The effect of age and gender on epidermal nerve fiber density

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Objective: Sensory neuropathies often involve small-diameter myelinated and unmyelinated nerve fibers, and neurologic and electrophysiologic findings may be normal unless larger nerve fibers are involved. The small (intra)epidermal nerve fibers (ENFs) now can be visualized with immunohistochemical techniques using the panaxonal marker anti-protein gene product 9.5 (PGP 9.5). Using this technique, the authors have established a reference range for ENF in a healthy white population and evaluated the reliability of the method.

Methods: Two punch biopsies, 3 mm in diameter, were taken from the distal part of the leg in 106 healthy volunteers (mean age, 49.0 ± 19.6 years). Fifty-micrometer frozen thick sections were incubated with rabbit polyclonal antibodies to human PGP 9.5. The number of ENF/mm then was reported as the mean of counts in six sections (three sections from each of the two biopsies).

Results: The mean number of ENFs was 12.4 ± 4.6 mm. In a multiple regression model, the density of ENF depended on age and gender ($Y = 13.92 + 2.25 \text{(gender)} - 0.06 \times \text{age}$). The mean difference in ENF by intraobserver analysis was 0.2 ± 1.2 ENF/mm, and by interobserver analysis, it was 0.4 ± 1.5 fibers/mm.

Conclusion: Normal means and ranges for the density of epidermal nerve fibers in a reference population have been established. The density of epidermal nerve fibers decreases with age and is lower in men compared with women. Intraobserver and interobserver analysis proves the reliability of the method.