Restless legs syndrome (RLS)/Willis-Ekbom disease (WED) is a common disorder, occurring at least twice a week and causing at least moderate distress in 1.5% to 2.7% of the population. It is important for primary care physicians to be familiar with this disorder and its management. Much has changed in its management since our previous algorithm was published in 2004, including the availability of several new drugs. This revised algorithm was written by members of the Medical Advisory Board of the Willis-Ekbom Disease Syndrome Foundation based on scientific evidence and expert opinion. It considers the management of RLS/WED under intermittent RLS/WED, chronic persistent RLS/WED, and refractory RLS/WED. Non-pharmacological approaches, including mental alerting activities, avoiding substances or medications that may exacerbate RLS, and the role of iron supplementation, are outlined. Chronic persistent RLS/WED should be treated with either a nonergot dopamine agonist or a calcium channel $\alpha_2\delta$ ligand. We discuss the available drugs, the factors determining which to use, and their adverse effects. We define refractory RLS/WED and describe management approaches, including combination therapy and the use of high-potency opioids.

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Experience with calcium channel $\alpha_{2-\delta}$ ligands, including gabapentin and pregabalin, has increased. Several long-acting drugs have become available, including the rotigotine patch \cite{14,15} and the gabapentin prodrug gabapentin enacarbil.\cite{16} The role of opioids in the management of refractory RLS/WED has become better defined,\cite{12} and there have been a variety of studies of iron therapy.\cite{17,19} Long-term therapeutic studies extending over 5 to 10 years have been published.\cite{11,12,15} As a result of these developments, the Willis-Ekbom Disease Foundation MAB decided that the time was right to issue a revised algorithm. Where no changes are recommended from the 2004 algorithm, the text has been left unchanged.

At the time that the 2004 algorithm was published, there were 2 available rigorous evidence-based reviews of the treatment of RLS/WED prepared under the auspices of the Standards of Practice Committee of the American Academy of Sleep Medicine.\cite{20,21} Since then, several more evidence-based articles have appeared, including an update from the American Academy of Sleep Medicine and a therapy guideline article jointly produced by the European Federation of Neurological Societies, the European Neurological Society, and the European Sleep Research Society.\cite{22,23}

Most recently, the International RLS Study Group has published evidence-based and clinical consensus best practice guidelines for the long-term management of RLS/WED.\cite{24} Although evidence-based reviews are valuable, they may not in isolation be helpful for the primary care clinician trying to determine the optimal therapy for a particular patient. Conclusions from such reviews are constrained by the breadth and quality of the published peer-reviewed literature. The highest level of evidence usually requires large multicenter studies that are almost always funded by the manufacturer of the drug to be tested. Thus, the degree of evidence to support a specific medication may depend on whether a pharmaceutical manufacturer has been willing to fund large studies. For similar reasons, few, if any, large comparative studies of different drugs have been published. Large controlled trials usually test short-term use of drugs, and long-term studies generally provide lower levels of evidence, being either uncontrolled prospective or retrospective studies. Nevertheless, data on continued use of medication in the community may be highly relevant for medical practice. For many of these reasons, evidence-based reviews generally make authoritative statements on the degree of evidence in support of the use of each medication for a defined disorder, but they are not always conducive to the development of practical algorithms for the management of disorders of varying severity and a lengthy natural history. For relatively rare conditions managed predominantly by specialists with considerable experience and a reasonable knowledge of the published literature, evidence-based reviews may be sufficient. However, for primary care physicians seeking a practical approach to common disorders, evidence-based reviews alone may be insufficient.

To prepare the revised algorithm, the Willis-Ekbom Disease Foundation MAB established a task force from among its members who produced and revised a draft that was submitted for approval to the other members of the board. The authors have had many years of experience in the treatment of RLS and have conducted original research on this disorder. Some have been members of task forces that have produced the previously discussed evidence-based reviews. The effort was supported by the board of directors and executive director of the Willis-Ekbom Disease Foundation, but this article is entirely the unpaid work of the physicians and scientists on the MAB. It is based on detailed knowledge of the literature, including evidence-based assessments, and on expert opinion from practical experience. We recognize that a different group of specialists might have produced a somewhat different algorithm, but we believe that our approach reflects current thinking about the management of RLS/WED. We expect that the development of new medications and further research on existing ones may alter clinical approaches in the future. Of note, the US Food and Drug Administration has approved pramipexole, ropinirole, the rotigotine patch, and gabapentin enacarbil for the treatment of RLS/WED, and, thus, all other drugs discussed are being used off label. Although we have attempted to produce an accurate document, it is the responsibility of individual physicians to familiarize themselves with all aspects of the medications they prescribe and to decide whether a specific drug is appropriate for a particular patient.
INTERMITTENT RLS/WED

Intermittent RLS/WED is defined as restless legs troublesome enough to require treatment but occurring on average less than twice a week (Figure 1).

Nonpharmacological Strategy

A nonpharmacological approach involves the following:

- Determining the patient’s iron status (early-morning fasting iron panel: iron, serum ferritin, total iron-binding capacity, and percentage of iron saturation). If the iron stores are low, administer iron replacement (see subsequent comment 1).
- Recommend mental alerting activities, such as video games or crossword puzzles, to reduce symptoms at times of boredom (see subsequent comment 2).
- Consider a trial of abstinence from caffeine (see subsequent comment 2).
- Consider whether antidepressants, neuroleptic agents, dopamine-blocking antiemetics (such as metoclopramide), or sedating antihistamines (including those found in nonprescription medications) may be contributing and whether discontinuation is possible without causing the patient harm (see subsequent comment 2).

Comments

1. Because RLS/WED may be the only clinical indication of iron deficiency, clinicians should consider evaluating the iron status in all patients with RLS/WED, especially those with a history of gastrointestinal blood loss, disorders or medications predisposing to gastrointestinal blood loss, menorrhagia, frequent blood donation, or recent onset or worsening of symptoms. If the serum ferritin concentration is in the abnormal range (usually <20 μg/L [to convert to pmol/L, multiply by 2.25] but adjusted based on age, sex, and the normative data from the specific laboratory) or percentage of iron saturation is low (<18%), a cause of iron deficiency should be pursued and replacement treatment instituted. A serum ferritin concentration lower than 45 to 50 μg/L has been associated with an increased severity of RLS/WED, and treatment of patients with ferritin levels less than 75 μg/L has been shown to improve symptoms. Therefore, therapy can be attempted in patients with levels in this low-normal range on a case-by-case basis. Note that serum ferritin is an acute-phase reactant and can be falsely elevated in the presence of acute infection or chronic inflammation.

A common therapeutic regimen is 325 mg of ferrous sulfate (65 mg of elemental iron) combined with 100 to 200 mg of vitamin C with each dose to enhance absorption 2 to 3 times a day. Oral iron therapy can cause constipation and abdominal discomfort, and the dose may need to be reduced in some patients, requiring a longer duration of therapy. Iron tablets should ideally be taken on an empty
stomach to enhance absorption, but if gastrointestinal symptoms develop, they can be taken with food. Iron should not be prescribed empirically because it may result in iron overload, especially in patients with previously unsuspected hemochromatosis. Follow-up ferritin level determinations are needed, initially after 3 to 4 months and then every 3 to 6 months until the serum ferritin level is greater than 75 μg/mL and the percentage of iron saturation is greater than 20%. Iron therapy can then be discontinued if an ongoing cause for iron deficiency has not been established. However, follow-up serum ferritin level determinations to ensure that levels do not decrease are recommended at least every 1 to 2 years, and earlier if RLS/WED symptoms worsen. Note that patients with RLS/WED do not always respond to an increasing serum ferritin concentration, even if it was low initially.

2. The recommendations to engage in mental alerting activities and to consider a trial of abstinence from caffeine are largely based on clinical experience rather than on scientific studies.

3. Clinical experience suggests that most antidepressant agents may sometimes be associated with initiation or worsening of RLS/WED. However, if antidepressants are deemed necessary, the symptoms can usually be treated in the same way as primary RLS/WED. Alternatively, use of bupropion can be considered because this antidepressant with dopamine agonist properties does not seem to induce or worsen RLS/WED.

**Medication**

Intermittent use of the following medications may be helpful:

- Carbidopa/levodopa, 25 mg/100 mg, or the controlled-release formulation, 25 mg/100 mg (see subsequent comment 4)
- Low-potency opioids, such as codeine, or opioid agonists, such as tramadol (see subsequent comment 5)
- Benzodiazepines or benzodiazepine agonists, such as temazepam, zolpidem, zaleplon, or eszopiclone (see subsequent comment 6)

**Comments**

4. Carbidopa/levodopa, 25 mg/100 mg (0.5-1.0 tablets), can be used for RLS/WED that occurs intermittently in the evening, at bedtime, or on waking during the night or for RLS associated with specific activities, such as airplane or lengthy car rides or theater attendance. Controlled-release carbidopa/levodopa, 25 mg/100 mg (1 tablet), can be used alternatively at bedtime for RLS that awakens the patient during the night. Even the controlled-release form has a relatively short duration of action and may not produce sustained efficacy if RLS/WED persists throughout much of the night. Controlled trials have shown the efficacy of both preparations. For maximal absorption, levodopa should not be taken with high-protein foods.

Problems with levodopa treatment include augmentation and rebound. Augmentation (see subsequent comment 7) may occur in up to 70% of patients taking levodopa daily, and the risk increases with daily doses of 200 mg or more. As a result, levodopa should be prescribed only for intermittent use, such as fewer than 3 times a week, although a lower risk of augmentation with such use has not been firmly established. Rebound, the recurrence of RLS/WED in the early morning, occurs in 20% to 35% of patients taking levodopa. (Because the action of dopamine agonists generally commences 90 to 120 minutes after ingestion, these agents cannot be used effectively once symptoms have started, and they are rarely prescribed for intermittent RLS/WED.)

5. Intermittent use of low-potency opioids or opioid receptor agonists, usually at bedtime, can be effective. Doses of 30 to 60 mg of codeine, usually available in combined preparations with acetaminophen, or 50 to 100 mg of tramadol can be taken at bedtime or during the night. Constipation or nausea may occur. Tramadol can rarely induce seizures, and it is the only non-dopaminergic drug associated occasionally with the development of augmentation.

6. Intermittent use of benzodiazepines or benzodiazepine receptor agonists before sleep may be useful, especially if the patient has another cause of poor sleep
in addition to RLS/WED, such as psychophysiologic insomnia. Short-acting agents, such as zolpidem (5-10 mg) and zaleplon (5-10 mg), may be helpful for sleep-onset insomnia caused by RLS/WED; intermediate-acting agents, such as temazepam (15-30 mg) and eszopiclone (1-3 mg), may be helpful for RLS/WED that awakens the patient later in the night. Long-acting agents, such as clonazepam, may result in more adverse effects, such as impotence in older men, unsteadiness during the night, and drowsiness or cognitive impairment in the morning, and should generally be avoided. There are no adequate controlled trials of benzodiazepines for RLS/WED, and it is likely that the drugs act by treating the associated insomnia rather than the sensory or motor symptoms of the disorder.

**CHRONIC PERSISTENT RLS/WED**

Chronic persistent RLS/WED is defined as RLS that is frequent and troublesome enough to require daily treatment, usually occurring on average at least twice a week and resulting in moderate or severe distress (Figure 2).

**Nonpharmacological Strategy**

The nonpharmacological approach to chronic persistent RLS/WED is the same as for intermittent RLS. Iron stores should be checked in all patients.

**Medication**

Choose between the following:

- A nonergot dopamine agonist (pramipexole, ropinirole, or the rotigotine patch) (see subsequent comment 7)
- An \( \alpha-2\delta \) calcium channel ligand (gabapentin, pregabalin, or gabapentin enacarbil) (see subsequent comment 8)

Table 1 lists clinical features that should be considered in the choice of an initial drug. Because the \( \alpha-2\delta \) ligands can cause depression and weight gain, a dopamine agonist is a more appropriate choice in the presence of these conditions. \( \alpha-2\delta \) Ligands can alleviate chronic pain and may be helpful in treating anxiety and insomnia, so the presence of any of these comorbidities may favor their use. For restless legs present through much of the day and night, consider the use of long-acting agents, such as the rotigotine patch or gabapentin enacarbil.

**Comments**

7. Nonergot dopamine agonists (Table 2) should be used because ergot agonists, such as cabergoline, are associated with cardiac valvular fibrosis and other fibrotic reactions. Pramipexole is usually commenced as 0.125 mg once daily, taken 2 hours before major RLS symptoms start. The dose is increased by 0.125 mg every 2 to 3 days until relief is obtained. Most patients require 0.5 mg or less, and patients taking higher doses should be carefully monitored for adverse effects, especially augmentation (see later herein). Experts differ on an acceptable maximum daily dose, but most agree that this should not exceed 0.75 or 1.0 mg. Ropinirole is usually commenced as 0.25 to 0.5 mg taken 1.5 hours before major symptoms start and is increased by 0.25 to 0.5 mg every 2 to 3 days. Most patients require 2 mg or less (note that 4-times higher equivalent doses are needed compared with pramipexole),
but total daily dosages up to 4 mg may be needed. Some patients require twice-daily doses of oral agonists, with an earlier dose in the late afternoon or early evening and a second dose before going to bed. The rotigotine patch is applied once daily, commencing at 1 mg and increasing, if necessary, to 2 to 3 mg. Minor adverse effects of the agonists include nausea and light-headedness that usually resolve within 10 to 14 days. Nasal stuffiness, constipation, insomnia, and leg edema occur less frequently and are reversible with cessation of treatment. Hypersomnia and sleep attacks may occur, often at higher doses. Application site reactions may occur with the rotigotine patch. Careful monitoring for adverse effects is essential, especially when higher doses are used.

Two major problems often limit the use of dopamine agonists. First, augmentation (a worsening of RLS symptoms earlier in the day after an evening dose of medication, including earlier onset of symptoms, increased intensity of symptoms, or spread of symptoms to the arms) occurs in 40% to 70% of patients using pramipexole for up to 10 years and probably a similar percentage with ropinirole. The frequency of augmentation with the rotigotine patch may be slightly lower at 36%. Second, 6% to 17% of patients experience impulse control disorders, such as pathologic gambling, impulsive shopping, or hypersexuality. These symptoms commence an average of 9 months after introduction of the drug, so patients should be questioned about them at every follow-up visit.

8. Gabapentin and pregabalin (Table 3) are usually administered as once- or twice-daily doses in the late afternoon or evening or before sleep. Treatment should commence at 300 mg of gabapentin or 100 mg of pregabalin daily and should be increased every few days as needed. Many patients require 900 to 1800 mg of gabapentin daily, but doses up to 3600 mg/d can be used. Because of nonlinear kinetics, the gabapentin dose does not always reflect the serum level. Effective pregabalin doses are usually in the range of 150 to 450 mg/d. Gabapentin enacarbil is a prodrug of gabapentin, converted to gabapentin after absorption. It is administered as a single daily dose of 600 mg at 5 PM. Doses of 1200 mg have been used. Class-specific adverse effects include drowsiness, dizziness, unsteadiness, weight gain, and depression. Patients should be carefully monitored for the development of adverse effects, especially if higher doses are used.

9. If augmentation develops with dopamine agonists, consider initially splitting the

<table>
<thead>
<tr>
<th>Variable</th>
<th>Pramipexole</th>
<th>Ropinirole</th>
<th>Rotigotine patch</th>
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<tr>
<td>Time to maximum blood level (h)</td>
<td>2</td>
<td>1-1.5</td>
<td>Stable plasma levels over 24 h</td>
</tr>
<tr>
<td>Elimination half-life (h)</td>
<td>8-12 (increases with decreasing glomerular filtration rate and age)</td>
<td>6</td>
<td>Stable plasma levels over 24 h (elimination half-life biphasic: 3 and 6)</td>
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<tr>
<td>Metabolism and excretion</td>
<td>Renal</td>
<td>Hepatic metabolism and renal excretion</td>
<td>Hepatic metabolism and renal excretion</td>
</tr>
<tr>
<td>Initial daily dose (mg)</td>
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<td>0.25 (&lt;0.5)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>1</td>
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<tr>
<td>Maximum daily dose (mg)</td>
<td>0.5 (&lt;1.0)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>4</td>
<td>3</td>
</tr>
</tbody>
</table>

<sup>a</sup>RLS = restless legs syndrome; WED = Willis-Ekbom disease.
<sup>b</sup>Values in parentheses differ from Food and Drug Administration—approved values.
dose with some of the drug administered earlier in the day.24 (Use of extended-release pramipexole or ropinirole can be considered, generally without increasing the total daily dose, although there are no data available on their use in RLS/WED.) If an increase in the total dose of agonist is deemed necessary, careful monitoring is essential to detect progressive augmentation, in which case the drug should be discontinued.

10. If the first drug is ineffective or poorly tolerated, consider a change to another agent in the same class.24 In particular, consider the rotigotine patch if progressive augmentation has developed while taking pramipexole or ropinirole. However, careful monitoring is needed if class-specific adverse effects occurred with the first drug, and should these recur with the second drug, further agents in the same class should not be used.

11. If 1 or more drugs in the first class tried are ineffective or poorly tolerated, consider a change to an agent in the other class (an \(\alpha-2\beta\) ligand for an agonist and vice versa). This can be achieved in 2 ways. The initial drug can be reduced slowly at the same time as the new agent is introduced, with an overlap period when the patient is taking both medications. Alternatively, the initial drug can be reduced and discontinued, with a drug holiday before introducing the new agent. Although this can allow for a new symptom baseline to be established, many patients find it hard to tolerate a period free of any medication. (Note that higher doses of dopamine agonists should never be discontinued abruptly because serious withdrawal effects can occur. Rates of reduction should not exceed 0.25 mg of pramipexole or 0.5 mg of ropinirole every 3 days.)

REFRACTORY RLS/WED

Refractory RLS/WED is restless legs unresponsive to monotherapy with tolerable doses of first-line agents due to reduction in efficacy, augmentation, or adverse effects (Figure 3).

The following approach should be used:

- Iron stores should be rechecked. If the serum ferritin level is less than 50 to 75 \(\mu\)g/L, oral iron supplementation should be prescribed. If this does not result in increasing serum ferritin levels owing to malabsorption or if oral iron intake is not tolerated, intravenous administration of iron should be considered (see subsequent comment 12).
- Other exacerbating factors should be sought, including the use of antihistamines or other medications that can worsen restless legs (see the “Intermittent RLS/WED” section), change in lifestyle (such as more sedentary behavior or shift work), or other causes of sleep disturbance, such as sleep apnea or chronic insufficient sleep.
- Consider combination therapy with drugs of different classes. Add a second agent and try to reduce the dose of the initial drug. Second agents may include a dopamine agonist for patients treated with an \(\alpha-2\beta\) ligand or vice versa, a benzodiazepine (if restless legs are present mainly at night with resulting insomnia), or a low- or high-potency opioid. Usually, the initial agent is continued at the same dose, but it may be possible to reduce the dose with time (see previous comments 5 and 6).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Gabapentin</th>
<th>Pregabalin</th>
<th>Gabapentin enacarbil</th>
</tr>
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<tr>
<td>Time to maximum blood level (h)</td>
<td>2</td>
<td>1.5</td>
<td>7-9</td>
</tr>
<tr>
<td>Elimination half-life (h)</td>
<td>5-7</td>
<td>6</td>
<td>Relatively stable plasma levels over 18-24 h (elimination half-life: 6)</td>
</tr>
<tr>
<td>Metabolism and excretion</td>
<td>Renal</td>
<td>Renal</td>
<td>Intestinal metabolism and renal excretion</td>
</tr>
<tr>
<td>Initial daily dose (mg)</td>
<td>300</td>
<td>100</td>
<td>600</td>
</tr>
<tr>
<td>Maximum daily dose (mg)</td>
<td>3600</td>
<td>450</td>
<td>600 (~1200)(^b)</td>
</tr>
</tbody>
</table>

\(^{a}\)RLS = restless legs syndrome; WED = Willis-Ekbom disease.

\(^{b}\)Value in parentheses differs from the Food and Drug Administration—approved value.
Consider substituting a high-potency opioid, such as oxycodone, hydrocodone, or methadone. In particular, consider low-dose methadone for severe refractory RLS resistant to other treatments. Daily effective doses of these drugs usually range from 5 to 20 mg in single or divided doses, depending on the time of symptoms. In some patients, a long-acting form of oxycodone may be most appropriate, but total daily doses should be kept low and should never approach the higher doses used for the management of chronic pain (see subsequent comment 13).

**Comments**

12. Intravenous iron should currently be restricted to patients with proven low or low-normal serum ferritin levels who are intolerant of oral iron or who are resistant to oral iron because of malabsorption. Iron gluconate, iron sucrose, iron dextran, and ferumoxytol are all infusion preparations available in the United States. Although iron dextran is associated with risk of anaphylaxis, the more recently developed low-molecular-weight iron dextran has a reduced incidence of anaphylactic reactions, estimated to be 1 per 200,000 infusions. A trial of ferric carboxymaltose in patients with RLS/WED had positive results, but the preparation is not currently available in the United States.

13. High-potency opioids may be highly effective in the management of RLS and should not be withheld from appropriate patients because of a fear of potential development of tolerance or dependence. Escalation of dose is uncommon, and dependence is infrequent in the absence of a history of substance abuse. Nausea and constipation are rare. Itch may be a problem due to mast cell degranulation rather than allergy. Daytime drowsiness, cognitive dysfunction, and unsteadiness resulting in falls, especially at night, are potential adverse effects. Opioids can precipitate or worsen obstructive sleep apnea and can induce central sleep apnea, especially in patients using continuous positive airway pressure (complex sleep apnea). Screening overnight oximetry or polysomnography should be considered for patients with RLS/WED taking opioids if there is a suspicion of sleep apnea. Generally, however, these medications are well tolerated at the recommended doses.

**ALTERNATIVE, INVESTIGATIVE, AND POTENTIAL FUTURE THERAPIES**

The management of RLS continues to evolve as new drugs become available and older ones are prescribed less frequently. Basic science studies to better understand the pathogenesis of RLS/WED will, with time, lead to the exploration of novel therapeutic agents. Further research is needed to understand the augmentation phenomenon associated with dopaminergic agents and to determine how best to reduce or avoid it. Long-term follow-up studies of the α-2-δ ligands are needed. Carbamazepine and clonidine have been used successfully in controlled trials but are not commonly used in clinical...
practice. Because carbamazepine may be effective, studies of other medications used to treat seizures should be considered. Controlled trials of high-potency opioids should be performed. An as-yet unpublished trial comparing pregabalin and pramipexole showed these drugs were equivalently efficacious (Richard Allen, PhD, written communication, July 2013). Further systematic studies of combination therapy are needed. Serum markers of iron deficiency may not reflect intracerebral iron concentration, and thus, intravenous iron has been suggested for patients without consideration of systemic iron stores. Results of controlled trials with iron sucrose have been negative, but a randomized double-blind trial of ferric carboxymaltose vs placebo in 46 patients with RLS and serum ferritin levels of 20 to 200 μg/L found symptomatic improvement in more than half of those treated. More work on intravenous iron therapy is needed. In 2004, we stated that this algorithm will undoubtedly need revision in the future as our understanding of RLS grows and new pharmacological agents are developed. This is again true in 2013.

CONCLUSION
Restless legs syndrome/Willis-Ekbom disease is a common disorder leading to considerable morbidity. A practical approach to its management includes accurate diagnosis, identification of reversible contributing factors, and appropriate use of nonpharmacological therapies, including iron replacement. Many pharmacological agents are effective in treating the condition. Appropriate choice of a drug depends on stratification of the disorder into intermittent, chronic progressive, and refractory subtypes; determination of individual patient factors, including other medical disorders; and consideration of potential adverse effects of the drugs. Standard medications for chronic progressive RLS/WED are noneergot dopamine agonists (pramipexole, ropinirole, and rotigotine) and calcium channel α2-δ ligands (gabapentin, gabapentin enacarbil, and pregabalin). Opioids should be considered when the disease is refractory to other agents.

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Abbreviations and Acronyms: MAB = Medical Advisory Board; RLS = restless legs syndrome; WED = Willis-Ekbom disease

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REFERENCES


