Leprosy as a neurological disease

On January 25 (World Leprosy Day), the International Federation of Anti-Leprosy Associations (ILEP) organised many events that tried to change the negative stereotypes still associated with the commonest treatable peripheral neuropathy in the world. As The Lancet Neurology went to press, the 17th International Leprosy Congress was taking place in Hyderabad, India, from Jan 30 to Feb 4, with an agenda to eradicate all forms of discrimination and stigma.

Progress has been made in controlling leprosy infection in recent years—according to WHO epidemiological records, the incidence rate decreased globally by 4% during 2007 compared with 2006—and effective antimicrobial treatment against Mycobacterium leprae is freely available. However, many patients are left with permanent disability due to nerve damage, and it is this neurological complication that leads to the visible impairments that cause stigma. Unless the focus moves from controlling the infectious disease of the skin to the identification and treatment of nerve impairment, leprosy disability—and therefore discrimination—will not be eradicated any time soon.

Epidemiological data on disability are not available, but they are likely to show a bleaker scenario than that depicted by incidence rates alone (the latest crude estimate put the number of patients with leprosy-related neuropathy at over 3 million worldwide). In disease-endemic countries, patients’ access to infection control has improved by its integration with primary-health services; however, non-specialised health staff usually lack training and tools for basic nerve-function assessment and in many patients nerve impairment remains undetected at diagnosis. Even in leprosy referral centres, most patients will never receive specialised neurological assessment. According to the ILEP Nerve Function Impairment and Reaction (INFIR) study investigators, the standard clinical tests applied in referral centers (semi-quantitative sensory testing and voluntary muscle testing) might be missing 20–50% of patients with sensory and motor neuropathy at diagnosis. Simple and cheap methods of electrophysiological and quantitative sensory testing that could enable extended surveillance of nerve damage are therefore urgent priorities.

Leprosy-related nerve damage is immune mediated and may start before diagnosis, during antimicrobial treatment, or even after completion of treatment. With time, the immune response can provoke spontaneous clinical manifestations, known as “leprosy reactions”, which are associated with inflammation and acute peripheral nerve damage. Although the different patterns of immune response to M leprae are controlled by host genetic factors, immunological markers that could predict disease susceptibility and disease progression have not been identified. Also unknown are the molecular mechanisms that trigger nerve damage and inflammation. Apart from their potential value in identifying patients at risk and establishing new therapeutic strategies, research on these areas may also serve as a model for nerve degeneration and axonal injury in other demyelinating neurodegenerative diseases, such as multiple sclerosis and Guillain–Barré syndrome.

Antimicrobial therapy—which consists of multi-drug therapy (MDT) with rifampicine, clofazimine, and dapsone—is safe and effective in treating M leprae infection. However, MDT does not stop the inflammatory impairment of nerve function. Although immunosuppressive treatment may reduce the risk of new immune-mediated neuropathy, the consensus is that steroids do not help if nerve impairment has lasted for more than 6 months, and a recent Cochrane review failed to find evidence of significant long-term benefit for prednisolone in improving nerve function even in patients with impairments of less than 6 months’ duration. More evidence is urgently needed to clarify both the prophylactic and therapeutic use of steroids and other immunosuppressants; further randomised clinical trials should also define optimum regime in newly diagnosed patients and in those with leprosy reactions.

With the endorsement of ILEP, WHO has implemented a set of operational guidelines to reduce the global burden of leprosy over the period 2006–2010. The strategy encourages every country to develop its own detailed guidelines to manage the disease. It is time to move beyond skin-deep paradigms and consider leprosy as a disease of the peripheral nervous system. In all local programmes, detection and treatment of nerve-function impairment at its earliest stage must be prioritised. Only the cooperation between dermatologists and neurologists in well equipped referral services will ensure optimum clinical care and speed up the fight against stigma. ■