. Generalised tonic-clonic and partial seizures were recorded separately.

Two patients withdrew after six and 10 days because of headache and lightheadedness. Another was non-compliant, and a further patient stopped taking all his drugs after six weeks. Thus nine patients completed one month and eight all three months of the study.

In the nine patients taking carbamazepine the mean trough, peak, and mid-afternoon concentrations did not change significantly from the baseline concentrations in the first 10 days of nifedipine treatment, and there were no long term alterations in the six patients who continued taking nifedipine for four months (Student's *t* test; 95% confidence interval (CI) -12% to +6%). The protein binding capacity in the serum of carbamazepine and circulating concentrations of its active metabolite carbamazepine 10,11 epoxide were also unaffected by nifedipine. The concentrations of the other anticonvulsants were unaltered.

The overall frequency of seizures in patients receiving adjuvant nifedipine was significantly less at one ( $p < 0.01$ ; 95% CI 23% to 36% reduction) and three months ( $p < 0.01$ ; 95% CI 25% to 57% reduction) compared with previous months (Wilcoxon matched pairs test) (figure). Five and four patients had >50% decreases in the number of fits after one and three months, respectively, while seven reported >25% reductions at both time points. Two patients, for the first time in many years, remained free of seizures for the whole three months.



Total number of seizures one and three months before and after starting nifedipine treatment (20 mg thrice daily) in patients who have intractable epilepsy.

Comparisons were repeated on an "intention to treat" basis, and the differences remained significant ( $p < 0.02$ ). It was not possible with such small numbers to separate out usefully differential effects on partial and generalised seizures, though a decrease in the frequency of partial events occurred in all patients after one ( $p < 0.02$ ) and three months ( $p < 0.01$ ) of nifedipine treatment.

### Comment

This study was not controlled for the placebo effect of giving a new drug or for that of a short admission to hospital. Nevertheless, the reduction in frequency of seizures supports the hypothesis that nifedipine has an anticonvulsant action. Calcium antagonists may have important potential as adjuvant, non-sedative, antiepileptic drugs.

Our grateful thanks go to Anne Somers for expert secretarial help.

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(Accepted 27 October 1987)

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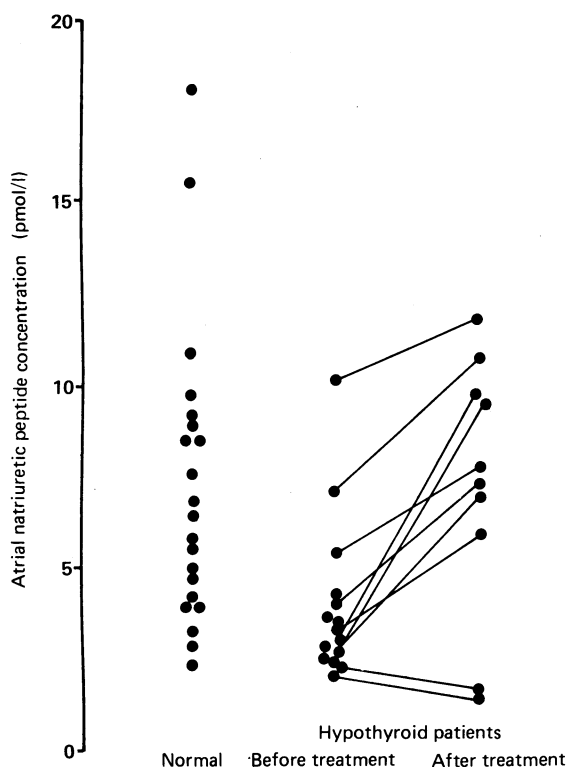
## Plasma concentrations of atrial natriuretic peptide in hypothyroidism

Atrial natriuretic peptide may play an important part in plasma volume homeostasis in normal humans because of its ability to cause natriuresis, diuresis, and vasodilatation. Hypothyroidism is accompanied by abnormalities in both the cardiovascular system and water balance.<sup>1,2,3</sup> Our study investigated the plasma concentrations of atrial natriuretic peptide in hypothyroidism.

### Patients, methods, and results

We studied a group of 15 patients in whom clinical and biochemical hypothyroidism had been newly diagnosed (mean age 49, range 23-73) and a group of 21 healthy normal subjects (mean age 43, range 27-86). In addition, 10 patients were restudied after treatment with thyroxine for six to 12 weeks. None had signs of heart failure, valvular heart disease, or hypertension (blood pressure >150/90 mm Hg). Venous blood from the forearm was drawn between 0900 and 1100 after 30 minutes of quiet sitting and placed into cooled tubes containing sequestrene and aprotinin. On the same day the peptide was extracted from plasma with octadecyl silica and methanol.<sup>4</sup> The mean recovery was 70%, and the results are given uncorrected for the losses.

The concentration of atrial natriuretic peptide was measured with a previously described radioimmunoassay using a polyclonal antibody to the carboxy terminus of atrial natriuretic factor 99-126 (Peninsula Laboratories) and an iodine-125 label (Amersham).<sup>4</sup> Intraassay and interassay variations were 10% and 12% respectively, and samples from before and after treatment were measured in the



Plasma concentrations of atrial natriuretic peptide in normal subjects and hypothyroid patients before and after treatment.

same assay. The concentration of plasma atrial natriuretic peptide increases in normal subjects who are receiving a high intake of sodium, so the 24 hour urinary sodium excretion was also measured on the day of the study. Diet was unrestricted. Because of the small numbers of subjects and the finding that plasma concentrations in each group showed a skew distribution the results are expressed as median and range, and the groups were compared with the Wilcoxon paired and unpaired tests.

The concentration of plasma atrial natriuretic peptide in the hypothyroid group (median 3.3 pmol/l, range 2.1-10.2 pmol/l) was lower ( $p < 0.01$ ) than in the controls (median 6.5 pmol/l, range 2.3-18.1 pmol/l) (figure). In 10 patients the median pretreatment value (3.0 pmol/l, range 2.1-10.2 pmol/l) increased significantly after treatment with thyroxine (median 7.6 pmol/l, range 1.4-11.8 pmol/l;  $p < 0.01$ ). There was no significant difference between the 24 hour urinary sodium excretion of the control group (median 148 mmol, range 45-288 mmol) and the hypothyroid group (median 130 mmol, range 65-191 mmol).

### Comment

The decreased median concentration of atrial natriuretic peptide in hypothyroidism confirms the results of a smaller study in which urinary sodium excretion was not measured.<sup>5</sup> By contrast, we have reported increased plasma concentrations of peptide in patients who have untreated hyperthyroidism,<sup>4</sup> a disease associated with an increased plasma volume.<sup>1</sup> A low plasma volume has been reported in myxoedema,<sup>1</sup> and this may decrease secretion of the peptide. A lack of circulating atrial natriuretic peptide may partly explain the impaired ability to excrete a water load, which recovers after treatment,<sup>2</sup> and the enhanced arterial pressor response to angiotensin II<sup>3</sup>—both are features of hypothyroidism.

The study was supported by the North East Thames Regional Health Authority locally organised research scheme.

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(Accepted 22 October 1987)

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## Rubber glove asthma

Rubber gloves are well known to dermatologists as causes of allergic dermatitis, the chemical responsible usually being an antioxidant or an accelerator added to the latex in its production.<sup>1,2</sup> So far as we are aware asthma provoked by vapour given off by rubber gloves has not been described, though rhinitis and anaphylaxis due to contact have.<sup>3</sup>

### Case report and investigations

A 36 year old male laboratory technician presented with a two year history of increasingly troublesome attacks of cough and wheeze. These tended to occur about one hour after starting work and lasted until evening. Two weeks before attending the clinic he had a prolonged and more severe attack which required treatment with prednisolone. For the past 10 years he had been performing serological investigations for hepatitis and, more recently, the acquired immune deficiency syndrome and he was required to wear gloves, which he changed frequently. He attributed his attacks to the starch with which the gloves were powdered. He recalled one attack after drinking red wine.

Over three weeks he recorded his peak flow rate four times daily. During a week at work it averaged about 530 l/min, whereas during two weeks on holiday it averaged about 570 l/min. During work he used an aerosol bronchodilator 14 times; he did not need it when off work.

Formal challenge tests with talc (control) and glove starch produced no reaction. Two sets of outwardly identical gloves were obtained from the manufacturers (Surgikos Ltd), microtouch and general purpose. The latter was the type he used at work. Putting on and taking off the microtouch gloves again produced no reaction, but after 10 minutes of the same manoeuvre with the