Diabetic peripheral neuropathy (DPN) is very common among patients with type 2 diabetes and a pivotal component of foot disease, therefore it is vital that physicians pay close attention to screening. The objectives of screening include identifying the risk of ulceration in order to avoid amputation, identifying early nerve injury, and evaluating areas for clinical research.

The International Neuropathy Guidelines define DPN as the presence of symptoms and/or signs of peripheral nerve dysfunction in people with diabetes after exclusion of other causes. Neuropathy can present with a loss of protective sensation, defined as a level of sensory loss sufficient for a patient to injure himself or herself without recognizing the injury.

**SCREENING INSTRUMENTS**

Most screening instruments for DPN are noninvasive, inexpensive, sensitive-specific and highly predictive of clinical endpoints. To evaluate a patient for neuropathy, clinicians need to ask patients about signs and symptoms, perform a thorough physical exam, including deep tendon reflexes, motor strength and vibration; as well as perform diagnostic studies such as nerve conduction velocities (NCV).

A single instrument may not be sufficient for sensory testing. Clinicians should use a history-symptom questionnaire, a physical exam, Semmes-Weinstein monofilaments (SWM), vibration perception threshold (VPT) evaluation and NCV.

Establishing a true sensitivity and specificity for VPT, SWM and nerve conduction is difficult because there is no true gold standard among these instruments. Several studies have reported a strong correlation between VPT, NCV results and subjective symptoms of neuropathy.

Several questionnaires are helpful in screening patients for DPN. These are the Michigan Neuropathy Screening Instrument (Table 1), Neuropathy Symptom Profile, Neuropathy Symptom Score, Diabetic Neuropathy Symptom Score (Table 2), and the UT Abbreviated Neuropathy Questionnaire.

The Diabetic Neuropathy Symptom Score has been evaluated in 73 diabetic studies, comparing it with clinical testing with SWM and VPT. It was found to have a reliability of 0.64, a sensitivity of 79% and a specificity of 78%.

A physical exam of the patient should include close inspection, with shoes and socks removed. The physician should perform deep tendon reflexes, vibration with a 128-Hz tuning fork; sharp, dull and light touch; and motor strength.

The North West Diabetes Foot Care Study predicted neuropathic foot ulcer risk in 9,710 diabetic patients followed for 2 years. It was a population-based study in the North West United Kingdom, carried out in six health care districts. To determine a neuropathic disability score (NDS), three sensory modalities were used: vibration with a 128-Hz tuning fork, pinprick with a
Neurotip device, and hot-cold rods. A score of 0 was normal and 1 was abnormal. The ankle reflex was scored 0 for normal, 1 for reinforcement and 2 for absent. The maximum total of 5 for each foot led to a potential maximum score of 10 (lower being less severely affected).

In this study, 291 ulcers developed. The researchers found that NDS was the best baseline predictor. A score of <6 translated to a 1.1% annual ulcer incidence and a score of >6 translated to a 6.3% annual ulcer incidence.

**MONOFILAMENT TESTING**

The SWM for sensory testing was popularized for the insensate foot from research and education courses taught at the Hansen Disease Center in Carville, La. (Figure 1). The monofilaments produce a characteristic force perpendicular to the contacting surface. The force of downward contact increases linearly until the monofilament buckles. The three digit numbers of the SWM are the common log of the characteristic force in grams plus the constant force. The set of forces range from 4.5 mg to 447 g and is nearly log-linear (Table 3).

While the SWM is accurate and durable, there are various recommendations for interpreting the data and inconsistent testing methods associated with it. There are also different sites of testing on the foot (Figure 2). Other variables affect the reproducibility and accuracy of SWM, such as the physical properties of the unit, is it calibrated or uncalibrated, the unit’s condition, as well as material wear and failure.

Studies have sought to determine whether SWM testing is accurate and reliable. Researchers have found that there is wide variability in the load characteristics at baseline and with continued loading. The reproducibility of testing decreased with repetitive loading, and recovery after 24 hours improved the test’s accuracy.

Studies have also evaluated the service life of a SWM. In a review of the New Touch-Test Sensory Monofilament (North Coast Medical), researchers found that the initial average force generated was 9.8 ±0.3 g (9.2 to 10.2 g). After 500 loading cycles, there was about a 1.3-g decrease to 8.6 ±0.3 g (8.1 to 9.0 g). They found that a 24-hour recovery period improved accuracy to 9.6 g (9.1 to 10.0 g).

Another study compared four commercially available 10-g SWM units. The investigators identified a large variation in loading forces and found that 20% to 100% demonstrated buckling ±1.0 g (9.0 to 10.0 g). Furthermore, repeated use of the devices throughout the day led to a far lower buckling force, thus leading the clinician to overdiagnose the loss of protective sensation.

Monofilaments can fail for several reasons: they can become damaged, old and uncalibrated. This contributes to lower loading forces and an overdiagnosis of peripheral sensory neuropathy. Monofilament units should be replaced frequently and only calibrated instruments should be used. Throwaway or give-away devices are of questionable quality and durability.

**VIBRATION PERCEPTION THRESHOLD**

VPT testing is the most widely used quantitative sensory testing approach. VPT is associated with large normative and neuropathy databases. VPT evaluation fulfills the key criteria that make it desirable for longitudinal cohort evaluation: The instrument is sensitive, specific and reliable.

Among diabetics, the coefficient of variation for vibration testing is in the range of 10% to 20%. VPT testing is administered at the distal pulp of the hallux, over the bony prominence. The voltage is increased on the base unit until the patient can perceive a vibration.

A prospective study of neuropathy and foot ulceration looked at 1,035 patients in multiple centers.
Patients had no history of ulcers, VPT >25 volts and palpable pulses. Patients had standardized education regarding foot care and three monthly visits. The annual incidence of foot ulcers was 7.2%, with an increase of 5.6% per volt VPT.

An advantage of VPT testing is that the instrument is calibrated so it should not vary with use. There is no potential for material failure and it does not need to be replaced.

NCV for DPN testing is noninvasive and readily available. The technique is most sensitive for detecting early changes and has a low coefficient of variation (peroneal nerve <10%). NCV can be used prior to the development of clinical signs and symptoms and it is helpful for predicting new ulceration.

NCV is not necessarily a screening instrument and it may be costly. It also may not provide actionable data or change the course of treatment.

In summary, because neuropathy is a common complication among patients with diabetes, evaluation and management of these patients is vital. Neuropathy is a major component of foot disease.

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**Figure 2. Ten-gram SWM: How many sites should be tested? How many missed sites are required to diagnose neuropathy?**

<table>
<thead>
<tr>
<th>SWM size</th>
<th>Force (gram)</th>
</tr>
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<tbody>
<tr>
<td>4.08</td>
<td>10</td>
</tr>
<tr>
<td>4.31</td>
<td>20</td>
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<td>260</td>
</tr>
<tr>
<td>5.88</td>
<td>600</td>
</tr>
</tbody>
</table>

1 to 8 g diminished light touch
10 to 60 g loss of protective sensation