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Johnson replies:

The point of our article *Local Autonomic Failure in a Limb* was to draw attention to isolated local autonomic failure causing sweating loss and change of temperature in the affected limb. In company with the authors of two other reports of similar patients,^{1,2} we were unable to give an explanation for the disorder other than that it appeared to be due to a discrete lesion in the spinal cord without any clear evidence that this was related to syringomyelia. In that we did not provide an explanation for the problem, the possibility of subsequent development of a Holmes-Adie pupil, as suggested by Dr Duncan, cannot be discounted.

However, Holmes-Adie syndrome consists of a tonic pupil in association with absent stretch reflexes but this association is not absolute. This is discussed in a review of the clinical features which also considers the occurrence of the autonomic abnormalities which are occasionally found.³ On clinical examination our patients neither had absent stretch reflexes nor a tonic pupil and little can be made of a possible autonomic similarity with the Holmes-Adie syndrome, for although autonomic disorders seem to occur more commonly than would be expected by chance, the lesions may not only be post-ganglionic but in some patients afferent rather than efferent.⁴ Our patients therefore have no similarity with the Holmes-Adie syndrome at present in their clinical findings related to pupils, reflexes or to autonomic dysfunction.

It must further be questioned whether development in the future of only one feature of the Syndrome, that of tonic pupils, would really assist in understanding the disorder we have described. The Holmes-Adie

syndrome is purely a clinical description of associations rather than an aetiological explanation.

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Local autonomic failure affecting one limb

Sir: The cases of autonomic failure affecting one limb described by Drs Johnson and Robinson¹ are of particular interest because all the cases affected by failure of sweating in the left arm. In the third case there was associated normal vasomotor function in the affected limb implying single modality autonomic failure.

Recently a 54 year old woman was referred with a mixed history of hyperhidrosis of the right arm and face and pain in both arms but worse on the left side. These symptoms had started 4 years previously after a "whiplash" injury in a road traffic accident. The hyperhidrosis was aggravated by stress and was such that she misted her right spectacle lens. On examination there was in fact anhidrosis of the left arm and side of face. There was no Horner's syndrome on either side. Thermographic examination using liquid crystal contact thermography showed vasomotor failure in the right arm and normal vasomotor response to the proximal application of ice on the left side. There were no other abnormalities. In this case there was single function (sudomotor) failure again on the left side. This must raise the query why is the left arm involved in this loss in four cases? In addition single function (vasomotor) failure was present on the contralateral side to produce a picture of bilateral but discrete and different autonomic failure.

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Schistosoma in the spinal cord

Sir: We are at present undertaking a longitudinal study examining the clinical, serological and radiological findings of schistosomiasis of the nervous system and therefore read, with interest, the letter by Kerr *et al.*¹ Over a period of 19 months we collected 14 patients with cord and/or root involvement. Two of these cases have already been published² while details of the others will be submitted for publication shortly. Of these, six had expansion of the conus and irregularity and matting of roots. One further patient showed root involvement alone. Two of these seven patients were subjected to laminectomy but the rest were treated on the basis of clinical findings, CSF changes and systemic evidence of schistosomiasis infestation. These patients showed remarkable clinical improvement. Serial CT myelograms showed reduction in the size of the conus.

We therefore support the suggestion that patients with the appropriate clinical and investigative profile be given a therapeutic trial of praziquantel before being considered for laminectomy.

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Aggravation of Parkinson's disease by cinnarizine

Sir: Marti Masso *et al.*¹ described exacerbation of Parkinsonian symptoms after cinnarizine intake. Recently we reported movement disorders including Parkinsonism, induced by cinnarizine and flunarizine.² Both have similar chemical structures and pharmacological profiles,

although the latter is more potent and has a longer plasma half-life.³

Given their mild D2 blocking effect in addition to their calcium entry channel antagonist activity, it has been speculated that either or both of these properties could account for their unwanted extrapyramidal effects. To date we have studied over 100 patients showing that these complications are not uncommon and may lead to permanent disabilities as in patients with tardive dyskinesias.

To provide a deeper insight into their mechanisms of action we studied the effects of cinnarizine, flunarizine and nifedipine on the release of ³H dopamine from the rat caudate nucleus.

Male Wistar rats (150–200 g body weight) were decapitated and 1.0 mm coronal brain slices prepared. Slices corresponding to 1.5–2.5 mm rostrally to the anterior commissure were selected and a prism of caudate nucleus removed. Krebs solution⁴ equilibrated with 95% O₂ at 37°C was employed. Endogenous stores of dopamine were labelled in vitro by incubating the tissue for 30 min with 10 µCi of (2,5,6-³H) dopamine. Following incubation, tissue samples were transferred to an open cylinder with a piece of nylon mesh of 100 filaments per cm² placed at the bottom and forming a small basket. The whole device was placed in tube containing 3 ml of Krebs solution. Tissue slices were then exposed to eight 1 min, then to ten 5 min and again to ten 1 min washing periods. The tissue was stimulated by 1 min exposure to medium containing 20 mM K⁺. Stimulation was immediately followed by several 1 minute washings until the basal level of tritium overflow had been reached.

Radioactivity released by the tissue into the medium was monitored by counting aliquots of the bathing solution. Total radioactive overflow elicited by the stimuli was expressed as a percentage of the radioactivity contained in the tissue at the onset of stimulation.⁵ Statistical calculations were performed according to conventional procedures. Differences were considered significant if $p < 0.05$.

As shown in the table, the stimulation of

isolated caudate slices by one minute exposure to 20 mM K⁺ induced a tritium overflow of 3.9% of tissue content. Cinnarizine, flunarizine and nifedipine at doses able to block calcium channels lowered the total tritium overflow elicited by potassium.

Since dopamine release by potassium stimulation depends on a calcium mechanism, our findings suggest that Parkinsonism induced by these drugs is caused by their calcium antagonism.

Further research is needed to evaluate any possible effect on dopamine presynaptic receptors.

Clinical and experimental evidence indicates that patients on calcium antagonist drugs should be closely monitored to disclose early extrapyramidal side-effects.

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Chronic relapsing inflammatory polyneuropathy complicating sicca syndrome

Sir: Dr Gross has described a patient known to have the sicca syndrome, who subsequently developed chronic relapsing inflammatory polyneuropathy.¹ His report has prompted us to describe a patient with the same association but in whom the sicca syndrome was only diagnosed after the development of her inflammatory polyneuropathy.

In April 1987, a 38 year old West Indian housewife was admitted to another hospital with a two week history of progressive weakness in her arms and legs. There was no previous history of weakness or sensory disturbance. On examination she had mild right facial weakness, slight weakness of finger extension and abduction bilaterally, and moderate (grade 4) weakness distally in her legs. Her ankle reflexes were absent, and her plantar responses downgoing. Sensation was normal. Examination of the cerebrospinal fluid revealed an increase in protein concentration (0.8 g/l), but no cells. On the basis of these findings, a diagnosis of Guillain-Barré syndrome was made.

Following transfer to our hospital her weakness progressed until, eight weeks after the onset, she was areflexic and her limbs were paralysed. Ventilatory function, however, remained normal, and sensation was only mildly impaired. Bilateral thickening of the ulnar nerves was noted. Median nerve conduction velocity in the forearm was 7 m/s, and sural nerve biopsy showed loss of myelinated fibres and extensive subperineurial oedema, consistent with a diagnosis of chronic inflammatory polyneuropathy. The patient was started on prednisolone 60 mg daily, and there was a dramatic clinical response. She was able to stand without support within four weeks, and had minimal residual distal muscle weakness after 10 weeks of treatment. Median nerve motor conduction velocity increased to 12 m/s after 2 weeks of prednisolone, and was 21 m/s 4 weeks later. Further investigation revealed a strongly positive antinuclear factor without DNA-binding antibody. Anti-Ro and Anti-La

Table Fractional release of ³H. Dopamine from slices of caudate nucleus by exposure to 20 mM K⁺

	M	N	Tritium overflow as a percentage of tissue content
Control	—	15	3.9 ± 0.25
Flunarizine	1 × 10 ⁻⁶	10	2.7 ± 0.30*
Cinnarizine	2 × 10 ⁻⁷	6	2.4 ± 0.30*
Nifedipine	2 × 10 ⁻⁷	6	2.78 ± 0.30*

Means ± SEM; * $p < 0.05$.