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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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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	