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Approach to Peripheral Neuropathy for the Primary Care Clinician

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ABSTRACT

Peripheral neuropathy is commonly encountered in the primary care setting and is associated with significant morbidity, including neuropathic pain, falls, and disability. The clinical presentation of neuropathy is diverse, with possible symptoms including weakness, sensory abnormalities, and autonomic dysfunction. Accordingly, the primary care clinician must be comfortable using the neurologic examination—including the assessment of motor function, multiple sensory modalities, and deep tendon reflexes—to recognize and characterize neuropathy. Although the causes of peripheral neuropathy are numerous and diverse, careful review of the medical and family history coupled with limited, select laboratory testing can often efficiently lead to an etiologic diagnosis. This review offers an approach for evaluating suspected neuropathy in the primary care setting. It will describe the most common causes, suggest an evidence-based workup to aid in diagnosis, and highlight recent evidence that allows for selection of symptomatic treatment of patients with neuropathy.

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KEYWORDS: Diabetes; Neuromuscular medicine; Peripheral neuropathy

INTRODUCTION

Peripheral neuropathy is among the most common neurologic problems encountered by primary care clinicians, but it can be challenging to recognize and evaluate because of its many diverse forms and presentations. Distal symmetric polyneuropathy is the most common form and is often encountered in the primary care setting as the most common systemic complication of diabetes mellitus. This review focuses on the presentation, evaluation, and management of distal symmetric polyneuropathy, but also offers suggestions for recognizing and evaluating other presentations.

CLINICAL PRESENTATION

Peripheral nerves consist of sensory, motor, and autonomic fibers. There are accordingly numerous symptoms that can prompt the clinician to consider neuropathy (**Table 1**). Patients usually present with sensory signs or symptoms before motor or autonomic symptoms prevail. Sensory fibers include large-diameter fibers mediating vibratory sensation and proprioception and small-diameter fibers mediating pain and temperature sensation. Symptoms vary on the basis of the relative involvement of large fibers and small fibers; most neuropathies affect both fiber types. Neuropathic pain occurs in one third of patients with peripheral neuropathy.[1] Some patients experience hyperesthesia, an accentuated sensation of tactile stimulation, or allodynia, the perception of normally nonpainful stimuli as painful. Autonomic symptoms are often underrecognized but common and can have great impact on quality of life. Orthostatic intolerance, gastroparesis, constipation, diarrhea, neurogenic bladder, erectile dysfunction, pupillomotor (eg, blurry vision) and vasomotor symptoms, leading to dry eyes, mouth, skin, or burning and flushing, are relatively common.[2,3] Rarely, autonomic symptoms may be the most prominent or only symptoms indicating neuropathy (**Table 2**).[4]

Delineating the pace of progression is critical. When symptoms of neuropathy develop acutely, the differential diagnosis is narrowed significantly (**Table 2**). Hyperacute onset of symptoms (eg, sudden wrist drop) in the absence of compression

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or trauma raises concern for a vasculitic process and merits urgent evaluation. Conversely, patients may not recognize long-standing symptoms or signs as being related to their presenting symptom. Asking about childhood clumsiness/poor athleticism, high arches, or ill-fitting shoes may reveal unrecognized signs of a chronic and perhaps hereditary neuropathy.

EXAMINING PATIENTS WITH SUSPECTED NEUROPATHY

The examination should focus on defining the anatomic distribution of findings and the extent of motor signs, sensory impairment, and absence of reflexes. The differential diagnosis for the causative process will vary on the basis of these classifications. Distal symmetric polyneuropathy is length-dependent: There is diffuse involvement of multiple nerves with symptoms and signs affecting the most distal segments first. Symptoms or signs in the legs usually reach the knees or just above before symptoms or signs occur in the fingers. A nonlength-dependent pattern or asymmetry may indicate a secondary process for which the differential diagnosis is different.

Other common patterns include mononeuropathy, such as median neuropathy at the wrist (ie, carpal tunnel syndrome), and radiculopathy, commonly caused by degenerative disease in the cervical or lumbosacral spine. Signs and symptoms will be restricted to the distribution of a single nerve, myotome, or dermatome in such cases. Multiple concurrent mononeuropathies, termed "mononeuropathy multiplex", may suggest a vasculitic etiology (**Table 2**). Because of the rapid, progressive course and potentially irreversible neurologic disability, it is important to suspect and investigate for vasculitis early.

CLINICAL SIGNIFICANCE

- Peripheral neuropathy is commonly encountered in the primary care setting, because it affects up to 8% of adults aged more than 55 years.
- Presentations of neuropathy are diverse, but distal symmetric polyneuropathy is the most common form.
- A relatively limited diagnostic investigation can efficiently identify the etiology of neuropathy in most patients.
- Suggested treatments for neuropathic pain include pregabalin, gabapentin, tricyclic antidepressants, and serotonin-norepinephrine reuptake inhibitors.

In addition to testing for weakness, the motor examination should look for muscle atrophy, which can be seen in chronic neuropathy. Distal calf atrophy, hammertoes, and pes cavus (high-arched feet) are characteristics of a long-standing neuropathy, often seen in hereditary neuropathies (**Figure**). When motor deficits are comparable to or greater than sensory deficits, demyelinating disorders such as chronic inflammatory demyelinating polyneuropathy and hereditary neuropathies must be considered (**Table 2**). Chronic inflammatory demyelinating polyneuropathy should also be considered if nonlength-dependent motor or sensory deficits are identified.

The sensory examination should test both large-fiber modalities (vibration and proprioception) and small-fiber modalities (pain and temperature). Proprioceptive deficits can manifest as sensory ataxia, mimicking cerebellar dysfunction. The Romberg sign is an effective screening tool for sensory ataxia. The patient stands with their feet directly together and then closes their eyes; the patient must rely on sensory information alone to maintain balance. If the patient is steady with eyes open but sways and takes a step to steady themselves with eyes closed, the test is positive.

Deep tendon reflexes may be diminished in a length-dependent pattern, with unobtainable ankle reflexes. Diffuse

Table 1 Symptoms and Signs of Neuropathy

	Symptoms	Signs on Examination
Motor	Weakness	Weakness
		Atrophy
		Fasciculations
		Areflexia
Large-Fiber Sensory	Numbness	Loss of vibratory sensation and/or proprioception
	Imbalance, falls	Pseudoathetosis
	Ataxia	Sensory ataxia
	Paresthesias	Areflexia
Small-Fiber Sensory	Numbness	Loss of pain and/or temperature sensation
	Pain	
Autonomic	Postural dizziness	Orthostatic hypotension
	Dry mouth, dry eyes, dry skin	Skin changes
	Early satiety	Loss of hair
	Coldness or flushing	Hyperemia or cold, pale feet
	Impotence	
	Bladder dysfunction	

Table 2 Etiologic Clues in Peripheral Neuropathy

Differential for Autonomic Neuropathy	Differential for Acute Neuropathy
Diabetes mellitus	Guillain-Barré syndrome
Amyloidosis	Vasculitis
Autoimmune autonomic neuropathy	Critical illness polyneuropathy
Paraneoplastic neuropathy	Porphyria
Vitamin B12 deficiency	Toxic exposure
HIV	
Sjogren's syndrome	
Prior chemotherapy	
Heavy metal toxicity	
Hereditary neuropathies	
Differential for Mononeuropathy Multiplex	**Differential for Motor-Predominant Neuropathy**
Vasculitis	CIDP
Amyloidosis	Multifocal motor neuropathy
Diabetes mellitus	Hereditary neuropathy (CMT)
Multifocal acquired demyelinating sensory and motor neuropathy	Paraneoplastic neuropathy
	Lead toxicity
	Porphyria
Multifocal motor neuropathy	Diphtheria
Hepatitis B and C	
Lyme disease	
Leprosy	
Compressive/traumatic neuropathies	
Hereditary neuropathy with liability to pressure palsies	

CIDP = chronic inflammatory demyelinating polyneuropathy; CMT = Charcot-Marie-Tooth disease; HIV = human immunodeficiency virus.

areflexia should prompt investigation for chronic inflammatory demyelinating polyneuropathy or hereditary neuropathy. Asymmetric reflexes, for example, if only 1 ankle reflex is absent, may suggest a superimposed mononeuropathy or radiculopathy. Accentuated deep tendon reflexes suggest superimposed central nervous system involvement, such as cervical spinal stenosis or vitamin B12 deficiency.

History alone may be insufficient to exclude a neuropathy in high-risk patients, such as those with diabetes. Many patients have only mild negative symptoms that go unnoticed but still put them at risk for injuries or foot ulcers.[5] The American Diabetes Association recommends that patients with diabetes be screened for signs of neuropathy annually.[6] The highest-yield bedside screening tests for large-fiber sensory dysfunction are use of a 10-g Semmes-Weinstein monofilament or testing vibratory sensation with a 128-Hz tuning fork.[7] The combination of both tests is approximately 90% sensitive and 85% to 89% specific for peripheral neuropathy in diabetic patients.[5] Testing of pinprick sensation should also be considered, because such patients with isolated small fiber neuropathy will not be identified if only monofilament and vibratory sensation testing are carried out.

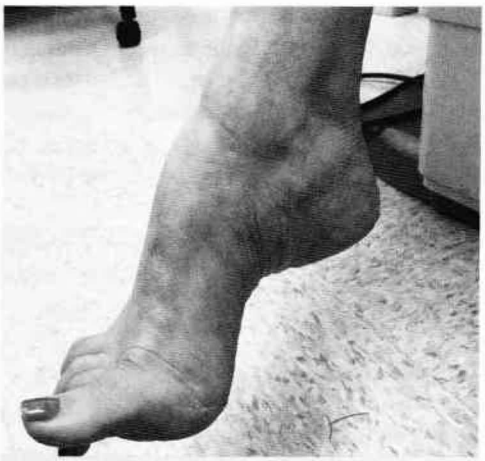

Figure Common lower-extremity findings in patients with hereditary neuropathy. High-arched feet (pes cavus), hammertoes, and atrophy of the distal calf—all evident in this patient with neuropathy—are common in patients with Charcot-Marie-Tooth disease. Hereditary neuropathy is an important, common, and underrecognized consideration in patients presenting with distal symmetric polyneuropathy. Patients present with disproportionately more weakness and atrophy relative to the degree of sensory involvement. Charcot-Marie-Tooth disease is the most common form of hereditary neuropathy.

DIAGNOSING NEUROPATHY

When the history and examination reveal symmetric, length-dependent signs and symptoms suggesting distal symmetric polyneuropathy, the differential diagnosis includes lumbosacral radiculopathy or myelopathy (process affecting the spinal cord). Low back pain, pain radiating into the legs, or bladder or bowel dysfunction may suggest radiculopathy. Hyperreflexia, spasticity, or sensory deficits in the trunk occur in myelopathy. In general, asymmetric or nonlength-dependent findings should prompt consideration of a process other than distal symmetric polyneuropathy.

Symptoms alone (eg, burning feet) have poor diagnostic accuracy for neuropathy.[8] Neurologic examination findings such as distal sensory loss or absent ankle jerks are more sensitive and specific. In one cohort, the presence of 2 of 3 of suggestive symptoms, abnormal temperature sensation, or diminished ankle reflexes was 87% sensitive and 91% specific for neuropathy.[9] Neuroimaging is not routinely indicated in patients with neuropathy, but should be considered when the neurologic examination suggests a concurrent myelopathy or when the diagnosis of neuropathy is not firmly established and lumbosacral radiculopathy remains in the differential diagnosis.

The most reliable diagnosis of neuropathy rests on the combination of symptoms, the neurologic examination, and the confirmatory findings on nerve conduction studies and electromyography.[8] It is debatable whether all patients with suspected neuropathy require electrodiagnostic evaluation. This

Table 3 Symptoms and Examination Findings that Should Prompt Electrodiagnostic Studies or Neurologic Consultation

Acute onset
Asymmetry
Nonlength-dependent weakness and/or sensory loss
Diffuse areflexia
Pure or predominant motor symptoms
Pure or predominant autonomic symptoms
Mononeuropathy multiplex

does not occur in current clinical practice. A study using a database of Medicare patients demonstrated that only 20% underwent electrodiagnostic evaluation within 6 months of their initial diagnosis of neuropathy.[10] If multiple symptoms and examination findings suggest distal symmetric polyneuropathy, electrodiagnostic evaluation may be low yield. In a sample of patients aged more than 65 years with a high prevalence of diabetes, for example, electrodiagnostic evaluation led to a change in diagnosis or management in <1% of patients.[11] By contrast, in samples of patients referred to academic medical centers for evaluation of neuropathy, electrodiagnostic evaluation led to a change in diagnosis in 24% to 43% of patients.[12,13] There are certain features in the history or physical examination; however, that should always prompt further neurologic consultation and possible electrodiagnostic evaluation (**Table 3**). Of note, patients with primarily small-fiber neuropathy will have normal findings on electrodiagnostic evaluation, because it evaluates motor and large sensory fiber function. Skin biopsy with measurement of the intraepidermal nerve fiber density has become the de facto gold standard for diagnosis of small-fiber neuropathy, with an estimated specificity of 95% to 97%, and can be performed in the office.[14]

FINDING A CAUSE

Once a diagnosis of neuropathy is made, focus should shift toward finding the underlying etiology. The type of neuropathy identified should guide the diagnostic workup, because the highest yield tests will vary. In cases of distal symmetric polyneuropathy, the search for a cause can be particularly daunting given the plethora of known causes (**Table 4**). Sending off an extensive, indiscriminate panel of tests is unnecessary and can be counterproductive. An organized approach can be applied to minimize unnecessary testing and efficiently reach a diagnosis (**Table 5**).

Review of the medical history, medications, and occupational exposures may reveal the cause of neuropathy in a substantial proportion of patients.[11] Screening patients for alcohol abuse is essential given the common association between long-standing alcohol overuse and neuropathy. A careful family history is also crucial, because many patients with Charcot-Marie-Tooth disease are not aware of affected family members' symptoms or have never connected them with their own symptoms. Specifically asking about family members with high arches, unexplained gait trouble,

Table 4 Common Causes of Distal Symmetric Polyneuropathy

Autoimmune	**Toxic**
Connective tissue disease	Ethanol
Vasculitis	Heavy metals
Inflammatory bowel disease	Organic solvents
Sarcoidosis	**Medications**
Celiac disease	Chemotherapy
Cancer Associated	Ado-trastuzumab emtansine
Paraprotein-Associated	Brentuximab vedotin
MGUS	Eribulin
Multiple myeloma	Etoposide
Waldenstrom's macroglobulinemia	Ifosfamide
Lymphoma	Platinums
Primary amyloidosis	Proteasome-inhibitors (eg, bortezomib)
Paraneoplastic	Taxanes
Endocrine/Metabolic	Thalidomide, lenalidomide, pomalidomide
Diabetes mellitus	Vincristine
Prediabetes	Amiodarone
Hypothyroidism/hyperthyroidism	Chloroquine
Chronic renal failure	Colchicine
Liver disease	Disulfiram
Infectious	Ethambutol
HIV	Hydralazine
HTLV-1	Isoniazid
Leprosy	Leflunomide
Inherited	Metronidazole
Charcot-Marie-Tooth disease	Nitrofurantoin
Familial amyloidosis	Nucleoside reverse transcriptase inhibitors
Nutritional	Phenytoin
Vitamin B12 deficiency	
Vitamin B1 deficiency	
Vitamin B6 deficiency or toxicity	
Vitamin E deficiency	
Copper deficiency	
Postgastric bypass	

HIV = human immunodeficiency virus; HTLV-1 = human T-cell leukemia virus type 1; MGUS = monoclonal gammopathy of unknown significance.

Table 5 Suggested Initial Etiologic Workup of Distal Symmetric Polyneuropathy

Detailed review of medical and family history, current and prior medications
Hemoglobin A1c and/or oral glucose tolerance test
Vitamin B12
Methylmalonic acid
SPEP with immunofixation
TSH
Comprehensive metabolic panel
Complete blood count

SPEP = serum protein electrophoresis; TSH = thyroid-stimulating hormone.

orunexplained pain may reveal previously unrecognized affected family members.

The American Academy of Neurology published guidelines in 2009 identifying blood glucose, vitamin B12 and metabolites (methylmalonic acid and homocysteine), and serum protein electrophoresis with immunofixation as the highest yield laboratory tests for evaluation of distal symmetric polyneuropathy.[2] A comprehensive metabolic panel and complete blood count are also commonly sent as part of the initial laboratory evaluation.[15,16] Many authors advocate for routine testing of thyroid-stimulating hormone in patients with distal symmetric polyneuropathy because it is a readily treatable cause.[16-18] A similar standardized workup was applied to a cohort of 138 patients with distal symmetric polyneuropathy in the primary care setting.[17] Serum protein electrophoresis with immunofixation, B12, thyroid-stimulating hormone, and an oral glucose tolerance test were tested in all patients; methylmalonic acid was also tested in patients with B12 levels between 200 and 300 pg/mL. Select patients had Sjogren related (Anti-Ro/SS-A and Anti-La/SS-B) antibodies and vitamin B6 tested. An etiology was found in 69% of these patients. Despite such evidence, there remains poor adherence to screening recommendations. Callaghan et al[15] found that hemoglobin A1c was tested in <20% of patients with neuropathy, vitamin B12 was tested in 41% of patients, and serum protein electrophoresis was tested in 19% of patients.

These tests correspond to the most commonly identified causes of distal symmetric polyneuropathy. Diabetes is the most common cause of neuropathy, and specifically distal symmetric polyneuropathy. Testing patients with unexplained distal symmetric polyneuropathy reveals abnormalities in blood glucose in approximately 11% of patients.[2] Epidemiologic studies have suggested that patients with prediabetes and specifically impaired glucose tolerance may also have increased prevalence of neuropathy.[9] The American Diabetes Association uses a hemoglobin A1c of 5.7% to 6.4% to define prediabetes and blood glucose of 140 to 199 mg/dL on 2-hour 75 g oral glucose tolerance testing to define impaired glucose tolerance.[19]

Approximately 10% of patients with chronic sensorimotor neuropathy have an associated serum paraprotein.[20] Testing immunofixation is recommended in addition to serum protein electrophoresis, because it is more sensitive.[2] Two thirds of neuropathy cases are associated with a monoclonal gammopathy of unknown significance, but neuropathy can also be seen in patients with multiple myeloma, Waldenstrom macroglobulinemia, amyloidosis, and other hematologic malignancies.[20] Patients with monoclonal gammopathy of unknown significance have a 1% annual risk of developing hematologic malignancy, and patients with concurrent neuropathy are at slightly higher risk, so these patients are best co-managed with a hematologist or oncologist.[21]

Vitamin B12 deficiency can be found in approximately 2.2% to 8% of patients with distal symmetric polyneuropathy.[2] Testing metabolites that become elevated when B12 is deficient—methylmalonic acid and homocysteine—increases sensitivity. Methylmalonic acid is more sensitive and specific than homocysteine; in one study, testing methylmalonic acid together with B12 increased diagnostic yield from 2% to 8%.[17] If not tested routinely, methylmalonic acid should be considered when B12 levels are borderline (200-500 pg/mL).

If the diagnosis remains uncertain after initial workup, additional testing can be considered tailored to the clinical situation. Many clinicians routinely test markers of inflammation and rheumatologic disease. In a cohort of patients with multiple types of idiopathic neuropathy, however, rheumatologic testing only led to a change in management in patients with known rheumatologic disease, symptoms suggestive of a rheumatologic disorder, or an atypical feature such as an acute or asymmetric presentation.[22] One exception may be celiac disease, in which neuropathy may precede or be the sole manifestation of the disease.[23]

Even after a complete laboratory workup, a specific cause will not be found in 18% to 26% of patients with distal symmetric polyneuropathy.[2] More invasive testing is rarely indicated. Cerebrospinal fluid analysis offers low diagnostic yield except in cases of demyelinating polyneuropathy.[2] Nerve biopsy should not be pursued simply because the cause of neuropathy remains uncertain. Although it is a minor procedure, permanent sensory loss in the distribution of the biopsied nerve is common and other adverse effects do occur. In one cohort of 67 patients who underwent sural nerve biopsy, 29.8% had chronic pain in the sural nerve distribution and 46.8% had persistent dysesthesia.[24]

MANAGEMENT

Even when a specific etiology is found and specific treatment can be offered, the progression of neuropathy may stabilize and symptoms may improve, but patients are usually left with some chronic residual symptoms. Supportive care and symptomatic management are paramount. Patients with sensory loss in the feet should be educated about routine foot care and surveillance for wounds and injuries. Patients with weakness may benefit from orthotic devices, most commonly ankle-foot orthotics. When gait and balance are affected, balance training and exercises to increase the strength of knee extension and ankle dorsiflexion may reduce the risk of falls.[25]

Patients with neuropathic pain may require symptomatic treatment. The first consideration is ensuring that the patient's symptoms are due to neuropathic pain, because discomfort can result from other causes, including joint deformities, foot ulcerations, and restless leg syndrome. Negative symptoms, such as numbness and coldness, do not respond to medications used to treat neuropathic pain.

There is a consensus that the anticonvulsants gabapentin and pregabalin, tricyclic antidepressants, and serotonin-norepinephrine reuptake inhibitors should be considered first-line for the treatment of neuropathic pain in patients with neuropathy (Table 6).[26,27] A meta-analysis examining the treatment of neuropathic pain in both central and peripheral nervous system disorders calculated the number needed to treat to achieve 50% reduction in pain in 1 patient: 3.6 for tricyclic antidepressants (most studies were of amitriptyline), 6.4 for

Table 6 Pharmacologic Agents for the Management of Neuropathic Pain in Patients with Neuropathy

Name	Instructions for Starting	Goal Dose	Maximum Dose	Good for Patients with:	Consider Alternatives if:	Common Side Effects
Gabapentin	100 mg TID or 300 mg at bedtime	300 mg TID	3600 mg/d	Seizure disorder	Renal insufficiency	Dizziness, sedation, gait disturbance, confusion, peripheral edema
Pregabalin	75 mg BID	150 mg BID	600 mg/d	Seizure disorder	Renal insufficiency	Dizziness, sedation, gait disturbance, confusion, peripheral edema
Amitriptyline/ Nortriptyline	10-25 mg at bedtime	50-100 mg at bedtime	150 mg/d	Insomnia Migraine	Cardiac disease, arrhythmia, other serotonergic medications	Dry mouth (more common with amitriptyline), sedation, dizziness, confusion, QT-prolongation, orthostatic hypotension
Duloxetine	30 mg/d	60 mg/d (daily or split BID)	120 mg/d	Depression, anxiety, fibromyalgia	Hepatic failure, other serotonergic medications, anticoagulants	Nausea, dyspepsia, constipation, sedation, dry mouth, dizziness, hyperhidrosis, sexual dysfunction
Venlafaxine	37.5 mg/d (XR)	150 mg/d (XR)	225 mg/d	Depression, anxiety	Uncontrolled hypertension, other serotonergic medications	Nausea, dyspepsia, sedation, dizziness, nervousness, insomnia, hypertension, sexual dysfunction

BID = 2 times per day; TID = 3 times per day; XR = extended release.

serotonin-norepinephrine reuptake inhibitors (duloxetine and venlafaxine), 7.2 for gabapentin, and 7.7 for pregabalin.[28]

Given the paucity of head-to-head trials, Griebeler et al[29] performed a comparative effectiveness network meta-analysis for painful diabetic neuropathy in 2014; Waldfogel et al[30] updated the analysis with recent trials in 2017. For each trial included, a standardized mean difference reflecting the effectiveness of each medication was calculated, allowing for comparisons between agents. The analysis concluded that pregabalin, tricyclic antidepressants, and serotonin-norepinephrine reuptake inhibitors were effective when compared with placebo. In contrast to the studies cited, the analysis concluded that gabapentin was not more effective than placebo. On the basis of calculated standardized mean differences, serotonin-norepinephrine reuptake inhibitors were found to be significantly more effective than pregabalin. There was no significant difference in effectiveness found between tricyclic antidepressants and either pregabalin or serotonin-norepinephrine reuptake inhibitors.

Hoffman et al[31] recently examined the use of opiates in the treatment of neuropathy. Patients with neuropathy receiving opioids were more likely to use gait-assist devices and had worse functional status. Opiate use did not improve functional status, but rather was associated with higher rates of depression, opiate dependence, and opiate overdose. Waldfogel et al's[30] network analysis also concluded that typical opiates were not effective for treating painful diabetic neuropathy. Atypical opiates—tramadol and tapentadol—have evidence supporting their use and are better alternatives to consider should first-line therapies fail.[26,27,30] If pain is localized, topical agents are appealing second-line agents because of their lack of significant drug interactions and low rates of systemic adverse effects. Options include capsaicin cream or patches, lidocaine patches, percutaneous electrical nerve stimulation, and botulinum toxin.[26,27,30]

An initial first-line agent may be chosen from the 3 classes listed on the basis of the patient's comorbidities, drug interactions, and cost. Unless there are prohibitive side effects, it is essential to increase to a therapeutic dose before concluding a medication trial has failed. In clinical trials, greater than 9% of patients stopped taking each of the suggested first-line medications because of perceived adverse effects.[30] If a medication is ineffective or not tolerated, trialing a medication from another class is appropriate. Combination therapy may be more effective than monotherapy, so this can be considered before trying second-line agents.[26,28]

CONCLUSIONS

Although the presentations of peripheral neuropathy are diverse, a standardized approach to taking a history and the neurologic examination allow the clinician to easily recognize many forms of neuropathy. Applying a standardized approach to the workup of neuropathy allows for the efficient recognition of the etiology in most patients with minimal testing. Offering supportive care to limit disability, prevent foot ulcers and falls, and ameliorate neuropathic pain is an essential task for the primary care clinician.

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