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Restless legs is a medical disorder and can be treated

Movement disorders have long been an interest of the Editor of *Neuropsychiatric Disease and Treatment* (Brimblecombe and Pinder 1972). Movement disorders can manifest as slowness or poverty of movement (hypokinesias) or as abnormal involuntary movements (hyperkinesias). Two of the commonest hyperkinesias are essential tremor, which has been described in a previous issue of the journal (Uccellini et al 2006), and restless legs syndrome (RLS), which occupies much of the current issue and was also reviewed in a recent issue (Byrne et al 2006).

RLS is a sensorimotor disorder characterized by an irresistible urge to move the limbs accompanied by uncomfortable sensations, leading to disturbed sleep and a poor quality of life. Symptoms usually begin or worsen during periods of rest or inactivity, and are partly or completely relieved by active movement. Symptoms tend to worsen in the evening and at night. Not all cases where legs are restless are due to RLS, and it can be distinguished from nocturnal leg cramps, positional discomfort, and akathisia. However, almost all RLS patients also experience periodic limb movements (PLMs) during sleep or while awake. RLS is a chronic neurological condition that occurs in two forms, a primary disorder independent of other disorders, and a form that is secondary to other conditions such as pregnancy, iron deficiency, and end-stage renal disease.

RLS affects about 5%–10% of the general adult population, but the risk increases in the elderly and in women. It can also affect children and adolescents, and is more common in children with ADHD. An early age of onset is indicative of a family history, while the familial nature of RLS is indicated by the demonstration of linkage to several chromosomal loci. The pathogenesis involves dopaminergic dysfunction, iron metabolism, and abnormalities in supraspinal inhibition.

Diagnosis is simple and based upon well-validated criteria. Nevertheless, RLS is misunderstood, frequently misdiagnosed, often classified as a psychogenic disorder, and patients can suffer inappropriate treatment and consequent distress. With correct diagnosis, counseling, and reassurance, many patients will not require pharmacological treatment which will be determined by the severity and nature of the symptoms. Treatment of secondary RLS should focus on the underlying cause where possible. Some drugs may exacerbate RLS, including antidepressants particularly tricyclics and fluoxetine, some antiemetics, calcium channel blockers, phenytoin, and excessive consumption of caffeine or alcohol especially at bedtime. Evidence-based treatment guidelines for RLS are available (Byrne et al 2006). Dopaminergic therapies are first-line treatments but there is also substantial, but lesser, evidence for the efficacy of some antiepileptic drugs especially gabapentin, for opioids like oxycodone and propoxyphene, for benzodiazepines particularly clonazepam, and for the α_2 -adrenergic agonist clonidine. Iron therapy, despite the evidence for the involvement of iron in the causality of RLS, has not been consistently shown to be effective, although it is recommended whenever serum ferritin levels are low.

In this issue of *Neuropsychiatric Disease and Treatment* the biopsychosocial aspects of RLS and particularly mental health problems like disturbances of mood and cognition are reviewed (Becker 2006), as well as the major influence that RLS has on sleep especially when it is accompanied by PLMs (Bogan 2006). Both authors

also briefly review treatment options and conclude that the evidence base is strongest for dopaminergic therapies and in particular ropinirole. Disturbed sleep, diminished quality of life, and mood symptoms are all alleviated by therapy with dopamine agonists. Individual dopaminergic agents are also reviewed. Ropinirole is currently the only FDA-approved therapy for RLS, a decision based upon several large scale clinical trials which established its safety and efficacy in treating the motor symptoms of RLS and improving sleep quality (Kushida 2006). Oral pramipexole (Benbir and Guilleminault 2006) and transdermal rotigotine (Bunten and Happe 2006), which are approved in many countries for the treatment of Parkinson's disease, have also undergone successful large-scale, randomized, and placebo-controlled trials in RLS. Data on pramipexole and rotigotine are promising, and both drugs should be soon added to the armamentarium of treatments for RLS. Other dopaminergic agents useful in RLS include L-dopa itself and the ergot derivatives pergolide and cabergoline (Becker 2006; Bogan

2006). Restless legs is a medical disorder that can be safely and effectively treated.

References

- Becker PM. 2006. The biopsychosocial effects of restless legs syndrome (RLS). *Neuropsychiatr Dis Treat*, 2:505-512.
- Benbir G, Guilleminault C. 2006. Pramipexole: new use for an old drug : the potential use of pramipexole in the treatment of restless legs syndrome. *Neuropsychiatr Dis Treat*, 2:393-405.
- Bogan RK. 2006. Effects of restless legs syndrome (RLS) on sleep. *Neuropsychiatr Dis Treat*, 2:513-519.
- Brimblecombe RW, Pinder RM. 1972. Tremors and tremorogenic Agents. Bristol: Scientechnica.
- Bunten S, Happe S. 2006. Rotigotine transdermal system: a short review. *Neuropsychiatr Dis Treat*, 2:421-426.
- Byrne R, Smita S, Chaudhuri KR. 2006. Restless legs syndrome: diagnosis and review of management options. *Neuropsychiatr Dis Treat*, 2:155-64.
- Kushida CA. 2006. Ropinirole for the treatment of restless legs syndrome. *Neuropsychiatr Dis Treat*, 2:407-19.
- Uccellini D, Grampa G, La Spina I, et al. 2006. Mirtazapine in the treatment of essential tremor: an open-label, observer-blind study. *Neuropsychiatr Dis Treat*, 2:95-100.