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Although Nocturnal leg cramps are not a surgical problem (as long as other diagnoses have been ruled out), as a vascular surgeon I very often get referred patients with “leg cramps”. Some of these, after careful questioning, actually turn out *not* to be from arterial insufficiency, but rather from the more benign (but not trivial!) “nocturnal leg cramps”.

I am not an authority on the management of nocturnal leg cramps, but in order to help my General Practitioner colleagues, I have come across this article in UpToDate, which I have re-produced here. All Copyright remains with the authors.

This article is **not** a guide for patients to treat themselves, as they need to be assessed by their GPs first, to rule out underlying disease.

## **Nocturnal Leg Cramps**

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### INTRODUCTION

Nocturnal leg cramps, a common lower extremity condition that produces pain and can disrupt sleep, are reviewed here. Other nighttime disorders of leg movement, including restless legs syndrome and periodic limb movements of sleep, are discussed separately. (See ["Restless legs syndrome"](#) and ["Restless legs syndrome", section on 'Periodic limb movements of sleep'](#).)

Nocturnal leg cramps are common and frequently unreported to clinicians [1,2]. They are present in nearly 50 percent of those over the age of 50, have an increased prevalence with age, and show no gender preference. Roughly 40 percent of those with nocturnal leg cramps report having such symptoms at least three times per week, and 5 to 10 percent report nightly cramping.

Leg cramps are characterized by sudden muscle tightness, most commonly in the foot, thigh, or calf, last from seconds to many minutes, and are relieved by forceful stretching of the affected

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muscles. The vast majority of individuals have such cramps only at night. Their primary morbidity is pain and sleep disturbance.

### ETIOLOGY

Leg cramps can be idiopathic (the most common), associated with structural disorders or leg positioning, or related to extracellular fluid volume depletion and electrolyte disturbances.

- Structural disorders such as flat feet, genu recurvatum, and the hypermobility syndrome may predispose to leg cramps. A family history is common in these circumstances.
- Prolonged sitting, inappropriate leg position during sedentary activity, or living or working on concrete flooring may be correlated with an increased occurrence of leg cramps.
- Leg cramps may result from extracellular volume depletion (eg, due to diuretics, excessive sweating without sufficient salt replacement, or fluid removal during hemodialysis) and the dialysis disequilibrium syndrome. (See "[Dialysis disequilibrium syndrome](#)".)
- Pregnancy-related leg cramps may be due, in part, to low serum magnesium, which may respond to magnesium supplementation, although results of trials using such therapy are mixed [3-5].
- Neurologic disorders including Parkinson disease, myopathies, neuropathies, radiculopathies, and motor neuron diseases are often accompanied by leg cramps [6,7].
- Metabolic diseases associated with leg cramps include diabetes, hypoglycemia, alcoholism, hypothyroidism, and metabolic myopathies [7].
- Exercise-associated muscle cramping (EAMC) is defined as an involuntary, painful contraction of skeletal muscle during or after exercise [8].
- Other causes of leg cramps include various medications and other medical conditions [7,9-17].
- Medications for which the evidence of an association with leg cramps is the strongest, although still unproven, include inhaled long-acting beta agonists (LABA), potassium-sparing diuretics, and thiazide-like diuretics. Analysis of a population-derived pharmacy database involving 24,417 individuals found that patients were more likely to receive a [quinine](#) prescription for nocturnal leg cramps during the year after starting a drug from one of these classes, compared with the preceding year (sequence ratios for LABA, potassium-sparing and thiazide diuretics of 2.42 [95% CI 2.02-2.89], 2.12 [95% CI 1.61-2.78], and 1.48 [95% CI 1.29-1.68], respectively) [17]. Only small increased risks were seen for loop diuretics and statins.
- Other medications that may cause cramps include other beta agonists, beta blockers with intrinsic sympathomimetic activity, angiotensin II receptor antagonists, benzodiazepines, paratide, teriparatide, [pyrazinamide](#), [raloxifene](#), [donepezil](#), [neostigmine](#), [tolcapone](#), clofibrate, [cisplatin](#), [vincristine](#), and oral contraceptives.
- Other unusual causes include anemia, Raynaud syndrome, opioid withdrawal, nonalcoholic cirrhosis, and bariatric surgery.

Patients with the most common form of leg cramps have no fluid or electrolyte imbalance.

Observed pathophysiologic changes include an increased frequency of muscle action potentials

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due to motor neuron hyperactivity [10]. This results in depletion of muscle adenosine triphosphate; cytosolic accumulation of calcium then prevents muscle relaxation.

### DIAGNOSIS

Patients may describe numerous types of leg pain as cramps. The physical examination may be helpful only in that it is usually normal with idiopathic leg cramps. A careful history and physical examination can exclude the majority of disorders in the differential diagnosis, including the following [9-11]:

- Contractures (which occur in metabolic myopathies and thyroid disease)
- Tetany (due to hypocalcemia, hypomagnesemia, and metabolic alkalosis)
- Dystonias (occupational cramps and those related to dopamine antagonists [eg, antipsychotic medications or antiemetics] or Parkinson's disease)
- Myalgias (due to some drugs such as [cimetidine](#) and [cholestyramine](#))
- Restless legs syndrome (which also occurs at rest, predominantly in the evening, and is characterized by a need to move the affected limb and at times, by involuntary brief movements, but does not involve sustained contraction of muscles) (see "[Restless legs syndrome](#)")
- Intermittent claudication (which occurs during limb use and is relieved by rest)
- Compartment syndromes (occurring after excessive running)
- Peripheral neuropathy (characterized by dysesthesias and/or muscle weakness but not sustained muscle contractions)
- Peripheral vascular disease

### MANAGEMENT

Diffuse, recurrent, or severe muscle cramping should prompt an evaluation for hypocalcemia, although the plasma calcium concentration is normal in patients with idiopathic cramps. (See "[Clinical manifestations of hypocalcemia](#)".)

The prevention and treatment of benign nocturnal leg cramps begins with nonpharmacologic therapy. Cramps often resolve on their own or with nonpharmacologic interventions alone. The best data for pharmacologic therapy is with [quinine](#), but this drug is no longer routinely recommended for nocturnal leg cramps. Weaker evidence exists for the efficacy of vitamin B complex, naftidrofuryl (though not available in the United States), and calcium channel blockers, and these medications should be tried before considering quinine or other less well-studied medications. (See '[Nonpharmacologic therapy](#)' below and '[Pharmacotherapy](#)' below.)

Nonpharmacologic therapy — Nonpharmacologic therapies are used for both the prevention and treatment of nocturnal leg cramps, but the evidence supporting the efficacy of any of these approaches is very limited [18].

The following preventive measures may be beneficial:

- In generally sedentary patients, riding a stationary bicycle for a few minutes before retiring

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- Stretching exercises. These exercises can be performed in the weight-bearing position. They are held for 10 to 20 seconds and are repeated three to five times in succession, four times daily for one week, then twice daily in the evening, and again before retiring thereafter ([picture 1](#)) [19]. One clinical trial, however, failed to confirm the benefit of this approach, although all of the trial patients were on [quinine](#) at baseline, and many continued the drug during the trial [19,20].
- Further support for the efficacy of stretching was provided by another randomized trial, which was not included in the 2012 systematic review [21]. In this trial, involving 80 patients over 55 years of age with a mean of 3.2 to 3.4 cramps nightly, a six-week program of calf and hamstring muscle stretching before sleep significantly decreased the frequency of nocturnal leg cramps compared with not stretching (mean difference of -1.2 cramps nightly, 95% CI -0.6 to -1.8). Additionally, cramp severity was decreased in the treatment group but not in the controls.
- Using long-countered shoes and other proper foot gear (see "[Joint protection program for the lower limb](#)")
- Keeping the bed covers at the foot of the bed loose and not tucked in
- Maintaining adequate hydration, particularly in older adults and patients on diuretics. Avoidance of alcohol and caffeine may also be helpful. Exercising in extreme heat should be avoided.

If a cramp occurs, nonpharmacologic interventions that may be beneficial include:

- Walking or leg jiggling followed by leg elevation
- A hot shower with the stream directed at the cramp area of the body, usually for five minutes, or a warm tub bath
- Ice massage
- Correction of fluid and electrolyte abnormalities, if present (see "[Etiology, clinical manifestations, and diagnosis of volume depletion in adults](#)")

### PHARMACOTHERAPY

[Quinine](#) has been the best-studied drug for nocturnal leg cramps and has been found effective in some well-designed randomized trials [22]. However, quinine is no longer routinely recommended for the treatment of nocturnal leg cramps due to the potential for serious and/or life-threatening side effects (eg, cardiac arrhythmias, thrombocytopenia, HUS-TTP, and severe hypersensitivity reactions) that occur in 2 to 4 percent of patients, important drug interactions, and evidence for only modest benefit [23]. An FDA warning issued in December 2006 and reaffirmed in 2010 stated that, due to these potential serious events, the risks associated with quinine use do not justify its use in the unapproved/unlabeled prevention and treatment of leg cramps [24,25]. (See "[Causes of thrombotic thrombocytopenic purpura-hemolytic uremic syndrome in adults](#)", section on 'Quinine'.)

Other medications have been less well-studied. A 2010 systematic review of prospective trials identified limited data to support the use of several agents [23]. These include:

- Vitamin B complex, including vitamin B6, 30 mg/day [26]
- Naftidrofuryl, which is unavailable in the United States [27]

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- Calcium channel blockers, including [diltiazem](#) (30 mg/day) and [verapamil](#) (120 to 180 mg at bedtime) [[28,29](#)].

The following medications have also been used for nocturnal leg cramps with variable success [[19,29-35](#)]:

- [Diphenhydramine](#) (Benadryl) 12.5 to 50 mg nightly
- Vitamin E [[30](#)], although the efficacy of this agent has not been confirmed in randomized studies [[31](#)]
- Muscle relaxants, including [carisoprodol](#) and [orphenadrine](#) [[34](#)]
- [Chloroquine](#) phosphate (250 mg daily for two to three weeks, followed by 250 to 500 mg once per week) [[33](#)]. We have also used [hydroxychloroquine](#) sulfate (200 mg daily for two weeks, then once per week) with good results.
- [Gabapentin](#) (600 mg daily with increased doses as necessary) [[36](#)]
- Shakuyaku-kanzo-to granule, used in hemodialysis patients [[35](#)]

A systematic review of randomized trials comparing magnesium supplementation with placebo identified four trials involving 322 patients with idiopathic (primarily nocturnal) leg cramps; meta-analysis of the trials found no evidence of significant benefit in the frequency or severity of cramping with magnesium therapy [[37](#)]. Three trials involving a total of 202 women with pregnancy-associated leg cramps were identified in the systematic review; only one found benefit.

We generally use pharmacotherapy only in patients who fail nonpharmacologic measures, given the risk of serious adverse effects of [quinine](#) and the relatively weak data for benefit of other agents. In these patients, we typically do the following:

- We use mineral and vitamin supplementation before using prescription medications, including assuring adequate supplementation with calcium; magnesium, the use of which is limited to patients with pregnancy-related cramps; iron, in patients who have iron-deficient anemia; and vitamins E and B6.
- We advise avoidance of drugs known to cause cramping. (See '[Etiology](#)' above.)
- If the measures above are ineffective, we first try [diphenhydramine](#) (25 mg) at bedtime, and, if it is ineffective, we prescribe a calcium channel blocker, such as [diltiazem](#) (30 mg) or [verapamil](#) (120 to 180 mg) each evening.
- In patients with muscle cramping that is persistent or severe or occurs in unusual locations, such as upper back or abdominals, the author has given a two-week trial of [chloroquine](#) 250 mg/day or [hydroxychloroquine](#) 200 mg/day. If cramps have resolved with this treatment, it is then withheld until symptoms return, but the cramping may remit for extended periods of time in the author's experience.
- We use [gabapentin](#) after the above measures have failed, with particular care in older patients because of the increased risk of side effects in such patients in the author's experience.
- If the measures above fail, [quinine](#) can be considered as long as the patient is informed of the potential adverse events and understands the level of risk relative to the benign (although painful) nature of leg cramps. The FDA specifically recommends that healthcare professionals should discuss with patients the warning signs of

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thrombocytopenia and that patients should be encouraged to read the Medication Guide given to them at the pharmacy before starting quinine sulfate and each time they get a refill [25]. However, the author advises the use of 6 ounces (180 mL) of tonic water, rather than prescription quinine, and only if cramps have persisted or are severe and disabling. We use such treatment rarely and do not use it on a daily basis.

Nocturnal leg cramps in children — Nocturnal leg cramps have been reported in 7.3 percent of children and adolescents [38]. Peak occurrence is 16 to 18 years of age, with no cases reported less than eight years of age. Pediatric nocturnal leg cramps are typically benign, self-limited, and infrequent [38,39].

### OTHER NOCTURNAL LEG MOVEMENT CONDITIONS

Sleep starts — Hypnic jerks, also termed benign hypnic myoclonus, are common sudden jerking contractures of the limbs that occur during the transition to, or very shortly after, falling asleep [40]. These sleep starts may awaken the patient, and the severity of the movement can occasionally be frightening. They seldom recur after falling back to sleep. No definite cause is known. (See "[Nonepileptic paroxysmal disorders in adolescents and adults](#)", section on '[Sleep starts](#)'.)

The condition is self-limited; treatment includes reassurance of the benign nature of the disturbance. Use of caffeinated beverages should be avoided. Occasionally, sleep starts and restless legs syndrome coexist.

Nocturnal myoclonus — Varieties of sudden movement that occur during sleep or sleep transitions are partial myoclonic jerks, massive myoclonic jerks (hypnic jerks), and periodic movements of sleep. These conditions are discussed in detail elsewhere. (See "[Classification and evaluation of myoclonus](#)", section on '[Jerks associated with sleep](#)' and "[Restless legs syndrome](#)", section on '[Periodic limb movements of sleep](#)'.)

Periodic movements of sleep (nocturnal myoclonus) consist of stereotyped dorsiflexion of the toes and feet, sometimes with flexion of the knees and hips occurring roughly every 10 to 30 seconds. These movements occur in relaxed wakefulness or during sleep, are common in restless legs syndrome (but can occur in those without this disorder), and can disrupt sleep. (See "[Restless legs syndrome](#)", section on '[Periodic limb movements of sleep](#)'.)

### SUMMARY AND RECOMMENDATIONS

- Nocturnal leg cramps are common, are frequently unreported to clinicians, and occur in all decades of life. The most important morbidity of benign nocturnal leg and foot cramps is that they produce pain and often disturb sleep. (See "[Nocturnal leg cramps](#)" above.)
- Leg cramps are most commonly idiopathic but may also be associated with structural disorders or leg positioning or related to extracellular fluid volume depletion and electrolyte disturbances. Other causes include neurologic and metabolic disorders and pregnancy. (See "[Etiology](#)" above.)
- Patients may describe numerous types of leg pain as cramps. The physical examination may be helpful only in that it is usually normal with idiopathic leg cramps. A careful

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history and physical examination can exclude the majority of disorders in the differential diagnosis. (See ['Diagnosis'](#) above.)

- Diffuse, recurrent, or severe muscle cramping should prompt an evaluation for hypocalcemia, although the plasma calcium concentration is normal in patients with idiopathic cramps. (See ['Management'](#) above.)
- The prevention and treatment of benign nocturnal leg cramps begins with nonpharmacologic therapy. The best data for pharmacologic therapy are with [quinine](#), but this drug is no longer routinely recommended for nocturnal leg cramps because of risks of serious adverse effects. Weaker evidence exists for the efficacy of vitamin B complex, naftidrofuryl (though not available in the United States), and calcium channel blockers, and these medications should be tried before considering quinine or other less well-studied medications. (See ['Nonpharmacologic therapy'](#) above and ['Pharmacotherapy'](#) above.)
- Sleep starts are a commonly occurring, sudden, jerking contraction of the limbs that occurs shortly after falling asleep and that may awaken the patient. They seldom recur after falling back to sleep. No definite cause is known. Treatment includes reassurance of the benign nature of the disturbance. (See ['Sleep starts'](#) above.)
- Periodic limb movements of sleep (nocturnal myoclonus) consist of stereotyped dorsiflexion of the toes and feet, sometimes with flexion of the knees and hips roughly every 10 to 30 seconds. These movements are common in the restless legs syndrome and can disrupt sleep. (See ['Nocturnal myoclonus'](#) above.)