Overview

Useful For
Investigation of polyneuropathies

Reflex Tests

<table>
<thead>
<tr>
<th>Test ID</th>
<th>Reporting Name</th>
<th>Available Separately</th>
<th>Always Performed</th>
</tr>
</thead>
<tbody>
<tr>
<td>SS2PC</td>
<td>SpecStain, Grp II, other</td>
<td>No, (Bill Only)</td>
<td>No</td>
</tr>
<tr>
<td>COSPC</td>
<td>Consult, Outside Slide</td>
<td>No, (Bill Only)</td>
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<tr>
<td>CUPPC</td>
<td>Consult, w/USS Prof</td>
<td>No, (Bill Only)</td>
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<tr>
<td>CRHPC</td>
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<td>MANPC</td>
<td>Morph Analysis, Nerve</td>
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<td>LV4RP</td>
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<td>Consult, w/Slide Prep</td>
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<td>EM</td>
<td>Electron Microscopy</td>
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<td>No</td>
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<tr>
<td>IHPCI</td>
<td>IHC Initial</td>
<td>No, (Bill Only)</td>
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</tbody>
</table>

Testing Algorithm
A battery of enzyme histochemical stains or immunostains are performed; other tests can be performed as indicated and will be charged separately.

Wet tissue for consultation: When adequately prepared tissue is provided, routine testing will include: PGP 9.5 immunostain, morphometric analysis, Congo red stain, and hematoxylin and eosin stain.

Slides and blocks sent for consultation must include PGP 9.5-reacted sections:

Special stains and studies performed on the case should be sent with the case for review. In order to determine an accurate diagnosis, some of these stains or studies may be deemed to warrant repeat testing at an additional charge at the discretion of the reviewing Mayo Clinic neuromuscular pathologist. In addition, testing requested by the referring physician (immunostains, molecular studies, etc) may not be performed if deemed unnecessary by the reviewing Mayo Clinic neuromuscular pathologist. For all consultations, ancillary testing necessary to determine a diagnosis is ordered at the discretion of the Mayo Clinic neuromuscular pathologist. An interpretation, which includes an evaluation of the specimen and determination of a diagnosis, will be provided within a formal pathology report.

See Pathology Consultation Ordering Algorithm in Special Instructions.

Special Instructions
- Epidermal Nerve Fiber Density Patient Information
- Epidermal Nerve Fiber Density Instructions
- Pathology Consultation Ordering Algorithm
Method Name
Calculation of Epidermal Nerve Fiber Density

NY State Available
No

Specimen

Specimen Type
Varies

Necessary Information
Neurology Clinical Notes information is required on Epidermal Nerve Fiber Density Patient Information (T702) in Special Instructions.

Specimen Required
Supplies: A Skin Punch Biopsy Kit containing fixatives, buffer, and cryoprotectant is required (no substitutions accepted). For ordering information, call 507-284-8065.

Preferred:
Specimen Type: Skin punch biopsy tissue

Preferred source: Distal leg, mid-thigh, dorsal foot, and lower abdomen

Collection Instructions:
1. The standard biopsy for evaluating distal small fiber sensory neuropathy includes two 3-mm skin punch biopsies from the same side of the body.

2. Prepare and transport specimen per instructions on the Epidermal Nerve Fiber Density Instructions (T703) in Special Instructions.

Specimen Stability: Refrigerated (preferred)/Ambient

Acceptable:
Specimen Type: Slides

Additional Information:
1. Slides reacted with PGP 9.5, using a PGP 9.5 protocol for visualizing epidermal nerve fibers, are required.

2. Hematoxylin and eosin-stained slides and Congo red-stained slides are optional.

Specimen Stability: Ambient (preferred)/Refrigerated

Specimen Type: Tissue block and PGP9.5-reacted slides
Additional Information:

1. Slides reacted with PGP 9.5, using a PGP 9.5 protocol for visualizing epidermal nerve fibers, are required.

2. Tissue block may be used to create hematoxylin and eosin-stained slides and Congo red-stained slides.

Note: Visualization of epidermal nerve fibers cannot be done on paraffin blocks.

Specimen Stability: Ambient (preferred)/Refrigerated

Forms

Epidermal Nerve Fiber Density Patient Information (T702) is required, see Special Instructions.

Reject Due To

All specimens will be evaluated at Mayo Clinic Laboratories for test suitability

Specimen Stability Information

<table>
<thead>
<tr>
<th>Specimen Type</th>
<th>Temperature</th>
<th>Time</th>
<th>Special Container</th>
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<tbody>
<tr>
<td>Varies</td>
<td>Refrigerated (preferred)</td>
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Clinical and Interpretive

Clinical Information

Small fiber peripheral neuropathy is a common neurological complaint and a frequent source of morbidity in many patient populations. Direct investigation of small fiber involvement has been limited as most classical techniques such as electromyography (EMG), nerve conduction studies (NCS), and nerve biopsy, focus on large diameter nerve fibers and may be normal in patients with small fiber neuropathies.

The advent of epidermal skin biopsies and PGP 9.5 immunohistochemistry allows the direct visualization and morphologic assessment of small sensory fibers innervating the skin.(1) Assessment of intraepidermal nerve fiber density has been used to reliably demonstrate pathologic abnormalities in small fiber neuropathy of various etiologies including diabetes, HIV, systemic lupus erythematosus, and neurosarcomiosis. Further, the technique has been validated, shown to have acceptable sensitivity and specificity, and is minimally invasive. The publication of normative data for commonly tested sites such as the distal and proximal legs and arms permits direct comparison of patients to age- and sex-matched controls facilitating localization and diagnosis.(2-4)

Based on class 1 evidence and American Medical Association CPT code review process acceptance, intraepidermal nerve fiber density (IENFD) measurements are now an accepted investigational method in the workup of polyneuropathy, including the characterization and diagnosis of varieties of length-dependent small fiber polyneuropathies. IEFND measurements have been incorporated in recent practice guidelines published by the American Academy of Neurology and the European Federation of Neurological Science.(5,6)

Reference Values

A consultative report will be provided.

Interpretation
The number of intraepidermally originating nerve fibers that cross the basement membrane between the dermis and epidermis are counted in several sections.(2,5) The total linear length of the epidermis is measured using standard morphometric techniques and a density of epidermal nerve fibers (number of fibers/mm) is reported. This value is compared to previously published normative data.

Cautions
Poor fixation, orientation, and improper handling of the tissue may hinder the neuromuscular pathologist's interpretation of the biopsy. See Epidermal Nerve Fiber Density Instructions in Special Instructions.

Supportive Data
Investigators at Mayo Clinic (Bolton, Winkelmann, Dyck) did previous work on cutaneous receptors preceding the recent work on intraepidermal nerve fiber densities. With recent findings, PJ Dyck and colleagues have developed the technique to national standards.(7)

Clinical Reference

Performance

Method Description

PDF Report
No
Test Definition: SPBX
Epidermal Nerve Fiber Density

Day(s) and Time(s) Test Performed
Monday through Friday; Varies

Analytic Time
12 days

Maximum Laboratory Time
20 days

Specimen Retention Time
Slides and blocks kept indefinitely

Performing Laboratory Location
Rochester

Fees and Codes

Fees
- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their Regional Manager. For assistance, contact Customer Service.

Test Classification
This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. This test has not been cleared or approved by the U.S. Food and Drug Administration.

CPT Code Information
88305-(if appropriate)
88313-(if appropriate)
88321-(if appropriate)
88323-(if appropriate)
88323-26-(if appropriate)
88325-(if appropriate)
88348-(if appropriate)
88356-(if appropriate)
88342-(if appropriate)

LOINC® Information

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