



Restless Legs Syndrome and Periodic Limb Movement Disorder in Children and Adolescents

A Guide for Healthcare Providers

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RESTLESS LEGS SYNDROME (RLS)

is a common, complex and treatable condition. RLS affects 5 to 10% of adults in many countries,^{1,2} with 2 to 4 percent of children and adolescents affected.³⁻⁶ In the United States alone, RLS is believed to afflict more than 10 million adults and an estimated 1.5 million children and adolescents. Although most research has focused on adults, RLS symptoms often begin during childhood or adolescence. About 35% of patients report RLS onset prior to age 20, and one in ten report that the syndrome appeared during the first decade of life.^{7,8} Multiple reports now document the occurrence of RLS, as well as the related problem periodic limb movement disorder (PLMD), during childhood and adolescence.⁹⁻¹²



RLS AND PLMD IN CHILDREN

Symptoms of both RLS and PLMD can range from mild to severe and can negatively impact a child's quality of life.^{3,13-15} Accurate diagnosis of RLS and PLMD in pediatric patients offers substantial benefits. First, understanding why a child is uncomfortable and irritable can be very important in engendering a supportive parental response. Second, there is reason to hope that early, specific treatment may reduce or eliminate RLS symptoms in children. Third, as larger numbers of children with RLS are identified, researchers can draw on this growing patient population to seek specific information and explore treatment options. Fourth, and most importantly, children who experience poor intellectual or emotional function due to these

sleep disorders can have their problems addressed more directly.

Signs and Symptoms of RLS

Like their adult counterparts, children with RLS tend to seek relief from their discomfort by moving their legs—often by fidgeting, stretching, walking, running, rocking, or changing position in bed. Parents or healthcare providers may mistakenly attribute the child’s discomfort to “growing pains.”¹⁶ In the classroom setting, attempts to relieve the uncomfortable feelings of RLS may be viewed as inattentiveness, hyperactivity, or disruptive behavior. Restless legs syndrome, however, is a real medical condition that calls for proper evaluation, diagnosis, and treatment. Unlike most adults with RLS, some children with RLS complain of the RLS sensations more during the day than at night.¹⁷



RLS and Sleep

Sleep disturbance is common among children and adults with RLS. In children, the sleep disturbance may precede or overshadow the complaint of leg discomfort.^{11,18} The quality and quantity of a child’s sleep are often diminished, and this sleep deprivation can result in moodiness, irritability, inattentiveness, fatigue, or hyperactivity.

Periodic Limb Movements in Sleep

Periodic limb movements in sleep (PLMS) are characterized by brief jerks (0.5 to 10 seconds in

duration) of the limbs during sleep, typically recurring at 20-to 40-second intervals. PLMS are more common in the toes, feet, and legs than in the arms. An affected individual is usually not aware of the movements or of the associated transient arousals that disrupt sleep continuity. Among adults, PLMS are present in an estimated 80% to 90% of individuals with RLS. In children, documentation of PLMS exceeding norms for age supports a diagnosis of RLS.^{17,19} On the other hand, PLMS are not specific to RLS; they can occur in other sleep disorders, and can be induced or aggravated by certain medications, particularly SSRI-type antidepressants such as fluoxetine (Prozac), sertraline (Zoloft), and venlafaxine (Effexor).^{20,21} Current research suggests that PLMS are possibly due to underactive dopaminergic function in specific brain pathways and that they are a marker of instability in the sleep system.

Periodic Limb Movement Disorder

A diagnosis of periodic limb movement disorder (PLMD) is based on three criteria: (1) PLMS exceeding norms for age (>5 per hour for children); (2) clinical sleep disturbance or impaired daytime function; and, (3) the absence of another primary sleep disorder or underlying cause (including RLS).²² In some children, a diagnosis of PLMD will evolve over time to a diagnosis of “RLS with PLMS” as the classic sensations of RLS develop.^{18,23}

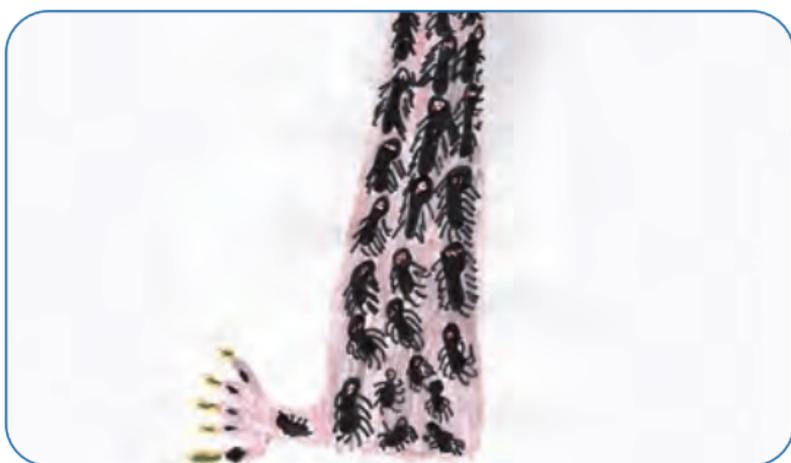
DIAGNOSIS OF RLS AND PLMD IN CHILDREN AND ADOLESCENTS

Because children may experience and present symptoms of RLS differently than adults, establishing a diagnosis of RLS in a pediatric patient can be challenging. At this point, few physicians have had extensive experience in the diagnosis and treatment of RLS in children, since the childhood manifestations of RLS have been defined only recently.²³⁻²⁵ In a pediatric patient, the presenting complaint is usually one of following: sensations of limb discomfort or

disturbed sleep.

RLS Sensations in Children

For some children, the urge to move and uncomfortable leg sensations are the main concern. In years past, and even today, many children with these symptoms have been presumed to have “growing pains”—vague, idiopathic episodes of leg pain.^{16,26} It is important to go beyond this and determine if the child truly has RLS. In response to the simple question “do your legs bother you,” children with RLS typically describe these sensations with age-appropriate terms: “want to move,” “have to move,” “got to kick,” “bugs,” “ants,” “tingling,” and “wiggly.”²⁴ It can be helpful to have the child draw a picture of their RLS feelings.²⁴ Non-RLS causes of lower limb discomfort in children include positional discomfort, sore muscles, sprains, and cramps, as well as transient nerve compression due to awkward positions.¹⁷



Sleep Disturbance

In other children, disturbed sleep and PLMS predominate as symptoms, while leg discomfort may be mild, intermittent, or even absent.²³ A longitudinal study reported chronic clinical sleep disturbance to precede the onset of specific RLS sensations by an average of 11 years in a group of children who presented with RLS in this manner.¹⁸ In such instances, a diagnosis of PLMD may be most appropriate before a definite RLS diagnosis can be made.

Family History

A thorough family history is of great importance because a dominant pattern of inheritance is common when RLS occurs at a young age.²⁷⁻²⁹ If a biologic parent has RLS, for example, then there is an almost 50:50 chance of passing the RLS trait on to each of his or her children. However, it is important to understand that a parent may receive his or her initial diagnosis of RLS in the course of medical attention for a child's symptoms. Thus, the child's evaluation should include an interview of the parents about RLS symptoms. The five essential criteria for adult RLS are listed below.

Physical Examination

In a child with RLS, the physical exam is typically normal. The finding of an associated underlying medical disorder in childhood RLS is unusual, except that a mild degree of iron deficiency may be present.



Sleep Testing

Most children evaluated for RLS and PLMD are described as “restless” in their sleep.²³ A sleep study (polysomnography) may be helpful in diagnosing pediatric RLS and, for PLMD, is necessary to document the sleep disturbance and PLMS. Simple observation of the sleeping child is not a reliable diagnostic tool for PLMS.^{10,30} The study should be carried out at a sleep center experienced in working with children, as proper technique and scoring are vital for accurate diagnosis.

RLS Diagnostic Criteria

Medical professionals have developed special considerations for diagnosing RLS in children and adolescents when applying the standard adult criteria.^{17,31}

THE CHILD MEETS ALL FIVE OF THE FOLLOWING DIAGNOSTIC CRITERIA:

1. There is an urge to move the legs.*
2. The urge to move begins or worsens with sitting or lying down.
3. The urge to move is partially or totally relieved by movement.
4. The urge to move is worse in the evening or night than during the day, or occurs exclusively in the evening or nighttime hours.
5. These symptoms are not solely accounted for by another medical or behavioral condition.

*the description of these symptoms should be in the child's own words.

THE FOLLOWING FEATURES, THOUGH NOT ESSENTIAL FOR DIAGNOSIS, ARE CLOSELY ASSOCIATED WITH AND SUPPORTIVE OF PEDIATRIC RLS:

1. PLMS >5 per hour
2. Family history of RLS among first-degree relatives
3. Family history of PLMS >5 per hour
4. Family history of PLMD among first-degree relatives

SPECIAL CONSIDERATIONS FOR THE DIAGNOSIS OF PEDIATRIC RESTLESS LEGS SYNDROME:¹⁷

- The child must describe the RLS symptoms in his or her own words.
- The diagnostician should be aware of the typical words children and adolescents use to describe RLS.
- Language and cognitive development determine the applicability of the RLS diagnostic criteria, rather than age.
- It is not known if the adult specifiers for clinical course apply to pediatric RLS.
- As in adults, a significant impact on sleep, mood, cognition, and function is found. However, impairment is manifest more often in behavioral and educational domains.
- Simplified and updated research criteria for probable and possible pediatric RLS are available.
- Periodic limb movement disorder may precede the diagnosis of RLS in some cases.

CAUSES OF RLS

Research into the causes of RLS is ongoing, and although answers are limited, three major themes have emerged. First, a strong genetic component is evident in early-onset RLS. Second, underactivity of the brain transmitter dopamine appears to be associated with both RLS and PLMD. Third, there is evidence for brain iron deficiency in early-onset RLS.

Genetic Component

Several family studies have demonstrated a high familial prevalence of early-onset RLS (RLS in which the onset of symptoms occurs before age 30).^{27,32-34} The likelihood in early-onset RLS that any first-degree relative of an affected individual

(i.e., parents, siblings, or children) will also have RLS is almost 50%. Researchers have identified several genetic variants that may mediate the expression of RLS as an inherited trait.^{35,36} Future research will aim to more precisely determine the role of genetics in RLS.

Dopamine and RLS

The brain transmitter dopamine plays a role in several neural networks, including those that control muscle movements, sleep, and “executive functions” (e.g., attention span, advanced planning, and impulse control). Pharmacologic studies and some brain-imaging studies provide evidence for an underlying dopamine abnormality in RLS and PLMD.

Iron and RLS

Because iron is vital to the function of the brain’s dopamine systems, the finding of iron deficiency as a causative or contributing factor for RLS begins to paint a more comprehensive model of RLS pathophysiology.³⁷

LEARNING AND EMOTIONAL PROBLEMS ASSOCIATED WITH RLS/PLMD

Attention Deficit/Hyperactivity Disorder

Several studies have reported an association between attention-deficit/hyperactivity disorder (ADHD), RLS, and PLMD in children.^{3,38,39} However, this appears to be a complex relationship. In some children, the sleep disturbance and/or restless legs sensations can induce or aggravate inattention and/or motor restlessness. Considerable evidence suggests that sleep deprivation in children can impair cognitive function, including attentiveness and memory.^{40,41} This is not to say that all children with ADHD have RLS or PLMD, but rather that an RLS subgroup may exist within the larger group of ADHD children. Conversely, not all children with RLS have ADHD, perhaps because of other modulating factors.⁴² Low iron and underactivity of dopamine have been

suggested to be the common factors between ADHD, RLS, and PLMD.⁴³

Regulation of Emotions

Less extensively studied is an association in children between mood problems, RLS, and PLMD.^{18,44} As most parents will attest, a child in need of sleep is often moody or “cranky” rather than overtly sleepy. Irritability, easy frustration, negative affect, and poor control of impulses and emotions can be induced or aggravated in children by lack of sleep.^{45,46} Given the common association between RLS, depressive symptoms, and anxiety in adults,^{47,48} further study of this relationship in children is indicated.

RLS/PLMD, IRON AND FERRITIN

Studies in adults and children have found correlations between low serum ferritin (a marker of body iron stores), RLS, and PLMD.^{11,49,50}

Current evidence indicates that systemic iron deficiency can induce or aggravate RLS and PLMS in children, even when the deficiency is not severe enough to cause anemia. Serum ferritin is the best single measure of peripheral iron stores, much more accurate than hemoglobin or serum iron tests. A low ferritin level, even one in the low-normal range, indicates a potential problem. Although recognition of the association between low iron stores and RLS/PLMD in children is recent, the fact that severe iron deficiency in children can affect brain development and function—likely via alterations in dopamine metabolism—has long been recognized.^{51,52} Infants, toddlers, and teenagers are at particular risk for iron deficiency. Studies in adults and children have shown that replenishing diminished iron stores can reduce RLS and PLMS symptoms.^{14,53-56} ADHD—a comorbidity in some children with RLS and PLMD—has also been associated with low ferritin levels.⁵⁷

TREATMENT OPTIONS

Nonpharmacologic Treatment

Nonpharmacologic interventions should always be included in the treatment plan, and in some children will provide sufficient management of RLS. In general, medication should be considered only when nonpharmacologic interventions are insufficient and an RLS-related sleep disorder is affecting the child's daytime function. The goals of therapy, both pharmacologic and nonpharmacologic, are adequate sleep quantity, good sleep quality, and suppression of RLS sensations, with a resultant improvement in daytime function.

Good Sleep Habits

All children and adolescents—especially those with sleep disorders—benefit significantly from establishing a routine of good sleep habits. Children and adolescents often test the limits of sleep, and for those with RLS the result can be sleep deprivation that significantly increases RLS symptoms and adversely affects daytime function. Parents should be made aware of the amount of sleep considered normal for age, and advised to help the child get sufficient sleep on a regular basis.

TYPICAL SLEEP NEEDS ARE AS FOLLOWS:

AGE	HOURS
2	12 (including one nap)
5	11
10	10
Teen years	9
Adulthood	7 to 9

A child or teenager should go to bed and awaken at about the same time every day, including weekends; avoid caffeine intake, especially late in

the day or evening; get regular exercise; and maintain a comfortable, quiet bedroom environment, free of stimulating activities. Teens should avoid the use of tobacco and alcohol, which are known to disrupt sleep, confine any napping to the afternoon hours, and avoid driving when tired.

Treatment of Low Ferritin

Iron supplementation should be given if the child's serum ferritin level is low or in the low-normal range, below 50-75 mcg/L.* While most labs have lower cut-off values than 50, it is clear that iron deficiency is common in the 10 to 50 range, as demonstrated by the 'gold-standard' measure for iron deficiency—bone marrow testing.⁵⁸ The dosage of therapeutic iron should be the same as that typically used to treat anemia in children, under medical supervision.⁶ A multivitamin that includes iron does not have enough iron to replenish low iron stores. Serum ferritin testing should be avoided when a child is ill, because the value can be falsely elevated by acute illness such as colds and other infections, for as long as 4 weeks after the illness.⁵⁹ Studies in children have shown decreased signs and symptoms of RLS and PLMD in association with serum ferritin concentrations rising to levels above 50-75 mcg/L.^{14,34,50,55,56} The results of iron therapy should be medically monitored with follow-up testing. Due to growth it may be difficult to maintain levels above 50-75 mcg/L. Safe storage of iron is very important to avoid accidental ingestion, which can be fatal.

**note: mcg/L equals ng/mL*

Iron Absorption

Taking an iron supplement with vitamin C enhances absorption of the iron. Many beverages, such as orange juice and fruit drinks, contain vitamin C. Vitamin C tablets are also available. Ideally, food, calcium, and tea should not be taken within two hours of taking an iron supplement. These decrease iron absorption and

will delay full replenishment of the body's iron stores. However, it is better to take iron regularly than under ideal circumstances.

Medication Options

The potential risks of medication must be balanced against the long-term consequences of poor intellectual and emotional function due to these sleep disorders. Three medications found particularly useful to treat children with RLS or PLMD are gabapentin (Neurontin), clonidine (Catapres), and clonazepam (Klonopin). Gabapentin is beneficial in improving sleep quality and reducing sensory symptoms of RLS.^{60,61} It has a long history of safe use in children as young as three years for the treatment of seizures. Clonidine is the one of the most commonly used medications for children's sleep,⁶²⁻⁶⁴ and is especially beneficial in children whose RLS results in severe sleep-onset problems. An occasional side effect of clonidine is the induction or aggravation of sleep terrors. Clonazepam is prescribed for children with RLS to improve sleep quality and to decrease RLS discomfort.⁶ In some children, clonazepam can have an activating effect (paradoxical activation); it should be discontinued, if this occurs. As part of routine care it is wise to remind families about the safe storage of all medications in childproof containers and out of the reach of young children.

Medications that Increase Dopamine

Dopaminergics are commonly used medications for adults with significant RLS, having been shown to suppress RLS sensations and PLMS.^{65,66} These include pramipexole (Mirapex), ropinirole (Requip), and rotigotine (Neupro). However, the use of dopaminergics has not been studied extensively in children and concerns about augmentation (paradoxical worsening of RLS over time) and impulse control problems have tempered use in adults.^{65,66} Dopaminergics that have been found to be effective in adult RLS may be considered with appropriate caution in children and teenagers who manifest severe and refractory

RLS or PLMD, when other treatments have failed.⁶

Does Treatment for RLS and PLMD Help ADD/ADHD?

The relationship between RLS, PLMD, and ADHD is clearly a complex one. Considerable evidence suggests that the treatment of sleep disorders in children, including impaired sleep resulting from RLS, can reduce, or in some cases eliminate, symptoms of ADHD.⁶⁷ Research in this area continues. In children who need medication to treat ADHD in addition to treatment for RLS or PLMD, the usual stimulant-type medications (Ritalin, Adderall, others) have not been found to aggravate RLS or PLMD, as long as the stimulant effect has worn off by bedtime.^{38,68}

Importance of Monitoring

Any pharmacologic treatment prescribed for RLS must be closely monitored for safety and efficacy. The best treatment effectively addresses the individual patient's symptoms—there is no “one size fits all” in the treatment of RLS. Medication should be periodically reassessed, especially if the patient has been treated for iron deficiency.



A Family Affair

The effects of RLS can be felt by the whole family and not just the child with RLS. Parenting

a child who does not sleep well can be a real challenge. Numerous, excellent resource materials are available for parents who have a difficult child.⁶⁹⁻⁷¹ In some instances, working with a counselor may be valuable in helping both the child and family develop methods for dealing with this chronic condition. If a parent has untreated RLS or PLMD, help for the child should include treatment for the parent too. Well-rested parents are typically more effective parents.

CONCLUSION

Research suggests that RLS affects an estimated 1.5 million children and adolescents in the U.S., and confirms that RLS and PLMD are not unique to adulthood. Healthcare providers need to be alert to the signs and symptoms of these disorders, and be aware of ongoing research and available treatment options.

Despite its high prevalence, RLS continues to be greatly underrecognized and undertreated. Many cases remain undiagnosed in patients of all ages. A child's complaints of leg pain or discomfort should not be dismissed as vaguely defined "growing pains" without consideration of a differential diagnosis that includes RLS. If a child has poor sleep, the specific cause should be sought.

The RLS FOUNDATION leads the quest for better treatment options and, ultimately, a cure for RLS and related disorders. The Foundation provides starter funding for promising research projects, and in recent years several of these studies have progressed to qualify for National Institutes of Health (NIH)-sponsored grants. Substantial advances have been made in the areas of diagnosis and treatment, and important research is ongoing on several fronts. Scientific studies continue to focus on causes, better treatments, and potential cures for RLS. For additional information, visit the Foundation's website at www.rls.org.

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RESTLESS LEGS
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The RLS Foundation is dedicated to improving the lives of the men, women, and children who live with this often devastating disease. Our mission is to increase awareness, improve treatments and, through research, find a cure for restless legs syndrome.

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