Restless Legs Syndrome
Darlene Moyer, MD, Javier Zayas-Bazan, MD, and Danielle Miller, DO, HonorHealth, Phoenix, AZ

Restless Legs Syndrome (RLS) is a common condition that geriatricians and primary care clinicians can easily manage. This issue of Elder Care will review the most important information needed to diagnose and treat RLS.

What is RLS?
Patients with RLS suffer from a strong urge to move their legs or other body parts. Since the urge is brought on by rest and is worse in the evening, it results in significant sleep disruption and can lead to daytime somnolence and diminished quality of life.

How Common is RLS?
RLS is estimated to affect about 10% of all adults, and up to 25% of those over 65. Older adults with RLS tend to have more severe symptoms than younger people because of the natural progression of the disease.

Diagnostic Criteria
There are no physical exam or lab findings that definitively identify RLS, so expert panels have developed specific clinical criteria to help diagnose the condition. Diagnosis is based on history alone, and there are five “essential criteria” that must be present to make the diagnosis: (1) a strong urge to move the legs or other body parts that (2) is brought on by rest, (3) gets better with activity, (4) gets worse in the evening or night, and (5) cannot be accounted for by another medical or behavioral condition. These essential criteria are partially defined by the URGE mnemonic: U=urge to move, R=rest-induced, G=get better with activity, and E=evening or night-time accentuation.

In addition to the essential criteria, there are supportive features that are not required but help with diagnosis. They include the presence of periodic limb movements, a response to dopaminergic therapy, family history of RLS, and a lack of expected daytime sleepiness.

RLS can be classified as “chronic-persistent” (untreated symptoms occur ≥twice weekly for a year) or “intermittent” (untreated symptoms that occur less than twice weekly). In addition, RLS can be classified as “clinically significant” or “not clinically significant,” based on the amount of distress and impairment that results.

RLS must be differentiated from other disorders that can have similar symptoms. Table 1 summarizes a few other movement disorders that can be confused with RLS.

Table 1. Some Conditions That Can Mimic RLS

<table>
<thead>
<tr>
<th>Condition</th>
<th>What is Different than RLS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypnagogic jerks</td>
<td>Sudden, brief, involuntary jerks of arms or legs, typically at onset of sleep</td>
</tr>
<tr>
<td>Sleep-related cramps</td>
<td>Involve specific muscle groups. Relieved (or partially relieved) by stretching</td>
</tr>
<tr>
<td>Pain syndromes</td>
<td></td>
</tr>
<tr>
<td>Neuropathic pain</td>
<td>Pain may occur during periods of activity, rather than only during rest</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>Claudication (pain) evoked by activity, rather than by rest</td>
</tr>
<tr>
<td>Painful-legs/moving-toes syndrome</td>
<td>Continuous/semi-continuous involuntary toe movement with associated leg pain, usually in patients with spinal cord or foot/leg injuries</td>
</tr>
<tr>
<td>Drug–induced syndromes</td>
<td></td>
</tr>
<tr>
<td>Neuroleptic-induced akathisia</td>
<td>Day or nighttime restlessness (in patient taking neuroleptic) that is generalized, immediately relieved with movement, and recurs after stopping movement</td>
</tr>
<tr>
<td>Normal positional discomfort</td>
<td>Alleviated by change in body position without need for repetitive body movements</td>
</tr>
</tbody>
</table>

TIPS FOR TREATING RESTLESS LEGS SYNDROME
- Always check a ferritin level in patients with suspected RLS, and give iron therapy if ferritin is <75 µg/L.
- Recommend non-drug treatment as first-line therapy. It includes good sleep hygiene practices, daytime exercise, and avoiding substances that can aggravate RLS.
- If drug therapy is needed, consider the newer agents, pramipexole and ropinirole, as they are less apt to cause rebound and augmentation than are levodopa/carbidopa.
- Prescribe chronic opioids only for severe cases that don’t respond to other treatments.
Secondary Causes
The most common identifiable conditions known to cause RLS include iron deficiency, renal failure, medication side effects and, in younger adults, pregnancy. Screening for these secondary causes with a history, physical, and laboratory exams can eliminate these treatable causes of RLS. Ferritin levels should be checked in all patients with RLS symptoms and iron replacement therapy given if levels are <75 µg/L, even if the patient is not anemic. Consider checking TSH, vitamin B12, and vitamin D levels as well. There is also an association between RLS and mood disorders and patients should be screened for these conditions.

Non-Drug Treatments
Non-drug treatment options include instituting good sleep hygiene practices, increased daytime physical exercise, mentally stimulating activities, and avoiding stimulants and other substances that can exacerbate symptoms (Table 2). Patients might also consider trying pneumatic compression devices prior to the typical onset of symptoms.

Drug Treatment
Drug treatment aims to control symptoms and avoid augmentation. First line options include dopamine agonists, and gabapentin-related medications (Figure 1).

A major concern about drug therapy is augmentation, which occurs when patients on dopamine agonists begin to experience RLS symptoms earlier in the day compared to before therapy was started. Augmentation is not, however, associated with the gabapentin-related medications. Augmentation can be managed by switching agents or drug classes, decreasing dose, or implementation of a “drug holiday.”

Alternative drug treatments include chronic opioids. Therapy with these alternative medications must be reserved for severe cases, used with caution in older adults, and individualized to each patient’s comorbidities, and medication tolerance and response. Figure 1 provides a stepwise approach to drug therapy based on symptom frequency and severity.

<table>
<thead>
<tr>
<th>Table 2. Common Medications that Can Worsen Restless Legs Syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antihistamines</td>
</tr>
<tr>
<td>Caffeine and other stimulants</td>
</tr>
<tr>
<td>Calcium-channel blockers</td>
</tr>
</tbody>
</table>

Figure 1. Stepwise Approach to Treatment of Restless Legs Syndrome

**STEP 3**

**Refractory Symptoms (Changing Therapy)**
- First: change to a different first-line agent
- Next: consider changing to a different dopamine agonist or second-line agent
- Also: If augmentation occurs consider a “drug holiday” from dopamine agonists; use gabapentin-related agents or different dopamine agonists in the interim
- Finally: consider opioids for severe/resistant cases

**STEP 2**

**Daily Symptoms (Daily Therapy)**
- First-line treatments (level A evidence per American Academy of Neurology guidelines):
  - dopamine agonists (pramipexole, rotigotine)
  - gabapentin enacarbil
- Second-line treatments (level B evidence per American Academy of Neurology guidelines):
  - other dopamine agonists (ropinirole)
  - pregabalin

**STEP 1**

**Intermittent Symptoms (As-Needed Therapy)**
- First-line treatment: non-drug treatment, avoidance of triggering substances, treatment of secondary causes
- Second-line treatment: as-needed therapy with dopamine agonist (see step 2)

References and Resources
Muth CC. JAMA Patient Page. Restless legs syndrome. JAMA 2017; 317/780