



Quick guide to small fibre neuropathy (SFN)

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What is small fibre neuropathy?

Small fibre neuropathy (SFN) is characterised by damage to the A δ and Group C nerves. This damage causes autonomic and/or sensory dysfunction. It is often caused by, or comorbid with, conditions such as lupus, Sjögren's, connective tissue disorders, metabolic problems, rheumatic arthritis, B12 deficiency, etc.

What are the symptoms of small fibre neuropathy?

Symptoms are often systemic and can be all-consuming. A stocking-glove presentation is most classic, with symmetrical and length-dependent symptoms. However, more diffuse or patchy presentations can occur. Symptoms can include:

General:

- Fatigue
- Early satiety
- Hypersensitivity to touch
- Pain
- Restless legs (especially at night)

Eyes, mouth, nose, & throat:

- Dry eyes
- Dry mouth

Gastrointestinal:

- Constipation and/or diarrhoea
- Nausea and/or vomiting

Genitourinary:

- Bladder incontinence
- Nocturia
- Polyuria
- Sexual dysfunction

Muscle & connective tissue:

- Cramping in feet/calves
- Feeling of feet swelling or tightness
- Feeling of "walking on sand/golf balls/pebbles"
- Musculoskeletal pain

Neurological:

- Aching or stabbing pains
- Cognitive dysfunction
- Feeling of electric shocks
- Headaches
- Orthostatic intolerance
- Pins and needles

Skin:

- Difficulties/abnormal sweating
- Numbness
- Skin discolouration

Findings such as weakness, reduced proprioception, and absent deep tendon reflexes should not be seen in SFN, as they instead indicate large fibre problems or other pathology

How is small fibre neuropathy diagnosed?

Diagnostic criteria can vary, but some guidelines propose that SFN can be diagnosed as follows:

Possible: Symptoms are length-dependent and/or clinical signs (pinprick and thermal sensory loss and/or allodynia/hyperalgesia)

Probable: Symptoms are length-dependent, plus clinical signs of small fibre damage and normal nerve conduction studies

Definite: Symptoms are length-dependent, plus clinical signs of small fibre damage, normal nerve conduction studies, and altered intra-epidermal nerve fibre density at the ankle and/or abnormal quantitative sensory testing of thermal thresholds at the foot

Intra-epidermal nerve fibre density can be considered low if it is below the fifth centile relative to age- and gender-matched controls.

Research suggests combination testing is most effective at diagnosing SFN.

What tests are there for small fibre neuropathy?

Testing should include ruling-out conditions that can present similarly, and investigating any potential causes of SFN. Specific testing can include:

- **Nerve conduction test or needle EMG** (this tests large nerves so is expected to come back normal)
- **Skin biopsy**
- **Quantitative sudomotor axon reflex test or sweat test (QSART)**
- **Quantitative sensory testing (QST)**

Other tests and diagnoses should also be considered to improve the clinical picture, rule-out other causes, and/or offer potential treatment options:

- Full blood count; kidney and liver function tests; cholesterol panel; HbA1c, fasting glucose, and/or oral glucose tolerance test
- Erythrocyte sedimentation rate; C-reactive protein
- Antinuclear antibody; ENA screen
- Vitamin B12, methylmalonic acid, and homocysteine; thiamine; pyridoxine
- Tissue transglutaminase and antigliadin antibodies
- Human immunodeficiency virus (HIV) and hepatitis C virus antibodies
- Tilt table and/or other autonomic testing
- Angiotensin-converting enzyme
- Copper
- Serum and urine monoclonal protein analysis, nerve biopsy, and fat pad analysis
- Paraneoplastic autoantibody panel
- Ganglionic acetylcholine receptor antibodies
- SCN9A and SCN10A genes (hereditary SFN)
- GLA gene (Fabry disease)
- Transthyretin gene (familial amyloidosis)
- ABCA1 gene (Tangier disease)

What treatments are there for small fibre neuropathy?

Treatment can include treating the underlying cause (e.g. Sjögren's) as appropriate, if known. The NHS do not treat SFN directly, but research and clinical experience of others suggests the following may be helpful:

Target underlying immune dysfunction:

- IVIG
- Corticosteroids
- Other immunosuppressants

Target pain:

- Anticonvulsants (e.g. gabapentin, pregabalin)
- Antidepressants (e.g. amitriptyline, nortriptyline, SSRIs)
- Topical anaesthetics (e.g. 5 % topical lidocaine patch)
- Narcotics (e.g. tramadol)
- Non-narcotic analgesics (e.g. NSAIDs)
- Antiarrhythmics (namely Mexiletine)
- Inhaled cannabis

Target pain (non-pharmacological):

- Heat
- Ice
- Massage
- TENS
- Neuromodulation

Melatonin has been shown to promote peripheral nerve repair, so may have use in SFN, however, this needs to be verified in trials (one trial protocol has been published for neuropathic pain, and promising results have been found in non-clinical studies in the context of diabetic neuropathy)

Resources

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