

Autonomic Neuropathy: Diagnosis and Treatment

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Ask most people with diabetes what neuropathy means and they'll quickly refer to symptoms of burning feet or numbness in the extremities. But these well-known manifestations of peripheral sensory neuropathy only tell half the story; in fact, as many as 60 percent of people with diabetes may suffer from autonomic neuropathy, another less-mentioned form of peripheral neuropathy. And while autonomic neuropathy may actually be considerably more deadly than its more familiar cousin, awareness of the condition and its dangers is only beginning to grow among doctors and patients alike.

While diabetic sensory neuropathy damages the sensory nerves in the extremities, diabetic autonomic neuropathy involves damage to the nerves serving the heart, all internal organs, and other processes that are not under direct conscious control. Impairment of the nerves serving the bladder or genitalia may cause urinary incontinence or erectile dysfunction. Sweat gland function may be affected, leading to uncontrolled perspiration, or a lack of it, resulting in overheating and dry skin. Autonomic neuropathy may also affect the nerves that internally sense blood pressure, leading to blood pressure that is too high or too low. Yet another complication is gastroparesis, a dysfunction of the stomach's autonomic nerves that may lead to slowed digestion, bloating, constipation, diarrhea, nausea, and vomiting.

Recent research indicates that autonomic neuropathy's most common and life-threatening consequences may be cardiac. Cardiovascular autonomic neuropathy can affect both heart rate control and cardiovascular dynamics. Add these effects to the already-serious tendency of diabetes to raise blood lipids and you have a condition ripe for disaster. Studies indicate that the onset of later-stage, symptomatic diabetic autonomic neuropathy is associated with a 50 percent mortality rate over the following five yearsⁱ

Early detection and intervention are of prime importance in heading off the potentially serious consequences of autonomic neuropathy. Yet surveys indicate that as few as 8 percent of diabetes patients know what autonomic neuropathy is, and only 2 percent believe they have undergone screening.ⁱⁱ To compound the awareness problem, diabetic neuropathy has a slow and insidious onset, and many patients may suffer from the condition unknowingly for years. Case reports

abound in which autonomic neuropathy has gone undetected in patients with other chronic conditions such as Parkinson's disease. Studies indicate that as many as 60 percent of all people with diabetes have some form of neuropathy, although an estimated 30 to 40 percent of those are in the pre-symptomatic stage and are therefore unlikely to know of their condition¹.

In our practice, we make a concerted effort to quickly identify patients with pre-symptomatic and symptomatic autonomic neuropathy, and then use a variety of interventions to get their condition under control. We routinely measure patients' heart rate variability, which research shows can help detect diabetic autonomic neuropathy in its early pre-symptomatic stages.

The American Heart Association and the American Association of Clinical Endocrinologists both recently declared heart rate variability as a recommended test for detecting autonomic dysfunction in diabetesⁱⁱⁱ. Heart rate variability testing has previously been limited to the research lab setting due to the fact that it called for customized and computerized analysis of electrocardiograms, but today physicians nationwide can incorporate a heart rate variability test, such as the DyAnsyst System, into a single office visit.

Using the DyAnsyst test, we look at heart rate variability response. We are able to track patients' heart rate variability over an extended period of time. With these and other test results as our guide, we can quickly set an individualized treatment regimen. People with diabetes should be tested for heart rate variability at least once per year as part of their personal diabetes management routine.

More than 25% of diabetics achieve heart rate variability test scores below the 5th percentile (and therefore abnormal) for a healthy population. Therefore, this form of testing identifies a large group with autonomic dysfunction².

When we detect diabetic autonomic neuropathy, the first and most important focus of treatment is blood sugar control. We find that many of our patients, particularly those with Type 2 diabetes, have not been under tight control for some time. Until recently, researchers were unsure as to whether high blood sugar levels were actually responsible for complications of diabetes. In 1993, the results of the Diabetes Control and Complications Trial (DCCT) largely put those doubts to rest. The nationwide study looked at 1400 people with Type

¹ Ziegler D. Diabetic cardiovascular autonomic neuropathy: prognosis, diagnosis and treatment. *Diabetes Metab Rev* 10:339-383, 1994

² Ewing D, Martyn R, Young R, and Clarke B. The value of cardiovascular autonomic function tests: 10 years experience in diabetes. *Diabetes Care* 8:491-498, 1985.

1 diabetes, half of whom followed their regular self-treatment regimen, and half who adopted a tighter standard for blood sugar control. Early signs of kidney and eye disease were significantly lower in the tighter-control group, and their rates of diabetic neuropathy were 60 percent lower³. Tight blood sugar control appeared so beneficial that the study was stopped a full year early so that the results could be announced.

Tight blood sugar control is now the standard treatment for Type 1 diabetes, and additional studies from Japan and Europe indicate that controlling blood sugar slows the development of complications in people with Type 2 as well. Patients with Type 2, however, must walk a finer line; tight blood sugar may have the somewhat paradoxical effect of increasing weight in many patients, and weight gain exacerbates diabetes. Maintaining healthy blood sugar levels while controlling or reducing weight remains a challenge for many people with diabetes. Most diabetologists recommend that people who want to avoid neuropathy should work with an endocrinologist, a dietician and a diabetes nurse educator.

Those without diabetes begin treatment with ProArgi9 plus at a double dose and Mistica at a double dose. Retesting beginning at 30 days sets the pace for the time for reversal. If the situation is not progressing fast enough, the addition of Core Greens is necessary. Treatment continues until normal and then checked each 6 months until one year. Then it is checked yearly.

The consistent yearly check is necessary since the etiology is unknown. With diabetes we have a traditional series of measurements where all the neuropathy can be watched in addition to the autonomic neuropathy. New medications as Byetta and Januvia appear to add efficiencies to diminishing the swings of blood glucose and may add to success.

Type 1 diabetes can use all these therapies but in the past we have developed proven therapies that have shown to be quite useful.

We begin our intervention by introducing the patient to the use of an insulin pump, which we have found extremely effective in helping to control even the most “brittle” diabetic patients. The pump can deliver a slow, steady dose of insulin, mimicking the role of the pancreas, which normally supplies the body with insulin. At the same time, the pump can be set to deliver large “bolus” doses of insulin at mealtimes, again, just as the pancreas does. Our goal is to

³The DCCT Research Group. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. *The New England Journal of Medicine* 329: 977-986, 1993.

consistently bring patients' glycosylated hemoglobin levels below 7.0%, and using the pump, we can usually achieve this within one month.

We also use a number of other interventions to ward off coronary artery disease, including administration of 800 mg of the antioxidant vitamin E per day, and L-arginine, an amino acid that smoothes the internal lining of blood vessels.

Perhaps the most important things we can do for our patients with diabetes are to make them aware of autonomic neuropathy, to let them know whether they have it, and to help them keep blood sugar levels in an acceptable range. Doing so not only helps reduce the risk of heart disease, but also lowers the risk of diabetic eye, kidney and nerve disease, each of which patients dearly want to avoid.

Diabetic autonomic neuropathy has been called a "silent killer," because so few patients realize that they suffer from it, and yet its effects can be so lethal. With a brief, 15-minute test that we can administer in the office, and some relatively modest interventions, we can help many patients live longer, healthier lives.

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¹ Vinik, Al, MD, PhD, and Suwanwalaikorn, S, MD: *Autonomic Neuropathy*, In deFronzo, R.M. (ed). *Current Therapy of Diabetes Mellitus*. Yearbook Inc. 1997; 165-176.

² NFO Research, Inc.: *The Diabetic Autonomic Neuropathy Awareness Survey*, commissioned by Boston Medical Technologies, Wakefield, Massachusetts. March 2001.

³ *The American Association of Clinical Endocrinologists Medical Guidelines for the Management of Diabetes Mellitus: The AACE System of Intensive Diabetes Self-management – 2000 Update*, *Endocrine Practice* 2000; 6(1): 43-84; American Heart Association, 1999. *AHA Scientific Statement; Diabetes and cardiovascular disease. Circulation* 100:1134-1146.

