RESTLESS LEGS SYNDROME

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Definition

Irresistible urge to move, usually associated with disagreeable leg sensations, worse during inactivity, and often interfering with sleep.
Primary Features (IRLSSG Criteria)

- Desire to move the limbs, usually associated with paresthesias
- Motor restlessness
- Symptoms worse at rest, partially relieved by activity
- Symptoms worse in the evening or at night
Uncomfortable Sensations

- Creepy, crawly, tingly
- Like worms or bugs crawling under the skin
- Painful, burning, or achy
- Like water running over the skin
- Sometimes indescribable
Restlessness

- **Voluntary**: patients *choose* to move to relieve discomfort

- **Irrepressible**: patients *feel compelled* to move and almost cannot resist it (as a tic)
Influence of rest and activity

- Activity relieves the discomfort, but variably, temporarily, and partially.
- Patients develop habits and behaviors to relieve discomfort ("nightwalkers").
Circadian Variability

- Symptoms typically peak between midnight and 4 AM
- Circadian rhythm of symptoms persists even in “unconventional” sleep/wake cycles
Additional Features

- Sleep disturbance and its consequences
- Involuntary movements while awake
- Chronic course
RLS vs. PLMs

- RLS is a symptom
- RLS is diagnosed in the physician’s office
- 80% of people who have RLS will have PLM’s

- PLMs are an PSG finding
- PLMs are diagnosed in the sleep laboratory
- 30% of individuals who have PLM’s have RLS symptoms
Clinical Importance of PLMs in Relation to RLS

- PLMs are neither necessary nor sufficient for the diagnosis of RLS
- Asymptomatic PLMs do not require treatment
Pathogenesis of RLS

- Primary (idiopathic)
- Secondary (symptomatic)
Primary (idiopathic) RLS

- No identifiable cause
- Tends to occur in families
- Strong genetic component
Secondary (symptomatic) RLS

- Iron-deficiency anemia
- Uremia (30% of dialysis patients)
- Pregnancy (30%)
- Neurological lesions
  - Myelopathy
  - Peripheral polyneuropathy
- Drug-induced:
  - TCA, SSRI’s, lithium, dopamine blockers (e.g., neuroleptics), xanthines
Associated Conditions

- Diabetes (PN)
- Parkinson’s disease (7-fold increase prevalence in RLS)
- Rheumatoid arthritis
Differential Diagnosis

- Neuropathy
- Depression and other causes of insomnia
- Arthritis
- Vascular disease
- Akathisia
Pathogenesis

- RLS is a *neurologic* disorder
- Location of the lesion is not known
- Some evidence points to spinal cord abnormalities in patients with PLMs
Consequences of RLS

- Discomfort
- Sleep disturbance
- Excessive daytime somnolence
  - Subjective assessment (Epworth scale)
  - Sleep study: MSLT
Assessment-Making the Dx

- History: the most important
- Physical examination
- Laboratory tests
History: 4 Cardinal Features

- Unpleasant sensations
- Motor restlessness
- Precipitated by inactivity; relieved with activity
- Worse in evening or night
History: etiology

- Diabetes, anemia, medications, renal status and other associated conditions
- Duration of symptoms
- Other affected family members
- Precipitating and relieving factors (new medications, lifestyle changes)
Physical Examination in RLS

- Careful neurological examination (to look for Parkinson's, neuropathy, myelopathy)
- No objective findings for RLS
PLMs on PSG

- EMG bursts
- Duration 0.5-5 sec
- Periodicity 5-40 sec
- Amplitude 25% of calibration
- PLM index
- PLM with arousal index
Laboratory Evaluation of RLS

- Polysomnography is not necessary for the diagnosis of RLS!
- Serum ferritin
- Screen for uremia
- Screen for diabetes
- Other tests for potential secondary causes if suspected
Non-pharmacologic Treatment

- Listen, support, and validate
- Reconsider medications known to exacerbate RLS (lithium, SSRI’s, tricyclics, dopamine antagonists)
- Not helpful: sclerotherapy, electrical stimulation
- Possibly beneficial: hot baths, delayed sleep time/rise time, exercise, avoid alcohol and nicotine
Support and Validation

- RLS Foundation (RLSF): www.RLS.org
Pharmacologic Treatment

- Dopaminergic medications
  - Benzodiazepines
  - Opioids
  - Anticonvulsants
  - Others
Treatment Considerations

- Age
- Combination strategies +++
- Distribution/frequency/severity of symptoms
- Treatment is symptomatic, not curative
- In general, smaller doses are used than in other conditions
Iron Therapy

Replace iron in patients with serum ferritin levels $< 50 \text{ mcg/L}$
Dopaminergic medications

- Carbidopa-levodopa (Sinemet®)
  - 25/100CR to 100/400CR qhs

- Dopamine agonists
  - Bromocriptine
  - Pramipexole 1.5-4.5 mg/day
  - Ropinirole 3-24 mg/day
  - More coming… (patch)

Limitations: augmentation, rebound, nausea, insomnia
Benzodiazepines

- Clonazepam (Klonipin®): 0.5-4 mg
- Lorazepam (Ativan®): 0.5-4 mg
- Temazepam (Restoril®): 15-30 mg
- Diazepam (Valium®): 5-10 mg

Disadvantages: tolerance, somnolence, hangover, confusion, worsened snoring/SDB
Opioids

- Propoxyphene (Darvon®): 130-520 mg/day
- Codeine: 15-240 mg/day
- Oxycodone
- Methadone (Dolophine®): 5-30 mg/day
- Hydrocodone
- Tramadol hydrochloride (Ultram®)

Disadvantages: tolerance, constipation
Antiepileptic drugs

- Gabapentin (Neurontin®): 100-2700mg/day
- Carbamazepine (Tegretol®)
- Others:
  - Topiramate (Topamax®)
  - Lamictal (Lamictal®)
  - Levetiracetam (Keppra®)
  - Zonisamide (Zonegran®)
  - Oxcarbazepine (Trileptal®)
Others

- clonidine
- baclofen
- vitamin B12
- vitamin E
- magnesium
Conclusions

- RLS is common, treatable, and underdiagnosed
- The pathophysiology of RLS is unknown
- RLS can be both secondary and idiopathic
- The diagnosis is made by history
- Treatment is mainly pharmacologic