



Restless Legs Syndrome: A Sleepless Situation



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Restless legs syndrome (RLS) consists of an overwhelming urge to move the legs, usually caused by an unpleasant sensation. The sensations occur during periods of inactivity, becoming worse in the evening and at night and are relieved by movement of the limbs.

Janet's Sleepiness

History...

- Since she was a teenager, Janet has needed to move her legs prior to falling asleep.



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Is it inherited?

The exact cause of RLS is unknown. The majority of cases seem to be inherited or “primary” (Table 1). Primary RLS needs to be differentiated from RLS triggered by some underlying peripheral nerve problem or other systemic metabolic abnormality (“secondary”).

Why are people with RSL sleepy during the day?

RLS causes difficulty with falling asleep and is associated with involuntary jerking of the limbs during sleep (periodic leg movements of sleep, typically occurring every 20 to 40 seconds). These features combine to cause daytime somnolence.

- Janet was treated with fluoxetine at age 45 due to a mild depression.
- During the last six months, the problem with leg discomfort has become much more severe and prevents her from falling asleep.
- She is very sleepy during the day and reports trouble concentrating at work.

What is Janet's diagnosis? For the answer, go to page 83.

Table 1

Main features of RLS

Primary features:

- An urge to move the limbs, usually secondary to abnormal sensations.
- Motor restlessness
- Symptoms are accentuated by rest and are relieved by movement
- Worsening in the evening

Additional features:

- Problems initiating and maintaining sleep
- Periodic movements while asleep
- Normal neurologic exam
- Positive family history
- Onset at any age; increasing severity with advancing age

How is RLS diagnosed?

The diagnosis is based on history. The features consist of:

- an unpleasant lower limb sensation with an urge to move,
- motor restlessness,
- relief of the unpleasant sensation with voluntary movement and
- worsening in the evening when at rest.

If severe, RLS will interfere with sleep onset (Table 2). Bed partners will often report motor restlessness and leg kicking during sleep.

What triggers should I look for?

There are several known triggers, including:

- pregnancy,
- peripheral neuropathy,
- iron deficiency,
- renal failure,
- smoking and
- a sedentary lifestyle.



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The first step is to review the patient's medication list, as many medications can trigger worsening of RLS.

Next, the examination should specifically look for evidence of peripheral neuropathy by checking for distal muscle wasting, absent distal reflexes, as well as distal sensory loss to temperature, pinprick and vibration.

Causes of peripheral neuropathy, if clinically evident, should be screened for, including renal dysfunction, diabetes and vasculitis. Nerve conduction studies can complement the exam. Polysomnography can be done to confirm the diagnosis.

Table 2

RLS severity classification

Severity	RLS symptoms frequency	Sleep disruption	Daytime fatigue
Mild	Intermittent	Mild	None
Moderate	Less than twice per week	Moderate	Mild
Severe	More than twice per week	Severe	Marked

RLS: Restless legs syndrome

Janet's Diagnosis

Janet is suffering from restless legs syndrome aggravated by medications (fluoxetine).

Her symptoms returned to baseline a few weeks after stopping the fluoxetine.



Recommended lab work-up for RLS

- Complete blood cell count
- Antinuclear antigen
- Sedimentation rate
- Serum ferritin
- Vitamin B12
- Creatinine, urea
- Fasting blood glucose
- Thyroid stimulating hormone
- Nerve conduction studies
- Polysomnography

What are the treatment options?

Non-medication options

Advise the patient to avoid caffeine, alcohol, tobacco and medications that make RLS worse (Table 3). Good sleep habits, including trying to retire and get up at the same time every day, as well as sleeping in a quiet environment at a comfortable temperature will often help. A hot bath or a massage before bed, along with regular exercise early in the day, may help. Exercise that is too aggressive can make the symptoms worse.



Table 3

Medications known to aggravate RLS

- Calcium channel blockers
- Metoclopramide
- Antinauseants
- Antihistamines
- Neuroleptics
- Phenytoin
- Selective serotonin reuptake inhibitors

RLS: Restless legs syndrome

Medication options

Medications used for RLS include dopaminergic medications (levodopa, pergolide, pramipexole, ropinirole), benzodiazepines, opiates and anticonvulsants.

Initial therapy should be with iron supplementation if the ferritin is lower than 50 pmol/L.

The newer dopamine agonists—pramipexole and ropinirole—are currently recommended. Chronic use of the older ergot agonists has recently been linked to cardiac valvulopathy.

If dopamine agonists are to be used, it is recommended to split the dose, taking part after the evening meal and then two hours prior to bedtime. These drugs need to be titrated slowly to avoid the risk of postural hypotension and nausea. Although there is concern with agonists causing excessive daytime sleepiness, this should not be a significant issue if the treatment is effective for RLS.

- **Levodopa** is usually effective, but has a high tendency (80% by six months) to augment the symptoms in the early morning hours, as well as create a rebound effect (35%). For this reason levodopa should probably be used no more than a few times per week. The continuous release preparation may be less likely to worsen the symptoms when used chronically. If the patient starts to show augmentation or rebound, they should be switched to a different medication, at least temporarily.
- **Pergolide's** rate of augmentation is reported to be 15% at six months. The dose required is usually 0.25 mg per day.
- **Pramipexole** can be used in a dose of 0.125 mg to 1 mg two to three hours before bed or divided between the patient's evening meal and two hours before bed.

- **Ropinirole** can be used at a dose of 0.25 mg to 2 mg two to three hours before bed or in divided doses between the patient's evening meal and two hours before bed.
- **Opioids** (*e.g.*, oxycodone) have been demonstrated to be effective in placebo-controlled trials.
- **Clonazepam** is probably the best-studied medication for RLS. It consolidates sleep, thus providing an indirect effect on the well-being of the patient.
- **Gabapentin** has been proven in double-blind studies to be effective for RLS. The mean effective dose has been shown to be 1,800 mg. The reported augmentation rate is very low. This medication is particularly good for patients with foot pain.

Suggested reading

1. Ekbom K: Restless legs syndrome. *Neurology* 1960; 10:868-75.
2. Stiasny-Kolster K, Trenkwalder C, Fogel W, et al: Restless legs syndrome—New insights into clinical characteristics, pathophysiology, and treatment options. *J Neurol* 2004; 251(Suppl 6):VI/39-43.
3. Chaudhuri KR, Forbes A, Grosset D, et al: Diagnosing restless legs syndrome (RLS) in primary care. *Curr Med Res Opin* 2004; 20(11):1785-95.
4. Schapira AH: Restless legs syndrome: An update on treatment options. *Drugs* 2004; 64(2):149-58.

Web reading

- Restless Legs Syndrome Foundation: www.RLS.org
- Worldwide Education and Awareness of Movement Disorders: www.wemove.org

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