

# Restless Legs Syndrome

## Quick Facts:

Restless legs syndrome (RLS) is a sleep-related movement disorder that is diagnosed based on clinical history. RLS requires four cardinal symptoms; these symptoms can be remembered using the mnemonic URGE. RLS is characterized by the patient's (U)rge to move the legs because of uncomfortable sensations that may be difficult to describe; symptoms occur predominantly at (R)est or with inactivity; symptoms are relieved, at least temporarily, by (G)etting up and moving; and are worse in the (E)vening or night. The prevalence is 7-10%, with females reporting slightly higher rates. The nature and description of symptoms can vary. The sensations are generally reported bilaterally and below the knees but have also been reported unilaterally, more proximally in the legs, and even in the arms.



### Are my patients at risk of RLS?

RLS is associated with periodic limb movements of sleep (PLMS) in over 80% of patients; however, the presence of PLMS is not necessary for the diagnosis of RLS. PLMS are seen frequently in the general population, particularly in the elderly.

RLS has been linked to low iron stores and central dopaminergic neurotransmission. Genetic linkages have also been described. Approximately 50% of patients have a positive family history of RLS.

RLS may be seen more commonly in pregnancy, in patients with a source of pain in the lower extremities, and in those with chronic renal insufficiency, parkinsonism, multiple sclerosis, and epilepsy.

## Why It Matters

- RLS impairs quality of life. Patients with RLS may find it difficult to fall asleep or return to sleep after an awakening. This sleep disruption can result in chronic insufficient sleep and daytime sleepiness.
- RLS is associated with anxiety and depression.
- RLS can affect surgical outcomes. There may be significant worsening of RLS symptoms after surgery.
- RLS may be associated with cardiovascular disease. There is some data of an association between RLS and cardiovascular disease, but this area needs further study.

## What You Can Do

- Advise patients with RLS to avoid caffeine, alcohol and tobacco and to not donate blood.
- Encourage moderate physical activity. Mentally stimulating activities may help when the patient is at rest for prolonged periods of time, e.g., during a car or airplane ride.
- Review medications with anti-dopaminergic effects that can worsen RLS symptoms such as antiemetics, antihistamines and some psychotropic medications.
- Consider nonpharmacological treatments including warm or cool baths, massage, stretching, electric blankets and spontaneous compression devices. These may be effective in milder cases of RLS.

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- Check ferritin levels and consider iron supplementation if the level is less than 50-75 mcg/L. If the ferritin level is less than 10 mcg/L, consider other iron studies, evaluating for causes of iron deficiency and referral to a sleep medicine specialist for consideration of an intravenous iron infusion, particularly if symptoms are severe and/or the patient is unable to tolerate oral iron.
- Rule out RLS “mimics” such as peripheral neuropathy, pain, sleep-related leg cramps and akathisia.
- Consider a pharmacological treatment with a dopamine agonist (e.g., pramipexole, ropinirole, rotigotine) or  $\alpha 2\delta$  ligand (e.g., gabapentin) in cases where symptoms are frequent (e.g., occur more than half of the days of the week and/or result in difficulty initiating sleep). Those with infrequent but bothersome symptoms may respond to intermittent use of carbidopa-levodopa.
- Start the medication at low dose and increase gradually, stopping at the lowest effective dose. In the case of a dopamine agonist, the medication should be taken at least one hour (empty stomach) or two hours (with food) prior to the onset of symptoms.
- A dopamine agonist may be preferable if the patient has a history of depression, metabolic syndrome or falls. An  $\alpha 2\delta$  ligand may be preferred if there is a history of anxiety, pain or insomnia.
- Counsel the patient regarding potential side effects of medications including dizziness, sedation, the development of impulse control disorders (such as excessive gambling or shopping) and sleep attacks. Dopamine agonists can be associated with augmentation (new development or worsening of RLS symptoms), rebound, tolerance and withdrawal.

### When to Refer?

- Consider referral to a sleep medicine specialist in cases where symptoms are refractory to medication.

### Patient Information Websites:

- Restless Legs Syndrome Foundation [www.rls.org](http://www.rls.org)
- National Institute of Neurological Disorders and Stroke [www.ninds.nih.gov/disorders/restless\\_legs/detail\\_restless\\_legs](http://www.ninds.nih.gov/disorders/restless_legs/detail_restless_legs)
- American Academy of Sleep Medicine [www.sleepeducation.org/find-a-facility](http://www.sleepeducation.org/find-a-facility)

### References:

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2. <https://www.ninds.nih.gov/Disorders/Patient-Caregiver-Education/Fact-Sheets/Restless-Legs-Syndrome-Fact-Sheet>
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7. Winkelmann JW, Shahar E, Sharief I, Gottlieb DJ. Association of restless legs syndrome and cardiovascular disease in the Sleep Heart Health Study. Neurology. 2008;70(1):35-42.
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9. Silber MH, Becker PM, Earley C, et al. Willis-Ekbom Disease Foundation revised consensus statement on the management of restless legs syndrome, Mayo Clin Proc. 2013;88:977-986.
10. Allen RP, Picchietti DL, Auerbach M, et al. Evidence-based and consensus clinical practice guidelines for the iron treatment of restless legs syndrome/Willis-Ekbom disease in adults and children: an IRLSSG task force report. Sleep Med. 2018;41:27-44.
11. Garcia-Borreguero D, Silber MH, Winkelmann JW, et al. Guidelines for the first-line treatment of restless legs syndrome/Willis-Ekbom disease, prevention and treatment of dopaminergic augmentation: a combined task force of the IRLSSG, EURLSSG, and the RLS-foundation. Sleep Med. 2016;21:1-11.

### Referring Guidelines:

- [aasm.org/clinical-resources/practice-standards/practice-guidelines](http://aasm.org/clinical-resources/practice-standards/practice-guidelines)
- [n.neurology.org/content/87/24/2585](http://n.neurology.org/content/87/24/2585)