

CHILDREN AND RLS



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

A Guide for Healthcare Providers

RESTLESS LEGS SYNDROME FOUNDATION

RESTLESS LEGS SYNDROME (RLS) is a common and treatable condition. RLS affects 5% to 10% of adults in some countries.¹ 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.^{2,3} Multiple reports now document the occurrence of RLS, as well as the related problem periodic limb movement disorder (PLMD), during childhood and adolescence.⁴⁻¹²



INTRODUCTION TO 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. 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."¹³ 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.



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.^{12,14} 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 5.0 seconds in duration) of the limbs during sleep, typically recurring at 20- to 40-second intervals.^{15,16}

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 On the other hand, PLMS are not specific to RLS; they can occur in certain 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).¹⁸⁻²⁰

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; and (3) the absence of another primary sleep disorder or underlying cause (including RLS).¹⁶ 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. Current research suggests that PLMS are possibly due to underactive dopaminergic function in specific brain pathways, and are a marker of instability in the sleep system.²¹

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. 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"^{11,13}—vague, idiopathic episodes of leg pain. It is important to go beyond this and determine if the child truly has RLS. Further complicating the diagnostic picture, a child may describe these sensations with age-appropriate but nonspecific terms: "oowies," "boo-boos," "tickle," "bugs," "spiders," "ants," "want to run," or "a lot of energy in my legs." Non-RLS childhood causes of lower limb extremity discomfort include joint pains, sore muscles, and cramps, as well as transient nerve compression due to awkward positions.



SLEEP DISTURBANCE

In other children, disturbed sleep and PLMS predominate as symptoms, while leg discomfort may be mild, intermittent, or even absent. A recent 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.¹⁴ In such instances, a diagnosis of "probable" or "possible" RLS may be most appropriate before a definite RLS diagnosis can be made [see next page].

FAMILY HISTORY

A thorough family history is of great importance because an autosomal dominant pattern of inheritance is very common when RLS occurs at a young age.²²⁻²⁴ If a biologic parent has RLS, for example, then there is an approximately 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 four essential criteria for adult RLS are listed on the next page.

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. An association between kidney failure, diabetes, or peripheral neuropathy and RLS is found more commonly in adults than in children.

SLEEP TESTING

Most children evaluated for RLS and PLMD are described as "restless" in their sleep. A sleep study (polysomnography) is often necessary to document the sleep disturbance and PLMS; simple observation of the sleeping child is



not a reliable diagnostic tool for PLMD.⁹ 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.¹⁶

RLS DIAGNOSTIC CRITERIA

Medical professionals have developed special criteria for diagnosing RLS in children ages 2 through 12 years. Adolescents (13 years and older) are evaluated by means of standard adult criteria.¹⁷ The following criteria are used to determine whether a child between the ages of 2 and 12 years can be given a diagnosis of *definite*, *probable*, or *possible* RLS:

DEFINITE RLS

The child meets all four of the following adult 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.*

AND

The child describes leg discomfort using his or her own words. Examples of age appropriate descriptors: *oowies, tickle, tingle, static, bugs, spiders, ants, boo-boos, want to run, a lot of energy in my legs.*

OR

The child meets criteria 1-4 above

AND

Two of the three following supportive criteria:

1. *There is a clinical sleep disturbance for age.*
2. *A biological parent or sibling has definite RLS.*
3. *A sleep study has documented a periodic limb movement index of 5 or more per hour of sleep.*

PROBABLE RLS

The child meets these adult 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.*

AND

The child has a biological parent or sibling with definite RLS.

OR

The child shows signs of lower-extremity discomfort when sitting or lying down, with motor movement of the affected limbs. The discomfort has characteristics of adult criteria

2, 3, and 4: worsening with rest and inactivity, relief with movement, and worsening during evening and nighttime hours.

AND

The child has a biological parent or sibling with definite RLS.

POSSIBLE RLS

The child has periodic limb movement disorder (PLMD).

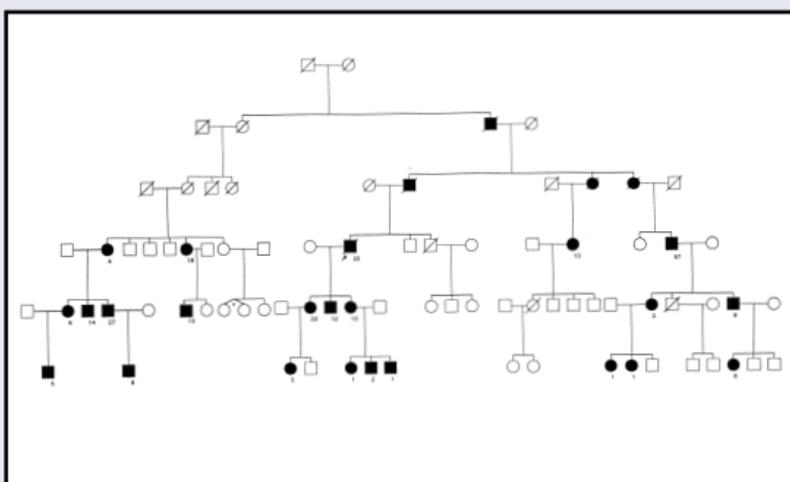
AND

A biological parent or sibling has definite RLS, but the child does not meet the criteria for definite or probable childhood RLS.

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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.



Family with dominant inheritance of RLS

GENETIC COMPONENT

Several family studies have demonstrated an autosomal-dominant hereditary pattern in early-onset RLS (RLS in which the onset of symptoms occurs before age 30).²²⁻²⁶ 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 chromosomes 9p, 12q, and 14q as possible genetic loci for the expression of RLS as an inherited trait.²⁷⁻³⁰ Future research will aim to more precisely locate RLS-specific gene sites and to determine the role of these genes.

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.³¹

THE ASSOCIATION OF RLS AND PLMD WITH LEARNING AND EMOTIONAL PROBLEMS ATTENTION DEFICIT/HYPERACTIVITY DISORDER

Several studies have reported an association between attention deficit/hyperactivity disorder (ADD/ADHD), RLS, and PLMD in children.^{6-8,10,32} 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.³²⁻³⁴ This is not to say that all children with ADD/ADHD have RLS or PLMD, but rather that an RLS subgroup may exist within the larger group of ADD/ADHD children. Conversely, not all children with RLS have ADD/ADHD, perhaps because of other modulating factors.³² A recent study indicates that adults with RLS are also at increased risk for ADD.³⁵ Underactivity of dopamine has been suggested to be the common factor between ADD/ADHD, RLS, and PLMD.^{36,37}



REGULATION OF EMOTIONS

Less extensively studied is a possible association in some children between mood problems, RLS, and PLMD. 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.³⁸⁻⁴⁰ Given the emerging association between RLS, depressive symptoms, and anxiety in some adults,⁴¹⁻⁴³ further study in children of a possible relationship between these factors is indicated.

RLS, PLMS, AND THE CONNECTION WITH LOW IRON LEVELS

IRON AND FERRITIN

Studies in adults have found correlations between low serum ferritin levels (a marker of body iron stores) and increased RLS symptoms,^{31,37} probably because of iron's vital role in brain dopamine function. Similarly, systemic iron deficiency can induce or aggravate RLS 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 new,^{12,44,45} the fact that severe iron deficiency in children can affect brain development and function—likely via alterations in dopamine metabolism—has long been recognized.⁴⁶⁻⁴⁸ Infants, toddlers, and teenagers are at particular risk for iron deficiency. Several studies in adults and two studies in children have shown that replenishing diminished iron stores can reduce RLS and PLMS symptoms.^{44,45} ADD/ADHD—a comorbidity in some children with RLS and PLMD—has also been associated with low ferritin levels.⁴⁹

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 FOR CHILDREN AND ADOLESCENTS

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 2: 12 hours (including one nap); age 5: 11 hours; age 10: 10 hours; teen years: 9 hours; and adulthood: 7 to 8 hours. 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 nap no longer than 45 minutes; and avoid driving when tired.

IRON SUPPLEMENTATION

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 35 mcg/L. While most labs have lower cut-off values than 35, it is clear that iron deficiency is common in the 10 to 35 range, as demonstrated by the 'gold-standard' measure

for iron deficiency—bone marrow testing.⁵⁰ The dosage and course of therapeutic iron should be the same as that typically used to treat anemia in children. A multivitamin that includes iron does not have enough iron to replenish low iron stores. However, once full replenishment of iron stores is obtained, a daily multivitamin supplement with iron can be used to help maintain 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. Studies in children and in adults have shown decreased signs and symptoms of RLS and PLMS in association with serum ferritin concentrations rising to levels above 35 to 50 mcg/L.^{44,45,51-53} The results of iron therapy should be monitored by follow-up testing. Unless there is concern about possible hemochromatosis (a disorder of iron overload) or another reason for particular caution, a daily multivitamin with iron should be used to help prevent the body's iron from becoming depleted during the growth years. (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.

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. Two medications found particularly useful to treat children with RLS or PLMD are clonidine (Catapres) and clonazepam (Klonopin). Clonidine is the most commonly used medication for children's sleep,⁵⁴⁻⁵⁶ 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. In some children, clonazepam can have an activating effect (paradoxical activation); it should be discontinued, if this occurs. Another option is gabapentin (Neurontin), which has shown promise in reducing sensory and motor symptoms of RLS, resulting in improved sleep quality.^{57,58} Temazepam (Restoril) and zolpidem (Ambien) are helpful to some adults whose RLS is accompanied by severe, chronically disturbed sleep, and might be considered for use in older children and teenagers with similar symptoms.^{53,59} As part of routine care it is wise to remind families about the safe storage of all medications (including Tylenol) in childproof containers, out of the reach of young children.

Medications that Increase Dopamine

Dopaminergics are the medications of choice for most adults with significant RLS, having been shown to suppress RLS sensations and PLMS more effectively and safely than medications in any other class.^{1,53,60} Dopaminergics commonly used to treat RLS in adults include levodopa (Sinemet, others), pramipexole (Mirapex), and ropinirole (Requip). While the use of dopaminergics has not been studied extensively in children, the safe use in treating the rare neurologic movement disorder dopa-responsive dystonia suggests that they are well tolerated in pediatric patients.⁶¹ Although medications such as methylphenidate (Ritalin) are not used to treat RLS or PLMS, they also raise dopamine levels and have a good long-term safety record in children.⁶² Dopaminergics that have been found to be effective in adult RLS may be tried with appropriate caution in children and teenagers who manifest severe RLS-related discomfort or significant PLMS.^{9,63,64}

Dopaminergic Medications and Augmentation

"More is not necessarily better." Augmentation—the worsening of RLS symptoms as the dosage of a dopaminergic medication is increased—is most commonly reported in patients taking levodopa, and is a less-frequent side effect of other dopaminergics.⁵³ Augmentation is typically managed by dose reduction or by switching to another dopaminergic medication.

Does Treatment for RLS and PLMD Help ADD/ADHD?

The relationship between RLS, PLMD, and ADD/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 ADD/ADHD.^{32,63} Research in this area continues. In children who need medication to treat ADD/ADHD in addition to treatment for RLS or PLMD, the usual stimulant-type medications (Ritalin, Dexedrine, others) have not been found to aggravate RLS or PLMD, as long as the stimulant effect has worn off by bedtime.^{7,65}

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.

FAMILY ISSUES

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.⁶⁶⁻⁶⁸ 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. Given the high prevalence of depression in adults with RLS, optimal treatment of depressive symptoms is important.^{42,43,69}

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 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 syndrome is a neurological disorder characterized by a distressing urge to move the legs and sometimes other parts of the body, usually accompanied by a marked sense of discomfort in the legs or other affected body parts. RLS is triggered by rest or inactivity, and its symptoms are temporarily relieved by movement. In adults, it follows a circadian pattern, meaning that symptoms vary by time of day – being most common and intense during the evening and nighttime hours. The disorder can be relatively mild or have profound disruptive effects on a patient's sleep and daily life.

*For more detailed information on the diagnosis,
pathophysiology, and treatment of RLS,
please see the RLS Foundation's
Medical Bulletin,
or visit <http://www.rls.org/literature/>*



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