



Peripheral Nerve Disorders: Chapter 10. The cutaneous nerve biopsy: technical aspects, indications, and contribution (Handbook of Clinical Neurology)

Svein Ivar Mellgren, Maria Nolano, Claudia Sommer

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Skin biopsy with a 3mm disposable circular punch is easy to perform and allows, after proper processing, the visualization of epidermal, dermal, and sweat gland nerve fibers. A technique of sampling the epidermis alone by applying a suction capsule, the “blister” technique, has also been developed. It is most common to stain immunohistochemically for the pan-axonal marker protein gene product 9.5 (PGP 9.5), an ubiquitin C-terminal hydroxylase. The sections are then observed and analyzed with bright-field microscopy or with indirect immunofluorescence with or without confocal microscopy. Most studies report quantification of intraepidermal nerve fiber density displayed in bright-field microscopy. Normative values have been established, particularly from the distal part of the leg, 10cm above the external malleolus. In diabetes mellitus early degeneration of intraepidermal nerve fibers is induced and there is slower regeneration even when there is no evidence of neuropathy. Skin biopsy is of particular value in the diagnosis of small fiber neuropathy when nerve conduction studies are normal. It may also be repeated in order to study the progressive nature of the disease and also has the potential of studying regeneration of nerve fibers and thus the effects of treatment. Inflammatory demyelinating neuropathies may also involve loss of small-diameter nerve fibers and IgM deposits in dermal myelinated nerve fibers in anti-MAG neuropathy. In some cases the presence of vasculitis in skin may indicate a nonsystemic vasculitic neuropathy and in HIV neuropathy intraepidermal nerve fiber density is reduced in a length-dependent manner. In several hereditary neuropathies intraepidermal nerve fiber density may be reduced but other abnormalities can also be demonstrated in dermal myelinated fibers. Some small swellings and varicosities may be present in the distal leg skin biopsy of healthy individuals but large axonal swellings are considered as evidence of a pathological process affecting the normal structure of nerves. The indirect immunofluorescence technique with confocal microscopy provides the opportunity to study the complex structure of sensory receptors and cutaneous myelinated fibers and the innervation of sweat glands, arrector pilorum muscles, and vessels.

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