

Letters to the Editor

Hereditary essential tremor and restless legs syndrome

Sir

Essential tremor is usually considered to be a monosymptomatic disorder with variable clinical expression, about half of all cases demonstrating an autosomal dominant pattern of inheritance.¹ Possible associations with other movement disorders have been described, including Parkinson's disease.² We report a patient with hereditary essential tremor and the restless legs syndrome.

A 71-year-old woman complained of a tremor in her right upper limb. This had affected her writing since her teens but had become worse in recent months, also affecting the left arm. The tremor was exacerbated by anxiety and fatigue; alcohol had no relieving effect. Tremulousness of the voice had made it increasingly difficult for her to sing in the church choir. She also complained of discomfort in the legs when sitting, unrelieved by massage but improved by getting up and walking about, and by taking a hot bath. She 'could not relax' because of an uncontrollable urge to move her legs when at rest. Although present throughout the day, this was particularly evident at night and often prevented her from falling asleep. This symptom had also been present since childhood when she had been labelled a 'fidget' at school because of her restlessness in class. A significant exacerbation of these symptoms occurred during pregnancy. Both her father and paternal grandfather had been troubled by a similar tremor of the arms. Moreover, her father had always been 'fidgety' and unable to settle. Her only sibling, a non-identical twin sister, was unaffected, likewise her only son (aged 47).

On examination, the patient had a distal tremor in the upper limbs, accentuated by posture. Writing showed intrusion of tremor and drawing of a spiral was impaired. Head titubation ('no-no') was also evident, and holding a single note revealed vocal tremor. Otherwise neurological examination was entirely normal; in particular, there were no dystonic features nor evidence of a peripheral neuropathy. Investigations (urea, creatinine, thyroid function tests, full blood count, serum vitamin B₁₂ and red cell folate) were normal. Treatment with propranolol (40 mg bid) marginally improved her postural tremor, but had no effect on her restless legs.

Clinically this patient had unequivocal hereditary essential tremor.¹ Furthermore, she fulfilled the suggested diagnostic criteria for restless legs syndrome.³ Previous accounts of an association between hereditary essential tremor and restless legs are few. Bornstein reported a pedigree in which restless legs and hereditary tremor coincided in three patients over two generations, with a similar time of onset in each patient, and opined that the syndromes were 'somehow associated'.⁴ Bain *et al* found restless legs in three of 93 patients with hereditary essential tremor; restless legs and tremor were found to co-segregate.¹ Jankovic has reported encountering several patients with the restless legs syndrome and an essential tremor-like tremor but gives no further details.⁵

The association between essential tremor and restless legs in our patient could be the chance concurrence of two relatively common

movement disorders. Alternatively, it may be indicative of an underlying link. The differing pharmacological responsiveness of the two disorders argues against a shared pathophysiological mechanism. A linkage at the genetic level would therefore seem more likely. Like hereditary tremor, restless legs syndrome has been reported to present in childhood and adolescence as an hereditary condition with probable autosomal dominant transmission.⁶ It may be that in this family, genes for essential tremor and restless legs have co-segregated. In such families, identification of the genetic locus for one condition may thus facilitate definition of the other.

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Hookworms to treat haemochromatosis?

Sir

Biological control strategies can be used to tackle ecological problems and plant diseases. For example, hydrocarbon-metabolizing bacteria are used to degrade oil spills and gardeners use parasitic organisms like the wasp *Encarsia formosa*, which preys on greenhouse whitefly. However, living organisms are rarely used for treatment of human disease, although Wagner von Janregy won a Nobel prize in 1927 for his work with malaria therapy for syphilis, now superseded by penicillin, and leeches are still valued by plastic surgeons. We should like to propose hookworms for the treatment of haemochromatosis.

Idiopathic haemochromatosis is an autosomal recessive inborn error of iron metabolism with accumulation of 20–40 g of iron resulting in multi-organ damage and death from cardiac failure or liver disease (normal body iron content is 3–4 g). Removal of excess iron reverses many of the biochemical and functional abnormalities.¹ Treatment includes weekly venesection of 450 ml of whole blood (equal to 0.2 g of iron) until iron stores return to normal, which may take

two to three years. Although some countries accept haemochromatosis sufferers as paid blood donors, asymptomatic patients in the UK may not perceive any tangible benefit from their weekly hospital visit and are excluded from blood donor panels.² Venesection is inconvenient and noncompliance can be a problem.

Ancylostoma duodenale is a nematode parasite of the human gut. The adult worms are 8–11 mm long, and attach to the mucosa of the upper small intestine with a set of cutting mouthparts. They live on blood and plasma protein sucked from the lamina propria, each worm consuming 0.2 ml of blood (about 0.09 mg of iron) per day. Worldwide, 700–900 million people harbour hookworms, making this infection second only to menstuation as the major global cause of iron deficiency.

The therapeutic potential of hookworms for haemochromatosis is obvious. To attain a daily blood loss equivalent to 450 ml per week, 300–400 worms would be required, depending on the amount of iron resorbed. *A. duodenale* lives for one to six years and autoinfection does not occur so blood loss is predictable. A three- or six-monthly blood count, albumin and ferritin would be used to monitor therapy. Commonly prescribed drugs would not kill the worms during their residence but once iron stores had returned to normal a two-day course of mebendazole should eradicate them. Hookworms are well adapted and, apart from anaemia, morbidity from natural worm infection is minimal. The practicalities of experimental human infection have been studied previously.^{3,4} Side-effects include pruritus at the site of cutaneous penetration, mild laryngeal and pulmonary symptoms during pulmonary passage and occasionally, upper gastrointestinal discomfort. In the UK there is no danger of transmission to others (except in the special case of miners working in warm damp tunnels) because the soil dwelling stage requires a high ambient temperature. The main problem is likely to be patient consent. There is a natural aversion to the idea of intestinal parasites and blood sucking creatures, and the knowledge that one was harbouring them could colour subsequent perception of abdominal symptoms. For long-term maintenance therapy only a little blood loss is required, so biannual venesection would be used. In conclusion, we feel that despite current enthusiasm for alternative and 'natural' medicine, the possibilities of hookworm therapy for haemochromatosis have been overlooked.

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