

## Leg Symptoms in Outpatient Veterans

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In a survey of outpatients at the Denver Veterans Affairs Medical Center for common leg symptoms—515 questionnaires returned in a 3-week period—56% reported nocturnal leg cramps, 29% reported the restless leg syndrome, and 49% reported symptoms of peripheral neuropathy. Only 33% of patients had no symptoms relating to their legs. Patients often did not report these symptoms to their physician but were more likely to do so if the symptoms were frequent. Conditions especially related to leg symptoms were hypertension, peripheral vascular disease, coronary artery disease, cerebrovascular disease, kidney disease, and hypokalemia. Most patients did not receive effective therapy for these symptoms.

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Several leg symptoms commonly seen in a primary care practice have never been adequately studied. Textbook statements that nocturnal leg cramps occur in about 15% of healthy young adults<sup>1(p1215)</sup> and as many as 70% of patients older than 50 years<sup>2(pp300-301)</sup> are not referenced. Nocturnal leg cramps are painful, involuntary contractions of muscles occurring at rest and causing a visible, palpable knot in a muscle, usually the gastrocnemius or soleus.<sup>3</sup> Pemberton reported in 1935 that 41% of arthritis patients had nocturnal leg cramps.<sup>4</sup> There have been no prevalence studies on general medicine clinic patients. Nocturnal leg cramps result from motor unit hyperactivity due to a variety of causes such as hemodialysis, lower motor neuron disease, electrolyte imbalance, and drugs.<sup>5-10</sup> Relief of these cramps requires stretching the contracted muscle, usually through passive dorsiflexion of the foot. Initial physical measures to prevent nocturnal leg cramps include calf stretching exercises and sleeping positions that minimize foot plantar flexion.<sup>11,12</sup> When these measures fail, various drug regimens have been suggested. Since 1940, quinine sulfate has been used to relieve night cramps.<sup>13</sup> Small double-blind studies have shown quinine superior to placebo in reducing the frequency and severity of leg cramps in elderly<sup>14,15</sup> and hemodialysis<sup>16</sup> patients but not in medical inpatients.<sup>17</sup> Other drugs whose use has been recommended but without good evidence of efficacy include verapamil, diazepam, diphenhydramine hydrochloride, phenytoin, dantrolene, procainamide hydrochloride, imipramine hydrochloride, and vitamin E.<sup>18-20</sup>

Ekbom renewed interest in a common but virtually ignored condition, the restless legs syndrome.<sup>21</sup> This is a clinical diagnosis based on the presence of peculiar creeping or crawling sensations, usually in the lower leg, felt deep inside the muscle or bones, occurring at rest and relieved by motion or exercise.<sup>22</sup> The restless legs syndrome is said to be less common than nocturnal leg cramps, again without supporting data, but does occur in 11% of insomnia patients.<sup>23</sup> The restless legs syndrome has been variously reported in 5% of healthy normal subjects,<sup>21</sup> 15% of surgical outpatients,<sup>24</sup> and 15% to 20% of dialysis patients.<sup>25</sup> Theories for the cause of the restless legs syndrome have included heredity, iron deficiency, uremia, pregnancy, anxiety or depression, and a variety of other causes.<sup>21,22,26</sup> Suggestions for treatment have

included the use of iron, vasodilators, propranolol hydrochloride, clonidine, baclofen, carbamazepine, clonazepam, and dopaminergic agents, and transcutaneous electric nerve stimulation.<sup>27-31</sup>

Peripheral neuropathy symptoms, especially due to diabetes mellitus, are common in an older population, but their prevalence in a primary care population has never been reported. Peripheral neuropathy is characterized by dysesthesias in the extremities, most often numbness and tingling or pain in the feet and lower legs.<sup>32(p1509)</sup> The long list of nerve-damaging processes resulting in these symptoms includes metabolic processes, particularly diabetes and vitamin deficiencies, toxins such as alcohol, antimicrobial or chemotherapeutic drugs, environmental chemicals, inflammatory diseases, neoplasms, and hereditary neuropathies. While several studies have examined the causes of neuropathy within specific patient groups, including the elderly,<sup>33</sup> inpatients in an Indian general hospital,<sup>34</sup> and patients referred to the Mayo Clinic with neuropathy of unknown cause,<sup>35</sup> the prevalence of peripheral neuropathy symptoms or dysesthesias in the primary care population has not been evaluated. Even among diabetic patients, "the incidence of neurological deficit in diabetes mellitus is not known."<sup>36(p977)</sup> Brown and co-workers estimated that 10% of all diabetic patients have symptomatic neuropathy,<sup>37</sup> but Clements reported signs and symptoms of polyneuropathy in half of all patients with diabetes observed for more than 20 years.<sup>38</sup> Recommendations for the treatment of both pain and paresthesias of peripheral neuropathy have been based on small series, mainly in diabetic patients, and have included the use of phenytoin, carbamazepine, amitriptyline hydrochloride, fluphenazine hydrochloride, and recently mexiletine hydrochloride.<sup>39-43</sup>

Because the causes of these nonfatal but often aggravating conditions are so poorly understood, recommendations for their treatment are largely empiric. We therefore studied patients at the Denver (Colorado) Veterans Affairs Medical Center (VAMC) to answer two questions: What is the prevalence of nocturnal leg cramps, the restless legs syndrome, and symptomatic peripheral neuropathy in an outpatient veteran population? What treatment regimens for these symptoms have been attempted, and which did the patients report most successful?

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**Methods**

We developed a two-page questionnaire for anonymous self-administration at the Denver VAMC. A patient's age and sex, clinic appointment, and underlying self-reported medical conditions including the presence of diabetes mellitus, hypertension, peripheral vascular disease, coronary artery disease, previous stroke, kidney failure, hypokalemia, and hypocalcemia were recorded. These associated conditions were selected from several reviews on the subject. Patients were asked about the presence and, if present, the frequency of symptoms, whether their physicians had been told of the symptoms, which drugs had been tried, and which worked best. The identifying questions for individual symptoms were as follows:

- For nocturnal leg cramps: Have you had trouble with cramps in your calves or feet at night?
- For the restless legs syndrome: Have you had trouble with restless or crawling sensations in your legs at night?
- For peripheral neuropathy: Have you had trouble with numbness or tingling in your legs or feet?

The study was approved by the Human Subjects Committee of the Denver VAMC. For each symptom, the patient was asked to circle any drugs that had been tried and then to specify which drug worked best. For cramps, the drugs listed were quinine, vitamin E, phenytoin, diazepam, procainamide, amitriptyline, diphenhydramine, and other (please specify). For restless legs, the drugs were iron, diazepam, clonazepam, amitriptyline, and other. For peripheral neuropathy, the choices were phenytoin, carbamazepine, amitriptyline, and other.

The primary care clinics at the Denver VAMC are staffed by general internal medicine faculty, internal medicine residents, and nurse practitioners. Over a three-week period the questionnaire was distributed to all patients attending the primary care, internal medicine, diabetes, hypertension, and geriatric clinics. The questionnaire was given to the patients by the nurse at clinic check-in, filled out while the patients were waiting for appointments, and collected by the primary care givers at the appointment.

Data analysis using the SPSS/PC [Statistical Package for the Social Sciences for use on a personal computer] program<sup>44</sup> centered on the frequency of the various leg symptoms according to demographic factors and reported chronic disease. Estimates of prevalence are reported with 95% confidence limits to provide an indication of the precision of our estimates. Odds ratio confidence limits were calculated using Miettinen's method.<sup>45</sup>  $\chi^2$  Tests without correction for continuity were used to test statistical significance.

**Results**

The self-administered questionnaire was distributed to 604 consecutive patients. Of these, 515 were returned, for a response rate of 85%. Because not all patients answered all questions, denominators may vary in the analyses. Of the respondents, 95% were men, with a mean age of 60.4 years (range, 26 to 91). Chronic medical conditions reported by the patients included hypertension (35%), coronary artery disease (25%), diabetes mellitus (24%), peripheral vascular disease (20%), previous cerebrovascular accident (8%), history of hypokalemia (14%), kidney disease (2%), and history of hypocalcemia (2%).

**TABLE 1.—Prevalence of Leg Symptoms**

Symptom	Patients, No./Total*	%	95% Confidence Interval, %
Nocturnal leg cramps . . . . .	276/490	56	52 to 61
Restless legs syndrome . . . . .	132/453	29	25 to 33
Peripheral neuropathy . . . . .	234/477	49	45 to 54
None of the 3 . . . . .	140/430	33	28 to 37
All of the 3 . . . . .	90/430	21	17 to 25

\*The total number of patients responding who had the symptom versus the number who answered the question. The denominators vary because not all patients answered all questions.

The prevalence of the three leg symptoms is shown in Table 1.

Associations of the three symptoms with self-reported chronic disease are shown in Table 2. Unexpectedly, diabetes mellitus was not correlated with any of these symptoms. Peripheral vascular disease was associated with all three symptoms ( $P < .001$ ). Hypertension, stroke, and kidney failure were associated with neuropathy symptoms, and leg cramps were associated with coronary artery disease.

Table 3 shows how frequently patients experience these leg symptoms. The frequency of symptoms strongly correlates with patients' reporting symptoms to physicians (Table 4). Of 64 patients with daily leg cramps, 52 (82%) had told their physician, while of 60 patients with 1 to 12 episodes per year, only 22 (37%) reported them. Of 276 patients with leg cramps, 213 answered questions regarding treatment and 77 (36%) reported some sort of drug treatment. Of those with daily cramps, 42 (55%) had received treatment. Quinine sulfate was used in 34 patients, followed by diazepam in 17, vitamin E in 12, amitriptyline in 10, phenytoin in 9, and diphenhydramine in 8. Some patients received more than one drug. Quinine was reported to be most effective in 50% of those receiving it. None of the other drugs were described as effective.

**TABLE 2.—Association of Leg Symptoms With Chronic Disease**

Disease	Odds Ratio	95% Confidence Interval	P
<b>Nocturnal Leg Cramps</b>			
Peripheral vascular disease . . . . .	3.49	2.11 to 5.76	.0001
Hypokalemia . . . . .	1.74	1.01 to 3.01	.047
Coronary artery disease . . . . .	1.68	1.10 to 2.56	.015
Hypertension . . . . .	1.35	0.92 to 1.97	.121
Kidney disease . . . . .	1.83	0.48 to 7.02	.378
Stroke . . . . .	1.07	0.55 to 2.06	.8392
Diabetes mellitus . . . . .	0.99	0.75 to 1.29	.9421
Hypocalcemia . . . . .	1.03	0.27 to 3.86	.9650
<b>Restless Legs</b>			
Peripheral vascular disease . . . . .	3.17	1.98 to 5.07	.0001
Hypocalcemia . . . . .	6.18	1.44 to 26.46	.0141
Hypertension . . . . .	1.54	1.02 to 2.34	.0421
Coronary artery disease . . . . .	1.58	1.01 to 2.48	.0465
Hypokalemia . . . . .	1.56	0.88 to 2.77	.1295
Kidney disease . . . . .	2.44	0.63 to 9.51	.1986
Stroke . . . . .	0.78	0.35 to 1.73	.5401
Diabetes mellitus . . . . .	1.11	0.69 to 1.78	.6664
<b>Peripheral Neuropathy Symptoms</b>			
Peripheral vascular disease . . . . .	5.07	3.07 to 8.37	.0001
Stroke . . . . .	3.48	1.67 to 7.25	.0016
Kidney disease . . . . .	9.52	1.73 to 52.35	.0096
Hypertension . . . . .	1.62	1.11 to 2.37	.0130
Hypocalcemia . . . . .	6.26	0.97 to 40.23	.0533
Hypokalemia . . . . .	1.62	0.96 to 2.73	.0705
Coronary artery disease . . . . .	1.41	0.93 to 2.14	.1048
Diabetes mellitus . . . . .	1.24	0.81 to 1.90	.3217

**TABLE 3.—Frequency of Leg Symptoms**

Frequency	Patients, No. (%)		
	Nocturnal Leg Cramps	Restless Legs Syndrome	Peripheral Neuropathy*
1-12/yr	60 (23)	14 (11)	28 (13)
1-3/mo	71 (27)	28 (22)	31 (14)
1-4/wk	67 (26)	33 (26)	45 (21)
Daily	64 (24)	54 (42)	115 (53)
<b>Total</b>	<b>262</b>	<b>125</b>	<b>219</b>

\*Includes dysesthesia symptoms.

**TABLE 4.—Patients Reporting to Physicians According to Frequency of Symptoms**

Frequency of Symptom	Patients, %*		
	Nocturnal Leg Cramps	Restless Legs Syndrome	Peripheral Neuropathy†
1-12/yr	37	21	31
1-3/mo	51	48	42
1-4/wk	63	70	68
Daily	82	68	78

\*Association between frequency of symptoms and reporting to physician ( $\chi^2$  test),  $P < .01$ .  
†Includes dysesthesia symptoms.

Although 70% of patients with frequent restless legs reported it to their physicians, only 29 of 104 (28%) patients reported receiving drugs. Diazepam was used in 16 patients, followed by amitriptyline in 9, iron in 5, and clonazepam in 3. None of these were reported by the patients as being particularly helpful.

More patients with numbness and tingling than with the other leg symptoms reported that their symptoms occurred daily (53% of 219), but still only 78% had discussed it with their physicians. Even fewer of them reported receiving treatment. Of 178 patients with dysesthesias who responded to treatment questions, only 34 (19%) of the total and 21% of those with daily symptoms reported receiving drug therapy. Of these, 14 had received phenytoin, 13 had received amitriptyline, 3 remembered having received carbamazepine, and 1 each was given chlordiazepoxide, quinine, tolmetin, and acetaminophen plus codeine. Only ten identified a drug as being effective—phenytoin in four, amitriptyline in two, and one each for carbamazepine, chlordiazepoxide, quinine, and acetaminophen plus codeine. Seven patients specifically wrote that no drug treatment worked.

Table 5 shows the percentage of patients with one of eight

self-reported diagnoses who had each of the leg symptoms alone or in combination. The restless legs syndrome rarely occurred alone. The combination of cramps and neuropathy was about as common as cramps alone. A surprisingly high number of patients had all three symptoms. Among patients with hypertension, 29% reported no leg symptoms and 28% reported all three symptoms of cramps, restless legs, and the dysesthesias of peripheral neuropathy. In diabetic patients surveyed, 29% had no symptoms and 23% had all three symptoms, while 14% reported dysesthesias alone, 10% reported cramps and dysesthesias, and 3% reported both restless legs and dysesthesias. Almost half the patients with peripheral vascular disease reported all three symptoms.

**Discussion**

In a recent review it was noted that the actual incidence of muscle cramps in internal medicine practices is unknown.<sup>46</sup> We have found that 56% of a veteran outpatient population experiences nocturnal leg cramps, with 12% reporting daily cramps. Only a third of these patients received drug therapy for cramps, most commonly quinine sulfate.

We likewise found that 29% of veterans describe restless legs, with 11% having daily symptoms. Only 28% of symptomatic patients reported drug treatment, most commonly with diazepam.

Finally, we found that 49% of veterans report numbness and tingling in the extremities. Only 21% of those with daily symptoms reported receiving drug treatment, with phenytoin and amitriptyline used equally often.

Conditions especially related to leg symptoms were hypertension, peripheral vascular disease, coronary artery disease, cerebrovascular disease, kidney disease, and hypokalemia. We were surprised that diabetes mellitus was not more closely associated. This lack of association was not due to a lack of study power, as the confidence limits on the odds ratio for diabetes are relatively narrow. Most of our diabetic patients are type II, and this may have accounted for the unexpectedly low rate of dysesthesias. Other factors such as the use of self-reported diagnoses and a lack of confirming data on medications may affect the relationships seen through misclassification and confounding. Further study of the associations found is needed to verify these findings.

In conclusion, we have shown that nocturnal leg cramps, the restless legs syndrome, and numbness and tingling in the legs are common in an outpatient veteran population. Only a third of our population is not bothered by at least one of these symptoms, and a fifth have all three. Yet less than half of

**TABLE 5.—Leg Symptoms According to Self-Reported Diagnoses**

Diagnosis	None		1 Symptom			2 Symptoms			All 3 Patients, %
			Nocturnal Leg Cramps (NLC)	Restless Legs Syndrome (RLS)	Peripheral Neuropathy (PN)	NLC & RLS	NLC & PN*	RLS* & PN*	
	Patients, No.	%	Patients, %						
Hypertension	151	29	11	0	7	3	18	2	28
Coronary artery disease	108	24	16	1	11	7	13	2	26
Diabetes	105	29	17	0	14	5	10	3	23
Peripheral vascular disease	83	10	10	0	12	4	18	4	43
Low potassium	56	23	13	2	9	9	18	4	23
Stroke	34	15	12	0	24	0	27	3	21
Kidney disease	8	13	0	0	25	0	13	0	50
Low calcium	7	0	0	0	29	14	0	14	43

\*Includes dysesthesias.

those with occasional symptoms and only 80% of those with daily symptoms can remember discussing them with their physician. The efficacy of treatment from patient reports is disappointing, even when given. While quinine use effectively relieves nocturnal leg cramps in half the treated patients, none of the regimens used for the restless legs syndrome or the dysesthesias associated with symptomatic peripheral neuropathy were effective. Further research is needed to develop effective treatments for these common and distressing conditions.

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