

## Small Fiber Sensory and Autonomic Neuropathies

**S**mall fiber neuropathy (SFN) results from damage to the small, unmyelinated nerve fibers. These nerves convey pain and temperature sensations from the skin, and mediate autonomic functions. Sensory symptoms can include numbness, hypersensitivity, and annoying or painful paresthesias such as burning, tingling, stinging, or aching sensations, among others. These are often present in the arms and legs, but can occur anywhere in the body including the torso and face (Walk et al, 2003; Lauria et al, 2005a). Autonomic manifestations can include such symptoms as dizziness resulting from postural hypotension or tachycardia, gastroparesis, incomplete bladder emptying, and sexual dysfunction (Low et al, 2003; Freeman 2007). The neurological examination, EMG and nerve conduction studies that measure the large nerve fibers are usually normal, so that the diagnosis can be missed if not suspected (Lacomis, 2002; Herrmann et al, 2004).

**The diagnosis of SFN can be made in the office by skin punch biopsy. Please refer to the tabs marked ENFD and SGNFD for more information.**

Making the diagnosis of SFN differentiates the condition from other causes of pain, and enables the physician to explain the symptoms, direct further testing for underlying causes, and institute appropriate treatment. Studies show that providing an explanation of the symptoms and reassuring the patients that their evaluation is complete is as important to patients as treatment of their pain (Petrie et al, 2005; McCracken et al, 2002).

The causes of small fiber neuropathy are diverse, and in some cases, the neuropathy is the first manifestation of an underlying systemic disease. Some common causes include diabetes mellitus or glucose intolerance, B12 deficiency, and Sjogren's syndrome (Brannagan et al, 2005; Devigli et al, 2008; Chai and Logigian 2010). A more complete listing of the causes of small fiber neuropathy, and the corresponding diagnostic tests are given in the table below.

In one study, approximately 40% of patients had no identifiable cause on initial evaluation, but in a 2 year follow-up, a cause was identified in 25%, and 13% of the patients developed a large fiber neuropathy (Devigli et al, 2008). Therapy is directed at the underlying cause as well as the symptoms.



Causes of Small Fiber Neuropathy	Evaluation
Diabetes Mellitus, glucose intolerance, hypothyroidism	Fasting glucose, glycosylated hemoglobin, glucose tolerance test, thyroid functions
Sjogren's syndrome	SSA-Ro and SSB-La antibodies, salivary or lacrymal duct biopsy
Lupus erythematosus, scleroderma, mixed connective tissue disease, psoriasis	ANA, dsDNA antibodies, SCL-70 antibodies, Sm antibodies, RNP antibodies, biopsy
Vasculitis	Biopsy of skin, nerve, or muscle, ANCA, cryoglobulins, HCV, RF
Sarcoid	Chest radiogram, biopsy
Inflammatory bowel disease	History, small or large bowel biopsy
Nutritional deficiency	Serum B12, B6, or B1 vitamins
Celiac disease	Gliadin and transglutaminase antibodies, duodenal biopsy
Lyme disease	Serological tests for Lyme antibodies
HIV-1 infection, HCV infection	Serological tests for HIV-1 or HCV antibodies
Fabry disease	Alpha-galactosidase A activity
Amyloidosis	Biopsy, free light chains, transthyretin mutations
Alcohol abuse	History
Toxins, drugs, vaccination	History of exposure, urine or blood toxin levels