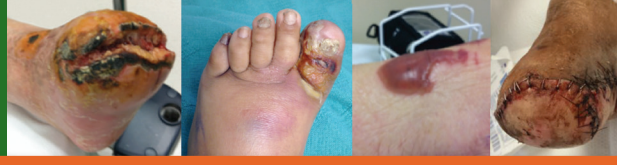

Diagnosing DPN

The authors take a closer look at the available screening tools.

BY MICHELLE BRANIGAN, BS AND STEPHANIE WU, DPM, MSC

Goals and Objectives

After completion of this article, one should be able to:

1) Identify and describe the different types of peripheral neuropathy.

2) Understand the basic pathogenesis of DPN.

3) Be familiar with the different screening tools that are available for the diagnosis of diabetic peripheral neuropathy.

Welcome to Podiatry Management's CME Instructional program. Our journal has been approved as a sponsor of Continuing Medical Education by the Council on Podiatric Medical Education.

You may enroll: 1) on a per issue basis (at $23.00 per topic) or 2) per year, for the special rate of $179 (you save $51). You may submit the answer sheet, along with the other information requested, via mail, fax, or phone. You can also take this and other exams on the Internet at www.podiatrym.com/cme.

If you correctly answer seventy (70%) of the questions correctly, you will receive a certificate attesting to your earned credits. You will also receive a record of any incorrectly answered questions. If you score less than 70%, you can retake the test at no additional cost. A list of states currently honoring CPME approved credits is listed on pg. 110. Other than those entities currently accepting CPME-approved credit, Podiatry Management cannot guarantee that these CME credits will be acceptable by any state licensing agency, hospital, managed care organization or other entity. PM will, however, use its best efforts to ensure the widest acceptance of this program possible.

This instructional CME program is designed to supplement, NOT replace, existing CME seminars. *The goal of this program is to advance the knowledge of practicing podiatrists. We will endeavor to publish high quality manuscripts by noted authors and researchers. If you have any questions or comments about this program, you can write or call us at:* ***Podiatry Management, P.O. Box 490, East Islip, NY 11730, (631) 563-1604 or e-mail us at bblock@podiatrym.com.***

*Following this article, an answer sheet and full set of instructions are provided (pg. 110).—**Editor***

Almost 26 million people, or about 8% of the population in the United States have diabetes, and diabetic peripheral neuropathy (DPN) is one of the most common and debilitating complications of this disease.[1,2] It is estimated that up to 25% of all diabetes patients have some degree of DPN, and this percentage increases to up to 50% in long duration patients.[2-6] DPN is a major clinical problem that often goes untreated and even undiagnosed.[6] Not only does DPN impose a significant negative effect on the quality of life, it is also the most common cause of non-traumatic amputation and leads to a plethora of other long-term complications that result in substantial economic loss.[2,4,7-8]

Cardiovascular autonomic neuropathy is a key cause of morbidity and mortality present in an estimated 20% of diabetes mellitus patients.

Diabetic neuropathy affects sensory, motor, and autonomic neurons of the peripheral nervous system. Sensorimotor neuropathy (distal symmetrical polyneuropathy), the most common type of diabetic neuropathy, is what most clinicians recognize as DPN. This type of neuropathy can be acute and is triggered by an episode of glycemic instability, but it is more commonly a chronic condition.[9-10] Not all patients with DPN experience symptoms, but when symptoms

Continued on page 104

DPN (from page 103)

are present, they are typically described as burning, tingling ("pins and needles"), sharp, shooting and/or aching in a stocking and glove distribution. These symptoms usually begin distally at the toes and ascend proximally as the disease progresses.[4,9,11-15]

In addition to sensorimotor neuropathy, there has been increasing awareness of the prevalence of autonomic neuropathies such as cardiovascular autonomic neuropathy (CAN), as well as gastrointestinal (GI) and genitourinary (GU) autonomic neuropathies. More specifically, CAN is a key cause of morbidity and mortality present in an estimated 20% of diabetes mellitus patients.[9]

While the pathogenesis of DPN is multifactorial, it is well established that the primary risk factor is hyperglycemia. Researchers have suggested several theories concerning the hyperglycemic-induced abnormalities in metabolism and blood flow that contribute to the progression of DPN. The major theories include: metabolic flux through the polyol pathway, advanced glycation end-products contributing to segmental dymyelination and axonal atrophy, activation of protein kinase C, and oxidative stress.[9,16-18] All of these abnormalities contribute to nerve dysfunction and microvascular issues such as basement membrane thickening and endothelial cell hyperplasia.[9,19]

Nerve Conduction Studies (NCS) are the most sensitive and specific diagnostic tool for detecting diabetic peripheral neuropathy.

Past studies support that both vascular and metabolic factors are involved in all stages of the pathogenesis of DPN, but why some patients develop severe, debilitating pain while others experience no symptoms remains unresolved.[11,20-21] One recent study using spectral analysis of heart rate variability (HRV) detected greater autonomic dysfunction in painful DPN patients compared to pain-free patients. The results of this study suggest that small, poorly myelinated and unmyelinated nerve fibers that mediate pain sensation and autonomic function may be vulnerable to the pathological processes that occur with diabetic neuropathy, and this may explain why some DPN patients experience pain.[20]

Still, further research is necessary to better understand the role of autonomic dysfunction in painful DPN, and other factors may contribute to differences in the pathophysiology of symptomatic versus asymptomatic DPN.

Cold temperature sensation is mediated by small myelinated A-delta fibers.

The loss of protective sensation caused by DPN puts the patient at an increased risk for foot ulcerations and other complications such as infections and amputations, and causes significant morbidity and mortality. Diagnosing DPN in a timely manner allows for preventive intervention. Currently, there are numerous diagnostic tools available to help in the identification of DPN, such as vibratory perception threshold and vibration discrimination stimuli, Semmes-Weinstein monofilament, nerve conduction studies, sudorimetry, and graded temperature stimuli. This review will take a closer look at some of the clinical tools used in the diagnosis of DPN.

Sudorimetry

Autonomic nerve dysfunction is a common and important aspect of DPN that is often overlooked and most likely under-diagnosed.[22] One diagnostic tool for early detection of DPN in diabetic patients includes testing sudomotor function, or the function of sweat glands. Sweat glands are innervated by small unmyelinated cholinergic sympathetic fibers that could be affected early in the course of diabetes mellitus, so diagnosing sweat dysfunction could be a quick and useful screening tool for DPN.[23,24] When evaluating sweating and cardiovascular function in patients with distal small fiber neuropathy, Stewart et al. found that sympathetic sudomotor fibers were more frequently affected than autonomic nerves controlling heart rate, making sudorimetry a useful diagnostic tool for peripheral neuropathy compared to tools that assess cardiovascular function such as HRV.[25]

The literature describes a variety of methods to test sudomotor function. The quantitative sudomotor axon reflex test (QSART) detects distal small fiber polyneuropathy with a sensitivity of around 80%.[26] QSART involves infusing acetylcholine into the skin to stimulate postganglionic nerves, and then sweat production is measured. Some limitations of QSART include that it could be time-consuming and it requires expensive equipment.[27]

Thermoregulatory sweat tests evaluate the pattern of sweating by increasing the skin temperature and then using an indicator dye. While these tests are not quantitative, they can be used to either screen the whole body, or just focal areas of sweat loss.[27] The silastic imprint method stimulates sweat via acetylcholine, and then silastic material is placed over the skin. Sweat beads indent the silastic material and can be quantified.[28] This test is easy to conduct, but the silastic material is prone

Continued on page 105

DPN (from page 104)

to artifacts such as dirt and hair.[27]

Another device that evaluates sweat gland function is based on an electrochemical reaction between electrodes and chloride of the sweat glands after stimulation by low-level voltage. Quantitative results are expressed as Electrochemical Sweat Conductance (ESC) for the hands and feet. One study tested 265 diabetic patients for clinical signs and symptoms of DPN and found lower ESC at the feet to be significantly associated with increasing VPT and CAN. The authors concluded that lower ESE was suggestive of sudomotor dysfunction and this may be a simple clinical test to alert physicians to early DPN.[29]

Sudomotor denervation is a significant presentation of diabetic neuropathy, and thus the use of sudorimetry during screening of diabetes patients may allow for a more comprehensive assessment of potential neuropathy. Because sudomotor dysfunction may result in dryness of the foot and skin and has been associated with foot ulceration, detecting sweat gland dysfunction early can enable the clinician to provide appropriate care to prevent ulceration due to anhidrosis.[30,31]

Graded Temperature Stimuli

Another method of detecting small fiber dysfunction in DPN is temperature discrimination. Temperature can be one of the first sensations that is affected in diabetes patients.[32] Lack of temperature sensation may predispose patients to burns and other thermal injuries, and so techniques to clinically diagnose temperature sensation dysfunction are of clinical relevance. Because warm temperature sensation is mediated by small unmyelinated C fibers and cold temperature sensation is mediated by small myelinated A-delta fibers, both warm and cold stimuli should be utilized when testing for temperature sensation.[32]

Most techniques for temperature discrimination utilize the Peltier principle, which involves a thermoelectric device creating a temperature change by passing current through two different types of metal. Devices can either be heated or cooled depending on the direction of the electric current.[33,34] While the use of such thermal techniques has largely been for research purposes, the availability of these quantitative tools may enable clinicians to integrate temperature stimuli into routine assessments.[35]

One hand-held device screens for DPN by testing the combination of graded temperature stimuli and vibration discrimination stimuli. This combination allows for the testing of small fiber disease via the patient's ability to discriminate a two-degree Celsius temperature change from a range of between 15 degrees to 40 degrees Celsius as well as large fiber disease by testing five amplitudes of the standard 128 Hz vibration frequency.

The quantitative sudomotor axon reflex test (QSART) involves Infusing acetylcholine into the skin to stimulate post-ganglionic nerves.

Vibratory Perception Threshold (VPT) and Vibration Discrimination Stimuli

VPT is the most widely used quantitative sensory diagnostic method, and is defined as the lowest voltage at which vibration can be detected up to 50% of the time.[13,36] Experts describe VPT as a quick, accurate and inexpensive (depending on what type of instrument is used) screening tool to assess high-risk patients for DPN.[37]

Generally speaking, the vibration is administered at the distal pulp of the hallux over the bony prominence, and voltage is increased at the base of the instrument until the patient perceives the vibration.[13] Cut off scores for patients who are at high risk and low risk for long-term neuropathic complications vary by the type of instrument that is used.[38] Common devices for measuring VPT include a graduated 128-Hz tuning fork and semi-quantitative electromechanical instruments such as the biothesiometer and neurothesiometer.

Patients are categorized as high risk if the vibratory perception threshold (VPT) in at least one foot is > 25V.

A standard, non-graduated 128-Hz tuning fork, while still widely used by many clinicians, has limited ability as it can only determine the presence or absence of vibration perception and is therefore psychophysical in nature. The standard, non-graduated 128-Hz tuning fork also lacks quantification of clinical findings and standardization of user technique. The graduated 128-Hz tuning fork uses vibration extinction threshold on a scale of 0 to 8, and still has the advantages of portability and ease of operation that the standard tuning fork has.[38] A cut-off score of less than 4 out of 8 would indicate that a patient is at high risk for long-term neuropathic complications with the graduated tuning fork.[39]

A novel 128-Hz electronic tuning fork (ETF) was recently developed to perform accurate timed vibration tests and help overcome limitations of traditional tuning fork exams. The ETF reproduces the same vibration output and decay rate as the traditional tuning fork and contains an integrated timer that facilitates performance of accurate and reproduc-

Continued on page 106

DPN (from page 105)

ible timed vibrations tests.[40] In a fifty-five patient study, the sensitivity and specificity of neuropathy detection for the ETF were noted to be 0.953 and 0.761 respectively.[40]

Semiquantitative electromechanical instruments, such as the biothesiometer and neurothesiometer, are quick, portable, and inexpensive.[38] Van Deurson et al. describes that one disadvantage of the biothesiometer is that it has a ceiling effect for patients with severe neuropathy as it limits scores to 50 V, and therefore cannot determine the maximum VPT for those patients.[41]

While there are advantages to determining maximum VPT, clinicians would still be able to categorize such patients as high risk since the cut off scores for semiquantitative electromechanical instruments are a VPT greater than 25 V in at least one foot for high-risk patients and a VPT less than 15 V for patients who are at a low risk for ulceration.[42]

Regardless of the instrument used, data has suggested that utilizing VPT as a diagnostic tool reduces the physical and economical burden of DPN.[43]

Vibratory Perception Threshold (VPT) is defined as The lowest voltage at which vibration can be detected up to 50% of the time.

Decreased vibration perception may be only one of many risk factors for DPN and its associated long-term complications, but research has shown that when implemented appropriately, VPT is a useful clinical measure for immediately identifying at-risk patients, which enables clinicians to provide the necessary treatment and prevention of ulcers for these patients.

Semmes Weinstein Monofilament (SWM)

Many experts agree that the 5.07, 10g Semmes-Weinstein monofilament (SWM) is the most widely used screening instrument for DPN.[12] The test is simple and inexpensive as it provides sensory testing for light touch perception using a 5.07 monofilament that produces a characteristic 10 g perpendicular force to specific contact points on the dorsal and plantar aspects of the foot.[13,14]

In general, patients are instructed to lie supine with their eyes closed during testing, and if a patient is unable to sense the SWM on any part of the foot, the patient should be provided with preventative care.[15,44] There is, however, a lack of standardization and conflicting recommendations when it comes to proper testing sites.[12-14,45]

Warm temperature sensation is mediated by small unmyelinated C fibers.

Methodology from past studies testing the sensitivity and specificity of SWM have described using anywhere from one to ten testing sites.[46] A systematic review by Dros, et al., evaluating SWM as a diagnostic test for DPN, found wide ranges in both sensitivity and specificity in past studies likely due to differences in monofilament site placement, the number and combination of sites tested, and the interpretation of the test.[47]

Because the SWM test is widely used, especially for diabetes patients, methodology should be standardized to make SWM an adequate clinical assessment for sensory loss. Ten common testing sites may include: the first, third and fifth metatarsal heads and toes, the medial and lateral plantar midfoot, the heel, and the space between the first and second toes on the dorsal surface of the foot.[44,48]

One study conducted SWM tests on the ten sites described above, and evaluated the impact of each site and combinations of the sites. Based on the results of the study, sensitivity and specificity of the test at the ten sites were 93.1% and 100%, respectively. Sensitivity and specificity at two sites, the plantar aspects of the third and fifth metatarsal heads, were the same as the ten-site test.[47] Overall, this study demonstrated that the commonly used ten-site test was highly sensitive and highly specific, but the two-site test could also potentially be clinically useful.

Nerve Conduction Studies (NCS)

Nerve conduction studies, electrodiagnostic tests that evaluate the ability of motor and sensory nerves to conduct electrical impulses, have been described as the most sensitive and specific diagnostic tool for detecting DPN.[49,50] Nerves are electrically activated via impulses on the skin, and a response is subsequently measured.[51]

Such tests, also known as nerve conduction velocity tests, are diagnostically helpful in patients who are suspected to have almost any PNS disorder, such as DPN.

Specific nerve conduction study techniques include motor nerve conduction studies, sensory nerve conduction studies, and F waves. Motor nerve conduction studies involve electrical stimulation of a nerve and the resulting compound muscle action potential (CMAP) from the surface electrodes that are placed on the muscle supplied by the nerve.[51] Sensory nerve conduction studies are performed by obtaining the sensory nerve action potential (SNAP) by electrically stimulating sensory fibers and recording the resulting action potential at a point further along that

Continued on page 107

DPN (from page 106)

nerve.[51] Lastly, F waves represent a late motor response.

When a motor nerve conduction test is performed, an impulse goes both distally (CMAP) and proximally to the anterior horn cell; this ultimately leads to a small muscle depolarization (F wave) of longer latency.[51] Essentially, F waves are useful for testing the proximal segments of nerves, and abnormal F waves can be indicative of peripheral nerve pathology.

Unlike VPT and SWM, NCS are objective and provide the clinician with a more reliable test for confirming polyneuropathy. It should be noted that because most NCS use surface electrodes which only measure fast conducting fibers, patients with small fiber neuropathies may still have normal velocities.[52] Still, NCS can be used before the development of clinical signs and symptoms which would be helpful for predicting new ulcerations.[13]

A 2013 Study by Parkhad and Palve found that NCV progressively decreased from the control group (non-diabetic) to the diabetes group with good glycemic control to the diabetes group with poor glycemic control.[50] These results suggest that slowing of nerve conduction velocities may indicate ongoing damage to the myelin sheath, which is accelerated by poor glycemic control. Utilizing NCS in patients with poor glycemic control could therefore provide an early assessment tool for predicting the onset of DPN so that immediate care can be provided when necessary.

Patients with small fiber neuropathies may still have normal nerve conduction velocities.

Summary

Peripheral neuropathy occurs commonly in the population with diabetes and its management continues to rely on early recognition. A direct correlation has been shown to exist between inadequate screening and under-utilization of preventative interventions that may decrease the rates of ulceration and amputation by up to 60% and 85%, respectively.[49]

No single standard for determining clinical neuropathic dysfunction currently exists, but early detection of DPN is critical for identifying at-risk patients and immediately implementing a preventative management plan.[52] Currently, the recommendation is to combine multiple diagnostic tools to ensure that neuropathic screening is comprehensive.[6] The improved diagnosis and management of this common and disabling complication will help prevent the deleterious sequellae associated with DPN and improve the quality of life in patients. **PM**

A cut-off score of less than 4 out of 8 using a graduated tuning fork would indicate that a patient is at high risk for long-term neuropathic complications.

References

[1] Centers for Disease Control and Prevention. National Diabetes Statistics Report, 2014. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention; 2014.

[2] Barrett AM, Lucero MA, Le T, Robinson RL, Dworkin RH, Chappell AS. Epidemiology, public health burden, and treatment of diabetic peripheral neuropathic pain: a review. Pain Medicine. 2007; 8(S2): S50-62.

[3] Dixit S, Maiya A. Diabetic peripheral neuropathy and its evalulation in a clinical scenario: a review. Journal of Postgraduate Medicine. 2014;60(1): 33-40.

[4] Davies M, Brophy S, Williams E, Taylor A. The prevalence, severity, and impact of painful diabetic peripheral neuropathy in type 2 diabetes. Diabetes Care. 2006;29: 1518-22.

[5] Boulton AJM, Malik RA, Arezzo JC, Sosenko JM. Diabetic somatic neuropathies. Diabetes Care. 2004; 27(6): 1458-86.

[6] Tesfaye S, Vileikyte L, Rayman G, Sindrup SH, Perkins BA, Baconja M, Vinik AI, Boulton AJM. Painful diabetic peripheral neuropathy: consensus recommendations on diagnosis, assessment and management. Diabetes Metab Res Rev. 2011; 27: 629-38.

[7] Gordois A, Scuffham P, Shearer A, Oglesby A, Tobian JA. The health care costs of diabetic peripheral neuropathy in the U.S. Diabetes Care. 2003; 26: 1790-95.

[8] Bruce DG, Davis WA, Davis TM. Longitudinal predictors of reduced mobility and physical disability in patients with Type 2 diabetes: the Fremantle Diabetes Study. Diabetes Care. 2005; 28: 2441-7.

[9] Duby JJ, Campbell RK, Setter SM, White JR, Rasmussen KA. Diabetic neuropathy: an intensive review. Am J Health-Syst Pharm. 2004; 61: 160-73.

[10] Boulton JM. Management of diabetic peripheral neuropathy. Clinical Diabetes. 2005; 23: 9-15.

[11] Tesfaye S, Selvarajah D. Advances in the epidemiology, pathogenesis and management of diabetic peripheral neuropathy. Diabetes Metab Res Rev. 2012; 28(Suppl 1): 8-14.

[12] Mayfield JA, Sugarman JR. The use of the Semmes-Weinstein monofilament and other threshold tests for preventing foot ulceration and amputation in persons with diabetes. The Journal of Family Practice;49(11):S17-29

[13] Lavery LA, Armstrong DG, Boulton A. Screening for diabetic peripheral neuropathy. Diabetic Microvascular Complications Today. 2004: 17-19.

[14] Cornblath DR. Diabetic neuropathy: diagnostic methods. Advanced Studies in Medicine. 2004;4(8A):S650-61.

[15] Mueller MJ. Identifying patients with diabetes mellitus who are at risk for lower-extremity complications: use of Semmes-Weinstein monofilaments. Phys Ther. 1996;76:68-71.

[16] Oates PJ. Polyol pathway and diabetic peripheral neuropathy. Int Rev Neurobiol. 2005; 50: 325-92.

[17] Sugimoto K, Yasujima M, Yagihashi S. Role of advanced glycation end

Continued on page 108

DPN (from page 107)

products in diabetic neuropathy. Curr Pharm Des. 2008; 14(10):953-61.

[18] Eichberg J. Protein kinase C changes in diabetes: is the concept relevant to neuropathy? Int Rev Neurobiol. 2002; 50: 61-82

[19] Malik RA. The pathology of human diabetic neuropathy. Diabetes. 1997; 46: S50-3.

[20] Gandhi RA, Marques JLB, Selvarajah D, Emery CJ, Tesfaye S. Painful diabetic neuropathy is associated with greater autonomic dysfunction than painless diabetic neuropathy. Diabetes Care. 2010; 33: 1585-90.

[21] Cameron NA, Eaton SE, Cotter MA, Tesfaye S. Vascular factors and metabolic interactions in the pathogenesis of diabetic neuropathy. Diabetologia. 2001;44(11): 1973-88.

[22] Papanas N and Ziegler D. New diagnostic tests for diabetic distal symmetric polyneuropathy. Journal of Diabetes and its Complications. 2011;25(1): 44-51.

[23] Yajnik CS, Kantikar VV, Pande AJ, Deslypere JP. Quick and simple evaluation of sudomotor function for screening diabetic neuropathy. ISRN Endocrinology. 2012; 2012: 103714.

[24] Summer CJ, Sheth S, Griffin JW, Cornblath DR, Polydefkis M. The spectrum of neuropathy in diabetes and impaired glucose tolerance. Neurology. 2003;60(1):108-11.

[25] Stewart JD, Low PA, Fealey RD. Distal small fiber neuropathy: results of tests of sweating and autonomic cardiovascular reflexes. Muscle Nerve. 1992;15(6):661-5.

[26] Thaisetthawatkul P, Filho AMF, Herrmann DN. Contribution of QSART to the diagnosis of small fiber neuropathy. Muscle Nerve. 2013;48:883-8.

[27] Illigens BMW and Gibbons CH. Sweat testing to evaluate autonomic function. Clin Auton Res. 2009;19(2):79-87.

[28] Stewart JD, Nguyen DM, Abrahamowicz M. Quantitative sweat testing using acetylcholine for direct and axon reflex mediated stimulation with silicone mold recording; controls versus neuropathic diabetes. Muscle Nerve. 1994;17:1370-77.

[29] Yajnik CS, Kantikar VV, Pande AJ, Deslypere JP: Quick and simple evaluation of sudomotor function for screening of diabetic neuropathy. ISRN Endocrinol. 2012;2012:103714.

[30] Tentolouris N, Marinou K, Kokotis P, Karanti A, Diakoumopoulou E, Katsilambros N. Sudomotor dysfunction is associated with foot ulceration in diabetes. Diabet Med. 2009;26:302-5.

[31] Luo K, Lue J, Hsieh S, Chao C, Hsieh P. Effect of glycemic control on sudomotor denervation in type 2 diabetes. Diabetes Care. 2012;35:612-16.

[32] Ziegler D, Mayer P, Wiefels K, Gries FA. Assessment of small and large fibre function in long-term type 1 (insulin dependent) diabetic patients with and without painful neuropathy. Pain. 1988;34:1-10.

[33] Zeigler D, Mayer P, Gries F. Evaluation of thermal, pain, and vibration sensation thresholds in newly diagnosed type 1 diabetic patients. Journal of Neurology, Neurosurgery, and Psychiatry. 1988;51:1420-24.

[34] Chong PST and Cros DP. American Association of Electrodiagnoistic Medicine review: quantitative sensory testing equipment and reproducibility studes. Muscle & Nerve. 2004;29:734-47.

[35] Lepow B, Bharara M, Armstrong DG. Thermography and thermometry: building a knowledge base. Podiatry Management. 2010: 145-51.

[36] Arezzo JC. New developments I the diagnosis of diabetic neuropathy. Am J Med. 1999;107(Suppl. 2B):S132-9.

[37] Krentz AJ, Acheson A, Basu A, Kilvert A, Wright AD, Nattrass M. Morbidity and mortality associated with diabetic foot disease: a 12-month prospective survey of hospital admissions in a single UK centre. The Foot. 1997;7:144-7.

[38] Garrow, AP and Boulton AJM. Vibration perception threshold—a valuable assessment of neural dysfunction in people with diabetes. Diabetes Metab Res Rev. 2006;22:411-9.

[39] Liniger C, Albeanu A, Bloise D, Assal JP. The tuning fork revisited. Diabet Med. 1990;7:8595-64.

[40] O'Brien T, Karem J. An initial evaluation of a proof-of-concept 128-Hz electronic tuning fork in the detection of peripheral neuropathy. J Am Podiatr Med Assoc. 2014 Mar;104(2):134-40.

[41] van Deurson RWM, Sanchez MM, Derr JA, Becker MA. Vibration perception threshold testing in patients with diabetic neuropathy: ceiling effects and reliability. Diabet Med. 2001;18:469-75.

[42] Young MJ, Breddy JL, Veves A, Boulton AJM. The prediction of diabetic neuropathic foot ulceration using vibration perception thresholds. Diabetes Care. 1994;17:557-60.

[43] Shearer A, Scuffham P, Gordois A, Olgesby A. Predicted costs and outcomes from reduces vibration dectection in people with diabetes in the US. Diabetes Care. 2003;26:2305-10.

[44] Rith-Najarian, SJ, T. Stolusky, DM Gohdes. Identifiying diabetic patients at high risk for lower-extremity amputation in a primary health care setting: a prospective evaluation of simple screening criteria. Diabetes Care. 1992; 15: 1386-89.

[45] Holewski, JJ, RM Stress, PM Graf, C. Grunfeld. Aesthesiometry: quantification of cutaneous pressure sensation in diabetic peripheral neuropathy. J Rehabil Res Dev. 1988; 25:1-10.Slater, 2013

[46] Lee S, Kim H, Choi S, Park Y, Kim Y, Cho B. Clinical usefulness of the two-site Semmes-Weinstein monofilament test for detecting diabetic peripheral neuropathy. J Korean Med Sci. 2003;18:103-7.

[47] Dros J, Wewerinke A, Bindels PJ, van Weert HC. Accuracy of monofilament testing to diagnose peripheral neuropathy: a systematic review. Ann Fam Med. 2009;7:555-8.

[48] Slater RA, Koren S, Ramot, Y, Buchs, A, Rapoport MJ. Pilot study on the significance of random intrasite placement of the Semmes-Weinstein monofilament. Diabetes Metab Res Rev. 2013;29:235-8.

[49] Perkins BA, Olaleye D, Zinman B (look up for rest of authors). Simple screening tests for peripheral neuropathy in the diabetes clinic. Diabetes Care. 2001;24:250-6.

[50] Parkhad, S and Palve S. Early diagnosis of neuropathy in diabetic patients using nerve conduction studies. National Journal of Physiology, Pharmacy & Pharmacology. 2014;4(2):158-60.

[51] Mallik, A and Weir AI. Nerve conduction studies: essentials and pitfalls in practice. J Neurol Neurosurg Psychiatry. 2005;76(Suppl. 2):S23-31.

[52] Horowitz SH. Criteria for the diagnosis of peripheral neuropathies. Occup Environ Med. 2002;59: 425-6.

Dr. Wu is Associate Dean of Research and Professor of Surgery, Professor, and Stem Cell and Regenerative Medicine Director at the Center for Lower Extremity Ambulatory Research (CLEAR) of the Dr. William M. Scholl College of Podiatric Medicine at the Rosalind Franklin University of Medicine and Science.

Michelle Branigan is a student at the Dr. William M. Scholl College of Podiatric Medicine at Rosalind Franklin University. Michelle is a NIH T35 funded research scholar and currently serves as parliamentarian for the Illinois Podiatric Medical Student Association (IPMSA).

SEE ANSWER SHEET ON PAGE 111.

1) Which of the following is a true statement regarding diabetic peripheral neuropathy (DPN)?
   A) Only symptomatic patients have DPN.
   B) Symptoms usually begin proximally and descend distally towards the toes as the disease progresses.
   C) Cardiovascular autonomic neuropathy is a key cause of morbidity and mortality present in an estimated 20% of diabetes mellitus patients.
   D) The incidence of DPN decreases in patients with long duration of diabetes.

2) What are nerve conduction studies (NCS)?
   A) Electrodiagnostic tests that evaluate the ability of both motor and sensory nerves to conduct electrical impulses
   B) Electrodiagnostic tests that evaluate the ability of only motor nerves to conduct electrical impulses
   C) Electrodiagnostic tests that evaluate the ability of only sensory nerves to conduct electrical impulses
   D) None of the above

3) Which of the following is described as the most sensitive and specific diagnostic tool for detecting diabetic peripheral neuropathy?
   A) Visual Analog Scale (VAS)
   B) Vibratory Perception Threshold (VPT)
   C) Electromyography (EMG)
   D) Nerve Conduction Studies (NCS)

4) Which of the following statements regarding the Semmes Weinstein Monofilament (SWM) are true?
   A) The 5.07, 10g SWM is one of the most widely used screening instruments for DPN.
   B) The 5.07 monofilament produces a characteristic 10 g perpendicular force to specific contact points on the dorsal and plantar aspects of the foot.
   C) There is a lack of standardization and conflicting recommendations when it comes to proper testing sites.
   D) All of the above

5) Cold temperature sensation is mediated by:
   A) Small myelinated A-delta fibers
   B) Large myelinated A-alpha fibers
   C) Small myelinated B fibers
   D) Small unmyelinated C fibers

6) Which of the following diagnostic tools is the least effective in detecting small fiber dysfunction in diabetic peripheral neuropathy?
   A) Temperature discrimination
   B) Quantitative sudomotor axon reflex test (QSART)
   C) Nerve Conduction Studies (NCS)
   D) The silastic imprint method

7) The quantitative sudomotor axon reflex test (QSART) involves ____.
   A) Evaluating patterns of sweating by increasing skin temperature
   B) Stimulating sweat glands with a low-level voltage
   C) Quantifying sweat beads
   D) Infusing acetylcholine into the skin to stimulate post-ganglionic nerves

8) The primary risk factor for DPN is _____.
   A) Hypertension
   B) Hyperglycemia
   C) Hypercholesteremia
   D) Obesity

9) Which of the following sudorimetric screening tools evaluates the pattern of sweating by increasing skin temperature and using an indicator dye?
   A) quantitative sudomotor axon reflex test (QSART)
   B) Silastic imprint method
   C) Thermoregulatory sweat test
   D) Electrochemical sweat conductance

10) The current recommendation for neuropathic screening is to _____.
   A) Utilize VPT and graded temperature stimuli to ensure an early diagnosis
   B) Combine multiple diagnostic tools to ensure that screening is comprehensive
   C) Always use NCS in addition to SWM since there is a lack of standardization
   D) Never use graded temperature stimuli because they should only be used for research purposes

11) Which of the following are specific NCS techniques?
   A) Motor nerve conduction studies
   B) Sensory nerve conduction studies
   C) F waves
   D) All of the above

12) Patients are categorized as high risk if the vibratory perception threshold (VPT) in at least one foot is _____.
   A) > 15V
   B) > 25V
   C) > 50V
   D) > 75V

13) Which of the following are common devices used to measure vibratory perception threshold (VPT)?
   A) Graduated 128-Hz tuning fork
   B) Biothesiometer
   C) Neurothesiometer
   D) All of the above

14) Vibratory Perception Threshold (VPT) is defined as _____.
   A) The lowest voltage at which vibration can be detected up to

Continued on page 110

50% of the time
B) The lowest voltage at which vibration can be detected all of the time
C) The highest voltage at which vibration can be detected all of the time
D) This highest voltage at which vibration can be detected up to 50% of the time

15) Warm temperature sensation is mediated by _____.
A) Small myelinated A-delta fibers
B) Large myelinated A-alpha fibers
C) Small myelinated B fibers
D) Small unmyelinated C fibers

16) Which of the following type of test typically utilizes the Peltier Principle?
A) Temperature discrimination
B) Vibration discrimination
C) Light touch perception
D) Nerve conduction tests

17) Sudorimetry specifically tests which of the following?
A) Sweat gland function
B) Autonomic nervous system
C) Somatic nervous system
D) Macrovascular function

18) Which NCS technique is useful in testing proximal segments of nerves?
A) Motor nerve conduction studies
B) Sensory nerve conduction studies
C) Autonomic nerve conduction studies
D) F waves

19) Which of the following is a true statement regarding nerve conduction studies (NCS)?
A) Most NCS use surface electrodes that only measure slow conducting fibers.
B) Patients with small fiber neuropathies may still have normal nerve conduction velocities.
C) When a motor nerve conduction test is performed, the impulse only goes proximally to the anterior horn cell.
D) F waves represent early motor responses.

20) What is the cut-off score when using a graduated tuning fork that would indicate that a patient is at high risk for long-term neuropathic complications?
A) Greater than 4 out of 8
B) 0 out of 8
C) less than 2 out of 8
D) less than 4 out of 8

SEE ANSWER SHEET ON PAGE 111.

PM's CME Program

Welcome to the innovative Continuing Education Program brought to you by *Podiatry Management Magazine*. Our journal has been approved as a sponsor of Continuing Medical Education by the Council on Podiatric Medical Education.

Now it's even easier and more convenient to enroll in PM's CE program!

You can now enroll at any time during the year and submit eligible exams at any time during your enrollment period.

PM enrollees are entitled to submit ten exams published during their consecutive, twelve–month enrollment period. Your enrollment period begins with the month payment is received. For example, if your payment is received on November 1, 2014, your enrollment is valid through October 31, 2015. If you're not enrolled, you may also submit any exam(s) published in PM magazine within the past twelve months. **CME articles and examination questions from past issues of *Podiatry Management* can be found on the Internet at http://www.podiatrym.com/cme.** Each lesson is approved for 1.5 hours continuing education contact hours. Please read the testing, grading and payment instructions to decide which method of participation is best for you.

Please call (631) 563-1604 if you have any questions. A personal operator will be happy to assist you.

Each of the 10 lessons will count as 1.5 credits; thus a maximum of 15 CME credits may be earned during any 12-month period. You may select any 10 in a 24-month period.

The* Podiatry Management Magazine *CME program is approved by the Council on Podiatric Education in all states where credits in instructional media are accepted. This article is approved for 1.5 Continuing Education Contact Hours (or 0.15 CEU's) for each examination successfully completed.

Home Study CME credits now accepted in Pennsylvania

Enrollment/Testing Information and Answer Sheet

Continuing Medical Education

Note: If you are mailing your answer sheet, you must complete all info. on the front and back of this page and mail with your credit card information to: ***Podiatry Management*, P.O. Box 490, East Islip, NY 11730.**

TESTING, GRADING AND PAYMENT INSTRUCTIONS

(1) Each participant achieving a passing grade of 70% or higher on any examination will receive an official computer form stating the number of CE credits earned. This form should be safeguarded and may be used as documentation of credits earned.

(2) Participants receiving a failing grade on any exam will be notified and permitted to take one re-examination at no extra cost.

(3) All answers should be recorded on the answer form below. For each question, decide which choice is the best answer, and circle the letter representing your choice.

(4) Complete all other information on the front and back of this page.

(5) Choose one out of the 3 options for testgrading: mail-in, fax, or phone. To select the type of service that best suits your needs, please read the following section, "Test Grading Options".

TEST GRADING OPTIONS

Mail-In Grading

To receive your CME certificate, complete all information and mail with your credit card information to:

Podiatry Management
P.O. Box 490, East Islip, NY 11730

PLEASE DO NOT SEND WITH SIGNATURE REQUIRED, AS THESE WILL NOT BE ACCEPTED.

There is **no charge** for the mail-in service if you have already enrolled in the annual exam CME program, and we receive this exam during your current enrollment period. If you are not enrolled, please send $23.00 per exam, or $179 to cover all 10 exams (thus saving $51 over the cost of 10 individual exam fees).

Facsimile Grading

To receive your CME certificate, complete all information and fax 24 hours a day to 1-631-563-1907. Your CME certificate will be dated and mailed within 48 hours. This service is available for $2.50 per exam if you are currently enrolled in the annual 10-exam CME program (and this exam falls within your enrollment period), and can be charged to your Visa, MasterCard, or American Express.

If you are *not* enrolled in the annual 10-exam CME program, the fee is $23 per exam.

Phone-In Grading

You may also complete your exam by using the toll-free service. Call 1-800-232-4422 from 10 a.m. to 5 p.m. EST, Monday through Friday. Your CME certificate will be dated the same day you call and mailed within 48 hours. There is a $2.50 charge for this service if you are currently enrolled in the annual 10-exam CME program (and this exam falls within your enrollment period), and this fee can be charged to your Visa, Mastercard, American Express, or Discover. If you are not currently enrolled, the fee is $23 per exam. When you call, please have ready:

1. Program number (Month and Year)
2. The answers to the test
3. Your social security number
4. Credit card information

In the event you require additional CME information, please contact PMS, Inc., at **1-631-563-1604**.

ENROLLMENT FORM & ANSWER SHEET

Please print clearly...Certificate will be issued from information below.

Name _____ Soc. Sec. #_____
Please Print: FIRST MI LAST

Address_____

City_____ State_____ Zip_____

Charge to: _____Visa _____ MasterCard _____ American Express

Card #_____Exp. Date_____

Note: Credit card is the only method of payment. Checks are no longer accepted.

Signature_____ Soc. Sec.#_____ Daytime Phone_____

State License(s)_____ Is this a new address? Yes_____ No_____

Check one:

_____ I am currently enrolled. (If faxing or phoning in your answer form please note that $2.50 will be charged to your credit card.)

_____ I am not enrolled. Enclosed is my credit card information. Please charge my credit card $23.00 for each exam submitted. (plus $2.50 for each exam if submitting by fax or phone).

_____ I am not enrolled and I wish to enroll for 10 courses at $179.00 (thus saving me $51 over the cost of 10 individual exam fees). I understand there will be an additional fee of $2.50 for any exam I wish to submit via fax or phone.

ENROLLMENT FORM & ANSWER SHEET *(continued)*

EXAM #8/14
Diagnosing DPN
(Branigan, Wu)

Circle:

1.	A	B	C	D	11.	A	B	C	D
2.	A	B	C	D	12.	A	B	C	D
3.	A	B	C	D	13.	A	B	C	D
4.	A	B	C	D	14.	A	B	C	D
5.	A	B	C	D	15.	A	B	C	D
6.	A	B	C	D	16.	A	B	C	D
7.	A	B	C	D	17.	A	B	C	D
8.	A	B	C	D	18.	A	B	C	D
9.	A	B	C	D	19.	A	B	C	D
10.	A	B	C	D	20.	A	B	C	D

Medical Education Lesson Evaluation

Strongly agree [5]	Agree [4]	Neutral [3]	Disagree [2]	Strongly disagree [1]

1) This CME lesson was helpful to my practice ____

2) The educational objectives were accomplished ____

3) I will apply the knowledge I learned from this lesson ____

4) I will makes changes in my practice behavior based on this lesson ____

5) This lesson presented quality information with adequate current references ____

6) What overall grade would you assign this lesson?

A B C D

How long did it take you to complete this lesson?

_____hour _____minutes

What topics would you like to see in future CME lessons ?

Please list :

_____

_____

_____

_____

_____