Introduction: Small Fiber Neuropathy results from damage to the small unmyelinated nerve fibers that connect the pain receptors in the skin to the spinal cord. The condition is diagnosed by demonstrating a reduction of the epidermal nerve fiber density (ENFD) in a skin punch biopsy. The diagnosis can be missed by routine EMG and nerve conduction studies, as these only measure the large fiber nerves. Making the correct diagnosis explains the symptoms, helps decide treatment and directs the evaluation of an underlying cause. The Epidermal Nerve Fiber Density is reported as the average number of nerve fibers that cross the basement membrane from the dermis to the epidermis, over 1mm length of skin.

Image 1: This image demonstrates skin with normal nerve fiber density (Epidermal Nerve Fiber Density). Arrow points to the small nerve fiber in the epidermal layer of skin, arrowhead points to the basement membrane that separates the dermis from the epidermis.

Image 2: Skin with low normal nerve fibers, consistent with small fiber neuropathy. The arrow points to the basement membrane of the epidermis.

Image 3: Arrowheads point to epidermal nerve fibers. Directly below an axonal bulb is shown. The mechanism of axonal swelling may be related to slowing of axonal transport during axonal degeneration. They may also be seen in regenerating axons and may have more than one cause. Arrows point to basement membrane.

Image 4: Amyloidosis observed with polarizing light microscopy. The arrow points to the apple-green birefringence of the amyloid deposit, previously detected by Congo Red staining, confirming the diagnosis.