THE IMPORTANCE OF SCREENING AND DIAGNOSING DIABETIC PERIPHERAL NEUROPATHY

Interview with Andrew J. M. Boulton, MD, DSc, FRCP

Professor Boulton is Professor of Medicine, University of Manchester and Consultant Physician, Manchester Royal Infirmary, Manchester, UK. He is also Professor of Medicine, Division of Endocrinology at the University of Miami, Florida. Professor Boulton graduated with Honours from medical school in 1976 and proceeded to earn the membership of the Royal College of Physicians (MRCP) in 1979 and was elected a Fellow of the Royal College of Physicians (FRCP) in 1992. His higher degree (PhD equivalent) was also from the University of Newcastle-Upon-Tyne in 1985. Before being promoted to Professor, he was Senior Lecturer then Reader in Medicine at the University of Manchester. He has previously been a Visiting Assistant Professor of Medicine in Miami from 1983 to 1984 and had worked in Sheffield. His clinical and research interests include diabetic complications, particularly in neuropathy and the foot, and he also has written more than 300 papers and 6 books on the above topic. In 2003, Professor Boulton received the Castelli Pedrolsi Prize for outstanding research in diabetic complications of the European Association for the Study of Diabetes and DSc Honoris Causa from the University of Cluj, Romania.

A senior clinical editor for Advanced Studies in Medicine (ASiM) interviewed Professor Boulton to discuss the current methods of screening for diabetic peripheral neuropathy in the office setting as well as the larger issues surrounding screening and diagnosis.

Patients with both type 1 and type 2 diabetes often develop peripheral neuropathy, a microvascular complication that may in some cases lead to substantial symptomatic pain for the patient. In advanced cases, diabetic peripheral neuropathy (DPN) may ultimately be a factor in the pathogenesis of nonhealing and infected foot ulcerations, gangrene, and the eventual amputation of the lower limb. Because of the increased risk for these negative consequences of neuropathy, screening and proper diagnosis are essential in this patient population. Many tools are available to screen for DPN in the primary care setting, yet in spite of the need for effective screening, there is no true gold standard approach used by clinicians.

What follows is an interview with Andrew J. M. Boulton, MD, DSc, FRCP, in which he discusses the importance of screening and diagnosing DPN, the various tools currently available along with their advantages and disadvantages, and other practical information on screening and diagnosis in the primary physician office setting.

ASiM: Why it is important to screen and diagnose DPN early?

Prof Boulton: It is important to uncover peripheral neuropathy early in the course of its slow progressive loss of nerve fibers for 2 reasons. Firstly, if treatment focusing on prevention is to be effective, it must be administered during the early natural history of this disease. We know that progressive loss of nerve function in neuropathy is clearly related to glycemic control in both type 1 and type 2 diabetes. Early intervention with tight, stable glycemic control may both provide needed symptomatic relief and also slow the progression of peripheral neuropathy. Otherwise, electrophysiologic abnormalities in the lower limb of a patient with type 2 diabetes who has chronic neuropathy will gradually increase over the years. Secondly, early screening and diagnosis is critical because patients at all stages of neuropathy are at a greater risk...
of developing insensitive foot ulcerations. In fact, the vast majority of foot ulcers have been shown to occur in patients with sensory loss. Such patients may not even be aware of the problem. These patients must be properly identified, and at the earliest possible time in the course of their disease, provided with appropriate education on regular (daily) self-foot care and medical management if appropriate in order to decrease their relative risk of foot ulcerations.

**ASiM: Who should clinicians screen for DPN?**

Prof Boulton: Clinicians should screen any patient who is diagnosed with type 2 diabetes for DPN beginning at the time of diagnosis, because current prevalence estimates reveal that 11% of these patients will already have evidence of peripheral neuropathy when initially diagnosed with diabetes. Peripheral neuropathy in those patients could be missed if screening did not begin for an arbitrary interval such as 5 or 10 years after diagnosis.

Type 1 diabetes is slightly different since the time of onset is relatively well defined. Patients diagnosed with type 1 diabetes in childhood should be screened for DPN annually beginning after adolescence.

An estimated 15% of patients with DPN will experience a foot ulcer at some point during their lifetime. Since medical evidence has shown foot ulcers precede the majority of all nontraumatic lower limb amputations in the United States, resulting in substantial morbidity and mortality in these individuals, it is therefore essential that every patient diagnosed with diabetes be screened for evidence of peripheral neuropathy.

If an individual without a diagnosis of diabetes presents with symptoms of DPN (that is, any complaint in the foot consistent with neuropathy) he/she should be screened for diabetes, as such symptoms could be the presenting feature of diabetes. Evidence of early neuropathy, especially small fiber neuropathy, has been reported even in prediabetic patients who have impaired glucose tolerance. Thus, these patients should be screened for diabetes.

**ASiM: What are some of the clinical indicators that a clinician should associate with DPN?**

Prof Boulton: DPN is a clinical diagnosis. Upon a diagnosis of diabetes, it is important to take a careful history, asking the patient for any symptoms of neuropathy he has experienced. Clinical indicators include positive symptoms such as burning pain, hyperesthesia (increased sensitivity of the skin), spontaneous electrical sensation, cramping, shooting, stabbing, and lancinating pain, altered or uncomfortable temperature perception, and various paresthesias, among others. Since many patients do not experience positive symptoms, such as whether the feet feel dead or numb, clinicians should then seek evidence of loss of sensation through various testing modalities such as pain, vibration, pressure, pinprick, light touch, joint-position sensation, and ankle reflexes.

**ASiM: How often should patients with risk factors for DPN be screened?**

Prof Boulton: I believe that patients who have been diagnosed with diabetes—even those without known major complications—should be screened at least every year in order to identify those patients who have potential risk of foot problems. The recommendation of the American Diabetes Association is for patients to be screened for neuropathy annually, at a minimum. Any patient who exhibits clinical evidence of DPN must be considered as being at risk of insensitive foot ulceration. While neuropathy by itself does not cause ulceration, the insensitivity typical of the condition combined with other causes will result in the development of foot ulcers. Results from the North-West Diabetes Foot Care Study showed that in the cohort studied, several independent factors were predictive of new foot ulcers. These factors included a history of past or present foot ulcers, an abnormal neuropathy disability score, any previous podiatry attendance or foot care advice, insensitivity to 10-g monofilament, a reduced number of pedal pulses, foot deformities, and an increasing abnormal ankle reflex score. Patients who have one or more of these risk factors for foot ulcers may require more frequent follow-up, with an emphasis on providing regular foot examinations to reinforce the educational message that the patient needs to himself perform regular self-care. Appropriate interventions should be undertaken with such patients.

**ASiM: Please give a brief overview of the types of DPN screening and diagnostic tools available to clinicians.**

Prof Boulton: It is said in medicine that 90% of diagnoses are made on history alone, but that is probably not true of neuropathy, because as many as half
the patients with neuropathy may not have any symptoms. Nonetheless, it is necessary when screening for DPN to first take a history of symptoms that would be suggestive of neuropathy. This includes positive symptoms and negative symptoms, as described above. Since a substantial number of patients might not have any symptoms whatsoever, a careful clinical examination must also be performed. It is not necessary to have sophisticated equipment to reach a clinical diagnosis of neuropathy; very simple diagnostic tools can be effective. A tendon hammer, a tuning fork (preferably 128-hertz frequency, which can be used to test for vibration as well as for cold sensation), a pin, and a monofilament that would impart pressure when it buckles at 10 g, are all simple tools that may be used for the clinical examination.

Thus, the diagnosis of neuropathy may be made with a good history and a careful examination of the lower limb. This should include an especially careful examination over the foot for loss of sensation of pain, vibration, temperature, and loss of appreciation of joint position. It is also important to assess the reflexes of the Achilles tendons, as well as the ankle reflex. The examination should also assess vascular conditions in the foot by taking peripheral pulses and assessing skin status, and also foot shape, by looking for claw toes, prominent metatarsal heads, or Charcot deformity.

Upon examination, the typical patient with moderately diffuse DPN would have reduced sensation to multiple modalities and a reduction in or loss of ankle reflex. Such a patient might not be able to perceive the 10-g pressure of the monofilament. These simple tests are sufficient to accurately diagnose neuropathy in day-to-day practice.

**A S I M:** Is there a gold standard approach to the screening and diagnosis of DPN?

Prof Boulton: The monofilament is taken by some to be the gold standard, although recent studies suggest that the monofilament may be problematic in terms of sensitivity.

Prospective data from a longitudinal study in a large patient population of 10 000 (the North-West Diabetes Foot Care Study) show that a simple composite score of 3 sensory modalities and a reflex is a superb predictor of foot ulcers. Using this approach, a composite score of 10 would be the maximum available, signifying a complete loss of sensation and loss of reflexes. In the study, patients with a composite score of 6 or greater had a 6-fold increased risk of getting a foot ulcer in the next year.

**A S I M:** What are some of the more complicated electrical devices and measurement techniques used to test for DPN?

Prof Boulton: In our clinics in Miami or in Manchester, England, I widely use a power source–required device called a biothesiometer or neurothesiometer, which measures a semi-quantitative vibration perception threshold. The device has a vibrating stylus with an adjustable frequency and gives readings on a scale of zero to 50. Most normal people can feel a vibration between 5 and 20. Two prospective studies have shown if the patient vibration perception threshold is recorded at 25 or more, there is substantially increased risk for not being able to sense a foot injury. Several more sophisticated tools with similar functions are available, as is equipment to do computer-aided sensory examination. Electrophysiology—used for clinical trials—is the most sensitive test and a very good predictor of ulceration, but even so, the results of electrophysiology will only reveal a deficit of large nerve fiber function. None of these tests will confirm that a neuropathy is actually caused by diabetes. Even with more sophisticated equipment, there is no gold standard test wherein an abnormal result equates to a definite diagnosis of neuropathy.

**A S I M:** What are the advantages and disadvantages of the simpler clinical screening/diagnostic techniques?

Prof Boulton: The advantages are that the simpler tests of sensation are inexpensive and can be performed quickly in the primary care setting, typically requiring no more than 5 minutes. Using these simple tests to reach composite score of 3 sensory modalities and a reflex—as I mentioned before—is a very effective way to screen for DPN.

The chief disadvantage of the simpler techniques—and this is true of the more sophisticated electric or computer tests of sensation as well—is that all of these
tests are highly subjective since they rely on the patient to give a response. Thus, all these tests have a rather high rate of variability, and some interobserver variability is also possible. Electrophysiology, by contrast, measures how far the nerve conducts between point A and point B, so the possible subjectivity of patient response is not an issue.

**ASiM: Are there any further issues related to the importance of screening and diagnosing DPN?**

Prof Boulton: Primary care physicians need to know that they can have a large impact on the management of DPN because they see a substantial proportion of the patients with type 2 diabetes, and, thus, are in a position to diagnose this condition earlier, and without the need for sophisticated equipment. The impression may be that all of the practitioners in the hospital setting are doing electrophysiology and detailed computerized testing on every patient, but that is not the case. Even in the teaching hospitals in the western countries, in clinical practice, most physicians are relying upon simple clinical examination. The primary care physician contribution in terms of screening and managing DPN at early stages can prevent many cases of diabetic foot ulceration, and ultimately reduce the number of amputations.

**REFERENCE**