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Autonomic Neuropathy in Leprosy

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Mycobacterium leprae is the only known bacillus that selectively invades human peripheral nervous tissue.[1] Darab K. Dastur[2] stated that leprosy is perhaps " the commonest peripheral neuropathy in the world..."; it certainly is the leading cause of severe neuropathy in the tropics and subtropics.[3] The peripheral neuropathy of leprosy has been neurologically classified by several investigators as 'mononeuritis multiplex'[4,5], because it is widespread, bilateral, but not homogeneous or systemic. All three components are affected: motor, sensory and autonomic nerves. Sensory loss and motor paralysis are the leading causes for morbidity and permanent severe disability in leprosy patients, and thus remain the prime focus of clinical concern and research. But what is the impact of autonomic neuropathy in leprosy? Reports in the literature are scarce.

Ermakova in 1936[6] demonstrated involvement of sympathetic chain and vagus nerve in leprosy. H.A. Arnold in 1949[7] was the first who studied the anhydrosis in denervated areas of skin in both lepromatous and tuberculoid leprosy. Later N.K. Mathur et al[8] quantified the sweat response. Several more reports followed, such as post ganglionic sympathetic nerve damage within the iris[9], pedal oedema due to autonomic nerve involvement of the capillaries of the legs[10], cardiac dysautonomia[11,12] and respiratory dysautonomia.[13]

The main clinical relevance of autonomic neuropathy in leprosy is peripheral dysautonomia[14]: Damage to vascular autonomic innervation in the skin is followed by loss of vascular tone and stasis of capillary blood resulting in impaired healing of ulcerations. Damage to peripheral sympathetic nerve fibres impairs sweating. Anhydrotic dry skin fissures easily, thus contributing to the vicious circle of secondary infection and ulceration. This is why patient education should not only stress the importance of daily hygiene and care of the anaesthetic limb but also include the necessity of regular lubrication of feet and hands.

Recent electrophysiological studies have looked at peripheral dysautonomia by testing for vasomotor and sudomotor function.[15,16,17] Methods used are the fingertip vasomotor reflex (VMR) and the sympathetic skin response (SSR). VMR measures the degree of fingertip vasoconstriction in response to an autonomic stimulus such as inspiratory gasp and is a method for the detection of subtle focal abnormalities of autonomic function.[18] The sympathetic skin response SSR measures the changes in voltage of the skin in response to exosomatic stimuli.[19] Several investigators found a high percentage of abnormal VMR[15,16,17] and absent SSR in leprosy patients.[17]

As sensory and/or motor impairment in leprosy may be partially or completely reversible with adequate and early treatment[20], is autonomic dysfunction in leprosy also reversible? Due to the lack of data, no conclusion can yet be made. A report from 1964[21] did not find any improvement in the sweating response in leprosy patients after treatment with DDS. Altered sweat function test, valsalva manoeuvre, histamine triple response and cold pressor test in patients with lepromatous leprosy and ENL reaction did not reverse with Clofazimine therapy.[22] However, these patients did not receive steroid treatment. There is now sufficient evidence, that anti-leprosy treatment on its own has no beneficial on leprosy reactions or leprosy neuropathy[23], but that corticosteroids need to be added.[24] In a pilot study[25] a small percentage of patients taking steroids for acute leprosy neuritis improved as tested by vasomotor reflex testing and sympathetic skin response - however, patient number and observation period were too small to be conclusive.

What is the potential value of testing for autonomic nerve function? The prevention of disability in leprosy depends on the early detection and treatment of neural impairment.[26] However, the early detection of leprous involvement of the peripheral nervous system can be difficult, as even before clinical signs of leprosy are evident, there is evidence that extensive nerve damage has already taken place.[27,28] As early detection of leprosy neuropathy is based on clinical sensory and motor testing,[29] a considerable amount of underlying neural damage is present at the time

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of diagnosis. There is histopathological and immunocytochemical evidence that initial damage occurs in small, poorly or unmyelinated nerve fibers.[27,28,30,31] Therefore neurophysiological tests for peripheral autonomic function may be useful in detecting early defects in leprosy. Using VMR testing in contacts of leprosy patients, recent studies[32] and our own group[16,33] have found a surprisingly high percentage of abnormal VMR in leprosy contacts. Also SSR testing showed a significant higher proportion of contacts had an abnormal result as compared to controls.[17]

Autonomic testing might shed new light on the pathogenesis and evolution of leprous neuropathy. Peripheral autonomic dysfunction in otherwise healthy leprosy contacts might either represent a very early stage of the leprosy disease process or an 'immunopathological scar' associated with a successful immune campaign against M. leprae.[33] Early treatment of leprosy prevents progression to deformity and disability and eliminates transmission of the disease. Consequently, early detection of leprosy should be the focus of research in the near future. Electrophysiological testing of autonomic parameters might be an important strategy to achieve the WHO declared goal of world-wide eradication of leprosy.[26,34] Well designed prospective studies are now needed to investigate whether autonomic nerve testing could eventually contribute to this goal.

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