

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; while some evidence suggests an association, further research is needed to better understand this relationship.

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 and bilateral high-frequency peroneal nerve stimulation. Treatment of coexisting obstructive sleep apnea may improve RLS symptoms.

- Check ferritin levels and transferrin saturation and consider iron supplementation if ferritin level is less than 75 mcg/L or transferrin saturation <20%. 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. Intravenous iron may also be considered if serum ferritin is between 75 and 100 mcg/L.
- Rule out RLS “mimics” such as peripheral neuropathy, pain, sleep-related leg cramps and akathisia.
- Consider a pharmacological treatment with a $\alpha 2\delta$ ligand (e.g., gabapentin, pregabalin) 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).
- Start the medication at low dose and increase gradually, stopping at the lowest effective dose.
- Dopamine agonists (e.g., pramipexole, ropinirole, rotigotine) are not recommended for standard use in RLS due to the risk of augmentation, but may be considered in patients who place a higher value on the reduction of RLS symptoms with short-term use and a lower value on adverse effects with long-term use.
- Counsel the patient regarding potential side effects of $\alpha 2\delta$ ligands including dizziness and sedation. Dopamine agonists can be associated with impulse control disorders (such as excessive gambling or shopping), sleep attacks, augmentation (new development or worsening of RLS symptoms), rebound, tolerance and withdrawal.
- In refractory RLS, consider referral to a sleep medicine specialist. Treatment options include combination therapy with a $\alpha 2\delta$ ligand and dopamine agonist, or monotherapy with a long-acting opioid in appropriate patients, in addition to non-pharmacological interventions and iron replenishment.

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
- National Institute of Neurological Disorders and Stroke <https://www.ninds.nih.gov/health-information/disorders/restless-legs-syndrome>
- American Academy of Sleep Medicine 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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9. Silber MH, Buchfuhrer MJ, Earley CJ, et al. The Management of Restless Legs Syndrome: An Updated Algorithm. Mayo Clin Proc. 2021;96(7):1921-1937.
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11. Garcia-Borreguero D, Silber MH, Winkelman 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
- n.neurology.org/content/87/24/2585