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Diabetic peripheral neuropathy: Person-centered care

BY JOYCE K. ANASTASI, PhD, DRNP, FAAN, AND CHLOE KLUG, BSN, RN

Abstract: Patients with diabetes mellitus may experience painful and nonpainful diabetic peripheral neuropathy (DPN). This article offers an overview of DPN and the clinical assessment and management of patients with DPN, as well as the nurse's role in supporting these patients.

Keywords: diabetes mellitus, diabetic neuropathy, diabetic peripheral neuropathy, DM, DPN, T1DM, T2DM, type 1 diabetes mellitus, type 2 diabetes mellitus

DIABETES MELLITUS (DM) has become a global burden, with 415 million adults living with DM as of 2015 and an estimated 55% increase to 642 million by 2040.¹ Under half of those with DM remain undiagnosed.² Patients with undiagnosed or untreated DM are at an increased risk for complications compared with those receiving treatment.² These complications include cardiovascular disease, nephropathy, retinopathy, Alzheimer disease, depression, and neuropathy.^{3,4}

Diabetic peripheral neuropathy (DPN), also called distal symmetric polyneuropathy, refers to signs and symptoms of peripheral nerve dysfunction in individuals with diabetes.⁵ It is the most common neurologic complication of diabetes, affecting the lower extremities and, occasionally, the upper extremities.^{6,7} DPN is a serious complication of both type 1 (T1DM) and type 2 diabetes mellitus (T2DM).⁸ If patients with DM are not treated

and develop DPN, it can lead to loss of protective sensation (LOPS), falls, foot ulcerations, chronic infections, and amputations.^{8,9} Patients with reduced sensation in their feet may not realize they have developed tissue damage or infections. If not addressed, these issues may lead to amputation.⁹

Advances in the treatment of T2DM have led to longer lives, but the cost of healthcare increases due to the associated complications of uncontrolled T2DM, such as DPN.² Patients with DPN may experience a twofold increase in healthcare costs, and those with severe, painful DPN may experience a fourfold increase. As of 2012, the annual healthcare costs related to diabetes in the US totaled \$245 billion, and approximately 27% of these costs could be attributed to DPN.¹⁰ According to the most recent statistics, the annual costs related to diabetes care have reached \$327 billion.¹¹

Normal anatomy and physiology

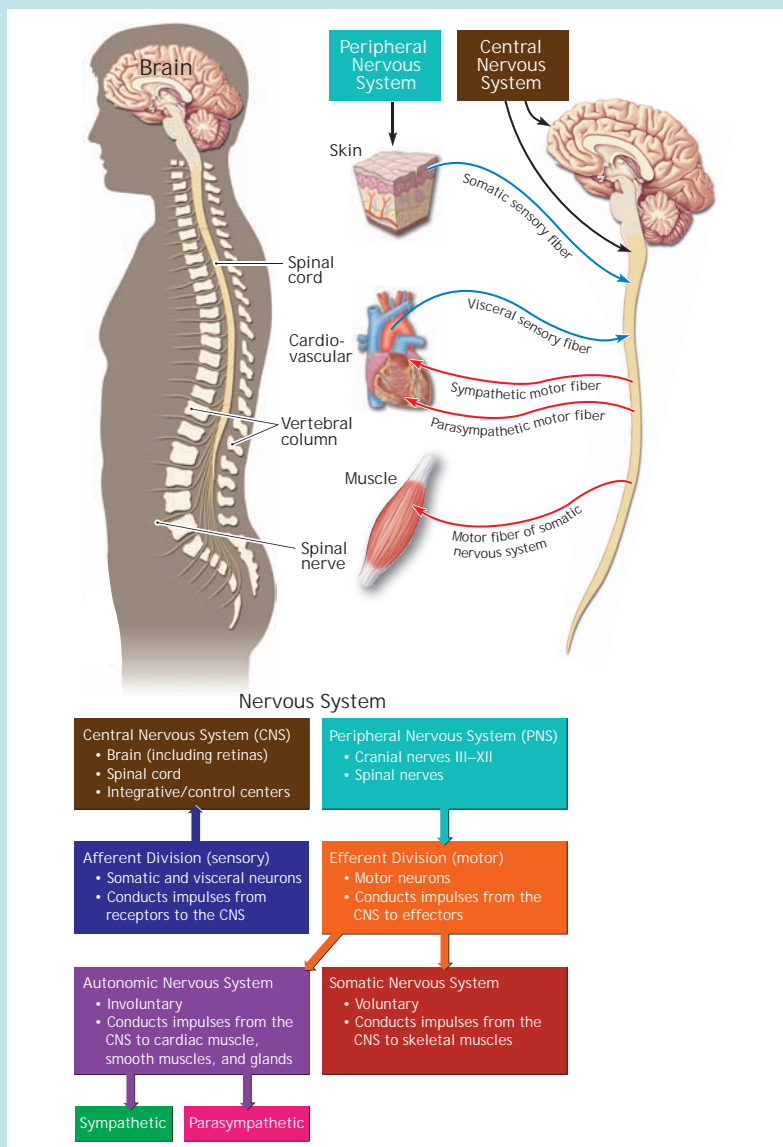
Anatomically, the nervous system can be divided into two basic components: the central and peripheral nervous systems. The central ner-

vous system (CNS) consists of the brain and spinal cord and is protected by the skull and vertebral column. The peripheral nervous system (PNS) includes the neurons outside the CNS (cranial nerves and

their ganglia, spinal nerves and their ganglia), which connect the brain and spinal cord with peripheral structures. The PNS relays somatic and visceral sensory (afferent) input to the CNS for processing and transmitting efferent or motor output from the CNS to effector organs throughout the body. (See *How the CNS and PNS compare*.)

How the CNS and PNS compare

The two divisions of the human nervous system are the CNS, which contains the brain (including the retinas), spinal cord, and integrating and control centers, and the PNS, which is made up of the cranial nerves and spinal nerves. The PNS further subdivides into the efferent (motor) division and afferent (sensory) division, which consists of the somatic nervous system and autonomic nervous system (sympathetic and parasympathetic divisions).



Source: McArdle WD, Katch FI, Katch VL. *Exercise Physiology: Nutrition, Energy, and Human Performance*. 9th ed. Baltimore, MD: Wolters Kluwer; to be published in 2022.

Pathophysiology

DPN is not well understood and there are multiple schools of thought regarding the exact cause, but it is largely considered to be a multifactorial process characterized by distal neuropathy in the longest sensory axons.^{12,13} It is also associated with metabolic and vascular abnormalities, such as dyslipidemia and hyperglycemia, and can cause small or large nerve fiber loss.^{10,14,15} DPN is associated with comorbidities that increase patient morbidity and mortality, including autonomic neuropathy, peripheral artery disease, cardiovascular disease, nephropathy, retinopathy, and medial artery calcification (MAC).⁸ MAC, or Mönckeberg's arteriosclerosis, refers to stiffening of the arterial wall due to aging and diabetes.¹⁶

When associated with T1DM and T2DM, these abnormalities can cause DNA damage, endoplasmic reticulum stress, mitochondrial dysfunction, cellular injury, and irreversible damage to nerve cells.⁸ The degree of nerve damage depends on patients' age, BP, weight, and the duration of their diabetes diagnosis.⁴ Patients with T1DM have an increased prevalence of DPN compared with those with T2DM, which implicates insulin deficiency and hyperglycemia as key factors in DPN.¹⁷ DPN can also occur in patients with prediabetes, which suggests that neuropathy secondary to diabetes correlates with the progression of hyperglycemia.¹⁸

Clinical manifestations

Fifty percent to 75% of patients with DM have symptoms of DPN, and 20% to 30% will experience neuropathic pain.^{1,8,10} Signs and symptoms of DPN depend on many factors, such as total hyperglycemic exposure and other risk factors such as dyslipidemia, hypertension, smoking, increased height, and high exposure to other potentially neurotoxic agents such as ethanol. Genetic factors may also play a role.¹²

There are positive and negative symptoms of DPN. Negative symptoms refer to dysfunction and nerve fiber loss, while positive symptoms refer to abnormal or reduced functions in the remaining nerve fibers, such as tingling and pain.¹⁹ The sensory nerves may be damaged in patients with DPN, and the signs and symptoms may differ depending on the sensory fibers involved.¹⁸

Signs and symptoms depend on the involvement of small and/or large sensory nerve fibers, with small fiber damage typically causing early symptoms of pain and dysesthesias.⁸ Between 15% and 20% of patients experience painful symptoms, and up to 25% may experience burning or stabbing pain.^{8,20,21} These patients may be at risk for foot ulcers and amputations. DPN affects the longest fibers and symptoms appear distally and symmetrically in the toes and feet, gradually spreading up the legs and in the hands. It results in paresthesias, LOPS, and poor balance.^{8,19,20,21}

Neuropathic pain may be the first symptom that requires a healthcare visit.⁸ Although pain may prompt a patient visit, healthcare professionals should be aware of the various DPN symptoms. As such, pain should not be the only factor prompting assessment or intervention.^{8,22}

Screening and diagnosis

The American Diabetes Association (ADA) recommends early diagnosis



Healthcare professionals should be aware of the signs and symptoms of DPN, and pain should not be the only factor prompting assessment or intervention.

and clinical management of patients with DPN. Diagnostic screening is crucial to early interventions.^{8,23} However, there is not currently a gold standard for DPN screening. As such, DPN symptoms are typically addressed through various patient-reported outcome measures for discomfort, sleep disturbance, and quality of life, few of which capture its complex symptomology.²⁴ The ADA recommends assessing patients who have had T1DM for 5 years or longer and all patients with T2DM for DPN annually. Similar assessments for patients with prediabetes are also recommended.⁸ In the authors' experience, however, it may be beneficial to assess all patients with DM for early warning signs

and symptoms of DPN during their annual visit. Similar assessments for patients with prediabetes are also recommended.⁸

After other possible causes have been excluded, DPN is diagnosed based on clinical criteria and patient history in patients with diabetes who present with peripheral nerve dysfunction.^{10,25} Referral to a neurologist may be required if the diagnosis is unclear or the patient presents with atypical signs and symptoms.²⁰ Clinical assessments should start distally bilaterally and move proximally. Clinical tools such as vibration perception, proprioception, monofilament, and ankle reflexes may indicate large fiber function, while pinprick and temperature sensation tests may be used to assess small fiber function.⁸ Pinprick tests assess a patient's ability to feel the pinprick and feel sharpness and dullness in a specific area.²⁶ Temperature sensation tests are neurologic exams to determine a patient's ability to sense heat and cold in a specific area.²⁷

The Semmes-Weinstein monofilament examination (SWME) is a standard assessment tool for DPN. Other diagnostic tools include the Michigan Neuropathy Screening Instrument (MNSI), which involves a 15-item questionnaire and foot exam; tuning fork tests, which assess vibration and temperature; neuromotor exams to evaluate muscle function; the

DPN medications^{33,35}

AEDs

- pregabalin
- gabapentin

SNRIs

- duloxetine
- venlafaxine

TCAs

- amitriptyline
- desipramine
- nortriptyline

Diabetic Neuropathy Symptom score, which assesses pain, ataxia, and numbness or tingling sensations; and the Diabetic Neuropathy Examination score, an 8-item assessment for polyneuropathy.^{19,26-31} The SWME is useful in predicting neuropathy.³²

Early diagnosis helps patients manage their disease and fosters early intervention. To better understand patient pain, nurses can conduct a comprehensive pain assessment and encourage patients to describe and report DPN-associated pain.

Pharmacotherapy

The following drug classes may help manage pain associated with DPN: antiepileptic drugs (AEDs), serotonin–norepinephrine reuptake inhibitors (SNRIs), and tricyclic antidepressants (TCAs) (see *DPN medications*).^{8,33} According to an ADA position statement on DPN, FDA-approved medications include pregabalin and duloxetine. Pregabalin and duloxetine may be considered first-line treatments for pain related to DPN. Atypical opioids such as transdermal buprenorphine, tapentadol, and tramadol are not recommended as either first- or second-line therapies despite different risks and mechanisms of action to other opioids.^{8,34} Additionally, topical medications include isosorbide dinitrate spray, lidocaine, and capsaicin cream.³⁵ Combination therapies may also provide effective treatment for DNP at lower doses.⁸

Tricyclic antidepressants such as amitriptyline, duloxetine, and nortriptyline can be used off-label and with caution due to an increased risk for adverse reactions.^{8,36} Non-steroidal anti-inflammatory drugs may be used as short-term therapies.³⁶ Gabapentin, desipramine, and venlafaxine are not approved by the FDA to manage pain associated with DPN, but they have also been prescribed off-label.^{8,18}



Adverse reactions to medications can be a key determining factor for patients who halt treatment or seek alternatives.

Adverse reactions can be a key determining factor for patients who halt treatment or seek alternatives. For example, common adverse reactions to SNRIs and AEDs include dizziness, nausea, and somnolence, while TCAs may cause xerostomia, somnolence, and insomnia.¹⁸ Due to the lack of treatments that target underlying nerve damage, prevention is the key component of patient care that may halt the progression of DPN-associated complications.⁸

The evidence supporting the effectiveness of many drugs is limited, making it difficult to determine which specific treatment will work for a specific patient. Healthcare professionals should be aware of medications and drug classes for treating DPN, but patient experience ultimately dictates their

effectiveness. Adverse reactions and the healthcare cost associated with DPN symptom management may contribute to negative patient outcomes and nonadherence to treatments. Nurses can promote adherence by educating patients and family members on the possible adverse reactions to DPN medications and how to manage them.

Nursing considerations

DPN causes significant morbidity, impairs quality of life, and increases risk of mortality. Limited options are available to treat it, so the focus of patient care is on prevention.³⁷ Nurses should screen patients for sensory deficits, help patients manage risk factors, and teach patients proper foot and skin care.^{20,38}

Without treatment, DPN can lead to ulcerations, falls, fractures, and amputations.⁸ For example, LOPS may prevent a patient from being aware of a foot injury, leading to foot ulceration, poor wound healing especially in the presence of peripheral artery disease, and potentially a lower extremity amputation. Nurses can educate and encourage patients to perform daily foot exams to identify and report foot injuries, ulcerations, and poor wound healing.^{3,8}

Functional impairments related to DPN can contribute to decreased quality of life. Depression affects up to 27% of individuals with DM and has a bidirectional relationship: depression increases the risk of T2DM, and its prevalence is doubled in individuals with T1DM and T2DM.³⁹ It may also affect treatment adherence and increase financial costs and the risk for complications, further affecting quality of life.⁴⁰

Although depression has been noted in patients with DPN, it is more prevalent in those with painful DPN than those without pain.^{39,41} It can affect patient outcomes and

adherence.^{4,39,41} Patients may be limited in their ability to manage and cope with neuropathy and require education based on their individual needs. Nurses should conduct screening and interventions, inform providers of any signs and symptoms or adverse reactions related to DPN medications, provide patient education on self-care, and encourage patients to discuss treatments that are not meeting their needs or expectations with health-care professionals.

Patient education is key to managing DPN. Modifiable risk factors include hyperglycemia, hypertension, hypertriglyceridemia, hypercholesterolemia, obesity, and smoking. Nurses can teach patients about risk factor modification, including glycemic control and lifestyle changes. A consultation with a registered dietitian regarding the specific dietary needs for a healthy food plan may be recommended.

Fall prevention is also important, as patients with DPN may experience loss of balance.⁸ Similarly, proper foot care and footwear is crucial. This includes daily foot inspections; keeping skin clean and hydrated; drying feet well and avoiding soaking; trimming toenails; and wearing proper footwear such as cotton or wool socks with appropriately sized shoes. Consultation with a podiatrist is essential to the management of patients with DPN.^{8,42}

Neuropathic pain can interfere with activities of daily living and lead to disability, psychosocial impairment, and diminished quality of life. Healthcare professionals can aid patients in the management of DPN by helping them identify effective treatments.

Consider what you say

Many individuals experience stigma associated with DM and may be less likely to seek care, which is essential

for nurses and healthcare providers in recognizing DPN. Avoid language with negative connotations, such as “uncontrolled” and “noncompliant,” and refrain from characterizing patients with DM as “diabetics.” Instead, use proactive, empowering language to motivate and encourage these patients. Supportive and proactive language focuses on “what is working” rather than language that denotes “what is wrong,” which may increase patient worries, concerns, and fears.^{43,44} For example, healthcare professionals can say, “You’ve made great progress with your weight loss.” ■

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At New York University in New York, N.Y., Joyce K. Anastasi is an Independence Foundation endowed professor and founding director and Chloe Klug is a former research assistant.

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