Restless legs? Or is it something else?

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Disclosures

- I have served on advisory boards
  - Abbvie Canada
  - Paladin Pharma
  - Sunovion Pharma
- I have received speaker honorarium
  - Abbvie Canada

Objectives

- Review the clinical features of restless legs
- Discuss the management
- Review other nocturnal movements
  - Rem Behaviour disorder
  - Periodic leg movements of sleep
  - Nocturnal cramps

Case history

- A 65 y o male has trouble sleeping
- He reports pain and “numbness” in his legs when he lies down
- He can’t fall asleep easily, needs to move his legs
- He wakes frequently
- His wife complains that he constantly moves and kicks his legs in bed which prevent her from sleeping

Diagnostic criteria Restless Legs syndrome

- Five hallmarks
  - **Urge** to move legs with unpleasant sensation in the legs
  - Worse in periods of **inactivity,** like sitting or lying down
  - Partially or totally relieved by **movement** such as walking or stretching
  - Symptoms are worse in evening or at **night**
  - **No other** condition can account for symptoms e.g. venous stasis

International Restless Legs Syndrome Study Group.
Sleep Med. 2014;15(8):860–873

Supportive clinical features

- Positive family history
- Response to dopaminergic medication
- Often co existence of period leg movements of sleep

International Restless Legs Syndrome Study Group.
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Unpleasant sensation

- Described as creepy, crawly, gnawing, horrid, burning, tingling
- Not real numbness (no loss of sensation)
- Most often in both legs but can be unilateral
- Can also involve the upper extremities
- In severe cases whole body
- **URGE** to move

Epidemiology

- Approx 10%-15% of population
- Increases with age
- Can start as early as adolescence
- Woman>men
- Family history
- Risk factors: pregnancy, iron-deficiency, dopamine blocking medications, uremia

Neurotherapeutics. 2021 Jan; 18(1): 140–155

Investigations

- History from patient and partner regarding sleep and PLMS
- CBC, electrolytes, BUN, creatinine, fasting glucose, serum iron, ferritin and iron saturation
- Nerve conduction studies can be performed if peripheral neuropathy is suspected
- Polysomnography should be performed if there is a clinical suspicion of sleep apnea or concurrent sleep disorder

Neurotherapeutics. 2021 Jan; 18(1): 140–155

Management

- Non pharmacological
  - Avoid caffeine late in day
  - Minimize alcohol
  - Hot bath, stretching
  - Avoid strenuous exercise late in day
  - Avoid contributing medication (anti depressants, dopamine blocking drugs, antihistamines)
- Treat iron deficiency! Ferritin <75 ug/L or ferritin saturation <45%
  - Start with oral ferrous sulfate, consider IV replacement in severe deficiency or if oral not tolerated

Neurotherapeutics. 2021 Jan; 18(1): 140–155
Mayo Clinic Proceedings 2021 961921-1937DOI: (10.1016/j.mayocp.2020.12.026)

Management: First line
Gabapentinoids vs dopamine replacement

- Gabapentin (can be give once or twice daily)
  - Doses range (900 mg -1800 mg/day)
  - Good option if unable to tolerate dopamine agonists or rebound
  - Also preferred in patients with pain and high anxiety
- Pregabalin (can be given once or twice daily)
  - Dose range (150-450mg/day)
  - As above

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Side effects Gabapentinoids

- Sedation
- Leg edema
- Dizziness
- Increased risk of falls in elderly

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Management (cont'd)
Dopaminergic replacement

- Dopamine agonists
  - Pramipexole start .125mg and titrate to efficacy (.25-.75mg) give an hour before bedtime, may need small dose in evening
  - Ropinirol start 1mg and titrate (1-2mg)
  - Rotigotine patch (1-2 mg)
- Levodopa
  - Levodopa/carbidopa 100/25 (1-2 tabs)
  - Best used PRN

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Side effects of dopaminergic medications

- Rebound
  - Recurrence of symptoms during night or early morning
  - Coincides with wearing off of medication

- Augmentation
  - Occurrence of symptoms earlier in the day
  - Shorter latency of symptoms when at rest
  - Spread of symptoms to involve upper extremities and trunk

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Impulse Control Disorders

- Highly associated with dopamine agonists
  - Pathological gambling
  - Hypersexuality
  - Compulsive shopping/ shop lifting
  - Compulsive eating
  - Punding

Voon, Neurology, 66,1750-1752.

Opioids

- Effective but high risk of dependency!
- Sedating so helpful in resolving insomnia
- Low potency opioids such as codeine or tramadol are better choice for episodic RLS
- More potent opioids such as oxycodone or methadone reserved for more refractory patients

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Benzodiazepines

- Do not improve the core symptoms but may help sleep quality
- May be used for on demand treatment
- Potential for dependence
- Might improve the PLMS

- Clonazepam .25-1 mg HS
- Can also try benzo receptor agonists

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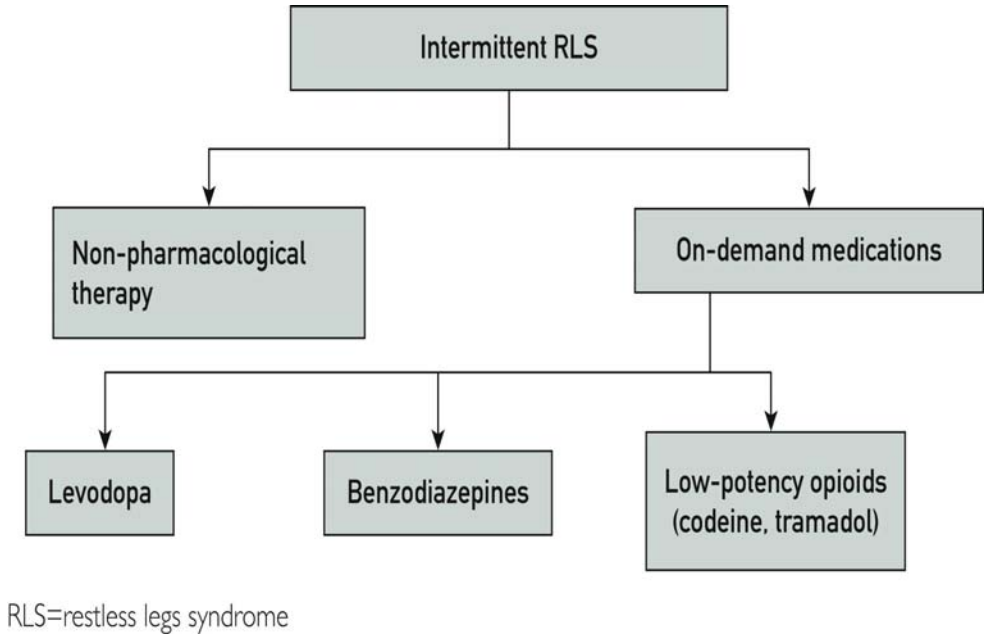

RLS=restless legs syndrome

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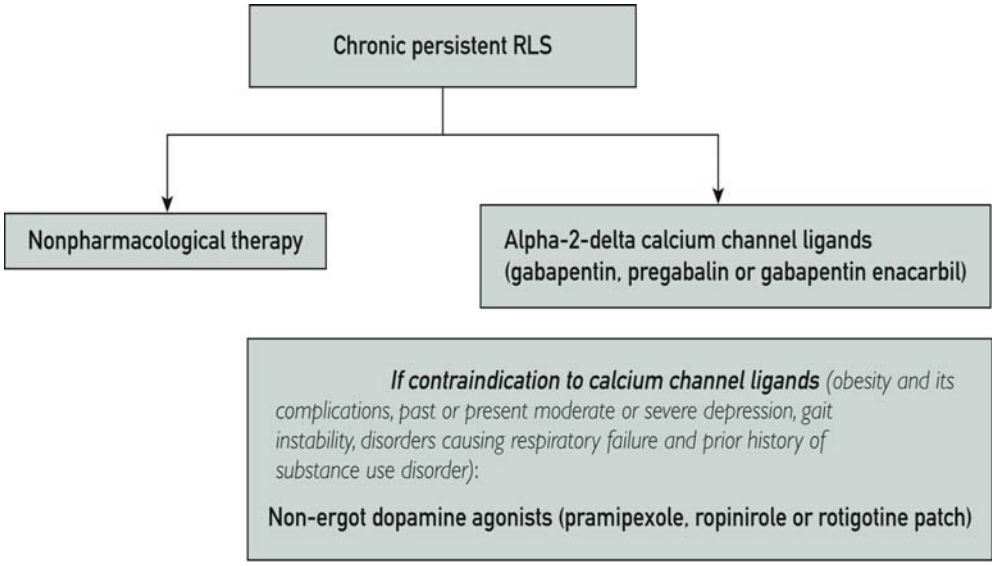

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Therapeutic tips

- Administer 1-2 hours before bedtime and gradually titrate to effective dose
- If one drug loses effectiveness, switch to another in same or different class
- If symptoms begin earlier in day, may need to prescribe in afternoon or morning
- Intractable RLS may need polytherapy
- Levodopa is most likely culprit of rebound and augmentation
- Monitor for impulse control if taking an agonist

Case history

- 67 y o male with recurrent nightmares
- Wife complains that he screams in his sleep
- He also kicks and has on more than one occasion punched her
- They are now sleeping in separate beds

- …… what could this be? What is it a biomarker of?

REM Sleep Behavior Disorder

- Dramatic, violent, and potentially injurious motor activity during sleep
- These behaviors include talking, yelling, swearing, grabbing, punching, kicking, jumping, or running out of the bed
- Patients have no recollection of the movements
- Dreams are usually violent, being chased
- Up to 50% of PD patients affected
- 80% of idiopathic REM sleep behavior develop PD up to 20 yrs later

How to treat RBD

1. Non pharmacological, safe sleeping environment
2. Remove triggers – antidepressants
3. Clonazepam (0.5 to 2 mg @ h.s.)
- helps 90% (observational only) – possible negative RCT?
- side effects: sleepiness, falls, cognition, dependence
4. Melatonin - 3 mg (up to 12 mg)
- two small-scale studies - helped >80%

Case history

- A 58 y o male reports poor sleep, wakes frequently
- Falls asleep easily but wakes often
- He has no urge to move his legs
- He never gets up to walk around
- Wife reports that he moves his legs throughout the night
- Her sleep is now interfered with

Periodic leg movements of Sleep (PLMS)

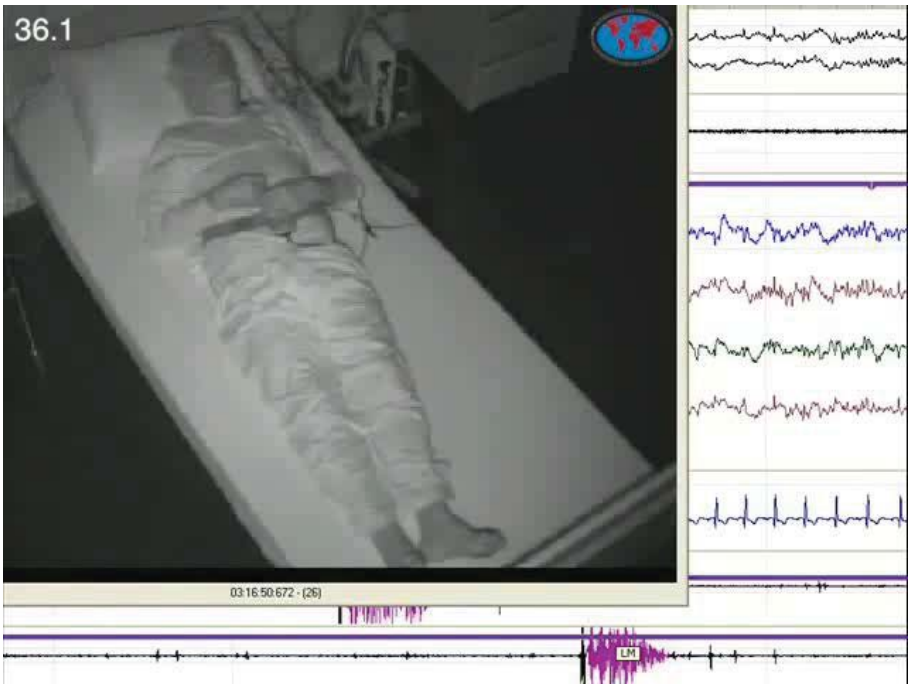
- Key word is in **sleep**
- Patient not aware, spouse is
- Very stereotyped movements of the legs
  - Dorsi flexion of ankle
  - Hip and knee flexion
  - Repeats every 20-40 seconds
  - At least 4 in 90 seconds
  - Can last minutes to hours
  - May be associated with Restless legs but may also occur alone

Sleep. 2012 Aug 1; 35(8): 1039–1062

PLMS epidemiology

- Can occur in 30% of people 65 and older
- Common in patients with RLS, Sleep apnea and narcolepsy
- Can occur at any age
- Males=females
- May be associated with diabetes, iron deficiency, uremia
- May be caused by antidepressants, antihistamines and antipsychotics

Sleep. 2012 Aug 1; 35(8): 1039–1062



Management

- Treat underlying cause if found ex. CPAP for apnea
- Don't treat PLMS discovered during polysomnography only
- Avoid caffeine
- Insufficient evidence to make specific recommendation
- May be improved by clonazepam, gabapentin, pregabalin, baclofen (uncontrolled studies)

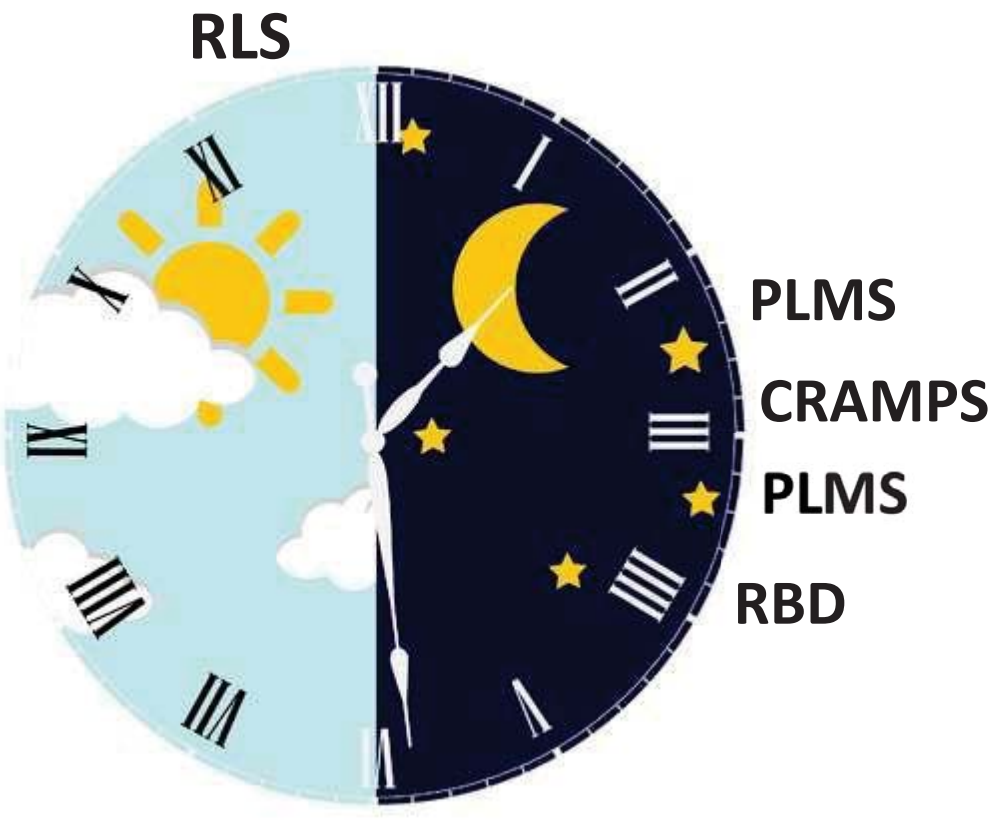
Sleep. 2012 Aug 1; 35(8): 1039–1062

Nocturnal Cramps
Diagnostic Criteria (American Sleep Association)

- A painful sensation in the leg or foot associated with sudden, involuntary muscle hardness or tightness, indicating a strong muscle contraction.
- The painful muscle contractions occur during the time in bed, although they may arise from either wakefulness or sleep.
- The pain is relieved by forceful stretching of the affected muscles, thus releasing the contraction.

Nocturnal cramps-management

- **No good treatment! No good evidence!**
- Stretching and massage
- Applying heat
- Quinine was useful but because of serious adverse effects, no longer recommended first line (arrhythmia, thrombocytopenia)
- Trial of Vit B complex
- Calcium channel blockers (diltiazem)-limited evidence
- Gabapentin-limited evidence that probably doesn't work
- Magnesium ? Cochrane says no evidence



Conclusion

- History helps diagnosis of nocturnal event
- Polysomnography can help when uncertainty exists
- Therapeutic choices for RLS with supportive evidence
- RBD, a predictor of alpha synuclein pathology
- No evidence-based treatment for cramps or PLMS