

TABLE 3. MANAGING RLS

In order to help pregnant women manage RLS, it is important to identify coping strategies that work for them. Encourage them to:

- Live a healthy lifestyle. Pregnant women with RLS should follow good sleep habits and eat a well-balanced diet.
- Find a low-impact exercise and include it into daily life.
- Identify aggravators. It is important for women with RLS to eliminate medications, foods, substances, or activities that produce or aggravate RLS symptoms.*
- Occupy their mind. Encourage those struggling with RLS to engage in activities which help take their mind off of RLS.
- Talk about RLS. Encourage each woman to share information about RLS with family and friends, and their health care provider.
- Don't fight it. Women should not suppress the urge to move. Encourage them to get out of bed and find an activity that takes their mind off of RLS.
- Rise to new levels. Women may be more comfortable if they elevate their desktop or bookstand to a height that will allow them to stand as they work or read.
- Stretch out their days. Encourage pregnant women with RLS to begin and end each day with stretching or gentle massage.

*A complete list of RLS symptom triggers is available on www.rls.org in the Members Only section.

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The Restless Legs Syndrome Foundation is dedicated to improving the lives of the men, women, and children who live with this often devastating disease. The organization's goals are to increase awareness of restless legs syndrome (RLS), to improve treatments, and, through research, to find a cure.

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PREGNANCY AND RLS



Vital Considerations in Treating a Pregnant Woman

*who has
Restless Legs Syndrome/
Willis-Ekbom Disease*



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RESTLESS LEGS SYNDROME (RLS), also known as Willis-Ekbom disease, is a common physical disorder characterized by an intense urge to move the legs, often associated with uncomfortable and unpleasant sensations^{1,2} (see Table 1). Sometimes the arms or other parts of the body are similarly affected. RLS is found at a significant increased frequency in individuals with iron deficiency (with or without anemia), with end-stage renal disease, and during pregnancy. A disturbance in the brain's dopamine systems, perhaps related to reduced iron in central neurons, seems likely to be the cause of RLS, resulting in altered central nervous system function.³

RLS during pregnancy poses a unique set of challenges.⁴ Symptoms of RLS may be difficult to differentiate from leg cramps – another common phenomenon in pregnancy – which also have the potential to disrupt sleep. But, unlike RLS, leg cramps involve painful and prolonged contraction and hardening of the muscle. RLS should also be differentiated from simple positional discomfort

TABLE 1. ESSENTIAL DIAGNOSTIC CRITERIA FOR RLS

These five essential features must be present for a diagnosis of restless legs syndrome:

1. There is an urge to move the legs, usually accompanied by or caused by uncomfortable and unpleasant sensations in the legs
2. The urge to move the legs and any accompanying unpleasant sensations begin or worsen during periods of rest or inactivity such as lying or sitting
3. The urge to move the legs and any accompanying unpleasant sensations are partially or totally relieved by movement, such as walking or stretching, at least as long as the activity continues
4. The urge to move the legs and any accompanying unpleasant sensations are worse in the evening or night than during the day or only occur in the evening or night
5. The urge to move the legs and any accompanying unpleasant sensations are not solely accounted for by another condition, such as leg cramps, positional discomfort, leg swelling, or arthritis

and leg edema.⁴ RLS can begin during pregnancy, or a woman already affected by RLS may notice that it becomes more severe during pregnancy.

RLS affects approximately one in five pregnant women in Western countries, less in some Asian countries.^{4,9} RLS symptoms are likely to occur or increase later in pregnancy, especially in the third trimester.^{6,8} For some women RLS is simply a nuisance.⁴ However, for others it can have major impact on sleep and daytime function. It is important to note that in the majority of cases, RLS symptoms resolve or improve significantly soon after delivery. About two-thirds of women with RLS during pregnancy have "transient" RLS, with onset and resolution related to pregnancy.¹¹ Predictors of developing RLS during pregnancy include a family history of RLS (8x risk), a history of RLS in a prior pregnancy (54x risk), a history of RLS in the past (13x risk), and low red blood cell count (2x risk).^{7,12-13} Although "transient" RLS related to pregnancy has a good short-term prognosis, long-term there is triple the risk of developing chronic RLS compared to women who do not experience RLS during pregnancy.¹¹ This and the strong family history of RLS in women who have RLS during pregnancy suggests a genetic predisposition that is unmasked due to pregnancy-related factors.

Factors specific to pregnancy that might account for the increased prevalence of RLS in pregnant women have not been well delineated. Potential contributors include low mineral or vitamin levels (iron, folate), sleep deprivation (due to nocturnal discomfort caused by changing body habitus, decreased bladder capacity, or prolonged caffeine half-life), hormonal changes, and increased sensory input (such as caused by lower extremity edema, varicose veins, and nerve compression).¹⁴

Very little research to date has been directed at the treatment of RLS in pregnancy. Most medications that have proven useful in treating RLS in the general population have been inadequately studied for safety in pregnancy, including pramipexole, ropinirole,

rotigotine, and gabapentin enacarbil.⁴

Before beginning or continuing treatment, women should discuss with their health care provider the risks and benefits of taking specific medications during pregnancy or while breastfeeding. In general, unless absolutely necessary, medications should be avoided during pregnancy unless the benefit clearly outweighs any concerns.

To help address the need for treatment guidelines, an expert panel published recommendations in 2015 for the treatment of RLS during pregnancy and lactation.⁴ That paper contains a broad, detailed analysis of the medical literature. Table 2 lists an abbreviated version of the most important guidelines.

Pregnant or lactating women with RLS should be encouraged to try behavioral approaches primarily (see Table 3), such as low-impact exercise and good sleep habits. Activities that maintain alertness seem to reduce RLS (such as knitting, engaging in intense discussions, or playing computer games). RLS typically subsides during the day, providing the opportunity for a morning or afternoon nap to obtain relief from fatigue after a sleepless night.

Prolonged immobility should be avoided and sleep apnea, if present, should be treated. The duration of caffeine is prolonged during pregnancy. It can aggravate RLS and interfere with sleep, even if taken earlier in the day.

Smoking and alcohol should be avoided. In addition to known harmful effects on the fetus, these have each been associated with increased sleep disturbance and increased RLS in pregnant women.¹⁵

Medications that make RLS worse should also be avoided, including sedating antihistamines such as diphenhydramine (Benadryl). Many medications prescribed for nausea and vomiting of pregnancy (NVP) can unmask or exacerbate RLS symptoms. In general, doxylamine, prochlorperazine, promethazine and metoclopramide should be avoided for NVP.

However, ondansetron does not appear to trigger RLS symptoms. Antidepressants and RLS are discussed in detail in the RLS Foundation brochure "Depression and RLS".

TABLE 2. GUIDELINES FOR THE TREATMENT OF RLS DURING PREGNANCY

- Accurate diagnosis is important.
- Severity/impact assessment guides treatment choices.
- Non-medication treatments are sufficient for most cases.
- Nonpharmacologic interventions include low-impact exercise and avoidance of exacerbating factors.
- Oral iron is recommended if serum ferritin is <75 mcg/L; IV iron may be considered if oral iron fails and serum ferritin is <30 mcg/L.
- If medication is used for refractory cases, the lowest effective dose and shortest duration possible are suggested.
- Periodic reassessment of medication is advised, particularly at delivery, when symptoms typically subside.

Oral iron is considered safe during pregnancy and lactation with potential benefits for both the mother and fetus. In addition, multiple lines of evidence implicate low iron stores as an aggravating factor for RLS.³ Importantly, it is not uncommon for women to require iron supplementation beyond that in prenatal vitamins during pregnancy, since there is heavy demand on iron stores during pregnancy and prenatal vitamins do not contain adequate iron to treat iron deficiency anemia or low iron stores.¹⁶

For women with RLS during pregnancy or lactation, additional oral iron is recommended if serum ferritin is <75 mcg/L.⁴ The ferritin level reflects iron stores in the body and is measured by a simple blood test. For RLS it is best for ferritin to be in the "middle normal" range, above 75 mcg/L. Iron supplementation should be supervised by a medical professional to avoid the rare but very

serious complication of iron overload. Also, iron should be stored out of the reach of children, because iron overdose in children can be fatal. IV iron may be considered if oral iron fails and serum ferritin is <30 mcg/L.⁴

If medication is felt to be needed for severe, refractory RLS, it should be chosen with care and in consultation with a health care provider, only after behavioral approaches and iron have failed. It should be used at the lowest dosage and frequency possible.⁴ The 2015 treatment guideline paper includes a detailed discussion of the risks vs benefits of medications for refractory RLS, including clonazepam (Klonopin) or carbidopa/levodopa (Sinemet) during pregnancy, as well as gabapentin (Neurontin) or clonazepam (Klonopin) during lactation.⁴ Also, bupropion (Wellbutrin) for depression during pregnancy and lactation is discussed.

Up-to-date, evidence-based information on the safety and risk of drugs during pregnancy, is available at Motherisk (www.motherisk.org), www.perinatology.com, or the Centers for Disease Control and Prevention (CDC) (www.cdc.gov/ncbddd/meds/).

In summary, there is much research to be done on RLS including RLS in pregnancy. Women should be reassured that RLS is likely to resolve or improve significantly soon after delivery. Measures that promote restorative sleep, such as avoiding sleep deprivation, abstaining from caffeine, and partaking in regular moderate exercise should be encouraged. Where ferritin levels are found to be low, supplementation should be given to bring these levels into the mid-normal range. Rarely, in refractory cases, IV iron or medication may be considered.⁴