Clinical aspects of nerve damage in leprosy
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SUMMARY
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Leprosy is a chronic infectious disease caused by the bacillus *Mycobacterium leprae*, a fact that is either unknown or of little interest to most of those affected by leprosy in Nepal and elsewhere in the world where this disease is still endemic. The World Health Organization considers leprosy a public health problem as long as the prevalence is over 1 case per 10,000 persons. For operational purposes only those who need or are under chemotherapy are considered "leprosy cases". With constant changes in the recommended (especially length of the) MDT regimens and with a lack of 10 years defaulter rates, it seems very questionable whether the prevalence rate of leprosy is a reliable parameter for weighing it as a public health problem. A more realistic parameter is the new case detection rate, a figure that has not come down in the last 15 years. Consideration can be given to viewing leprosy as a public health problem as long as the prevalence is more than 1/10,000 or when, after becoming less than 1/10,000, the new case detection has not come down in 3 of the 5 consecutive years. In the year 2000, 738284 new patients were registered world-wide. They may be confronted with the often-disabling consequences of leprosy neuritis, social isolation, mental stress, economical downfall and, when skilled assistance is offered, the difficult road towards rehabilitation. In order to understand the world of Nepali leprosy patients, an introduction into the country of Nepal and the clinical aspects of leprosy is given.

In the second chapter the intense mass survey of Lalitpur District, performed between 1986-1990, is discussed. Eighty-five percent of the 210,358 enumerated inhabitants were examined and 234 new cases were found. The new case detection rate was 2.6 per 10,000 per year and the child detection rate 0.8 per 10,000 per year. In 1999 the new case detection rate had dropped to 0.8 per 10,000 per year. Amongst the newly detected cases of the survey the multibacillary rate was 20% and the disability grade 2 rate was 12%. In 1999 of the 25 new cases, 17 had multibacillary leprosy.
Most of these multibacillary patients had worked and lived outside Lalitpur district for many years. It was concluded that adequate training of health post staff and village health workers can both improve compliance as well the earlier detection of nerve damage. Since then Anandaban Hospital has not only trained this staff of its own district but, at the request of the Ministry of Health, of all staff of this level in the Central Region of Nepal. Disability prevention has received the same priority and timing as the full implementation of MDT. It is concluded that an intense mass survey as conducted in Lalitpur district serves well as a scientific study, but that the costs per newly detected patient renders it far too expensive for such an area with a prevalence rate of less than 10 per 10,000 inhabitants.

In the third chapter we note that neuritis of the lateral femoral cutaneous nerve (meralgia paraesthetica) is observed more frequently in leprosy than in non-leprosy patients and the symptoms may mimic those of e.g. ischialgia. After confirmation of the diagnosis by a diagnostic block with a local anaesthetic solution, therapeutic measures like analgesics, anti-inflammatory drugs, bed rest and, in severe cases, therapeutic blocks containing a corticos-
teroid, can be successfully applied and may suffice. In our leprosy patients with a meralgia paraesthetica, surgical decompression of the affected lateral femoral cutaneous nerve was not needed.

In the fourth chapter it is stated that at present the administration of prednisone remains the first drug of choice for the treatment of nerve function loss in leprosy. However, in only a minority of patients restoration of sensation and muscle function up to a functional level is obtained. In those cases a definite improvement of sensation can still be obtained by our new microsurgical approach named “selective meshing of the epineurium (SME)” in which decompression is realized by the making of small overlapping incisions in the epineurium (much like in meshing a skin graft) while the epineural blood vessels are carefully spared. The improvement is the best when performed as early as possible, and a moderate and a definite improvement was found in 70% of the nerves operated when the procedure was performed within 6 months after loss of sensation, while a definite improvement was still found in 32% of the nerves when operated within 10 years after loss of sensation.

In the fifth chapter the observation is discussed that, due to the scarcity of the cardinal signs of leprosy, pure neural leprosy can be difficult to diagnose. Under such circumstances cytological needle aspiration of an affected nerve can be a safe and valuable tool to set the diagnosis. The method as developed by us at Anandaban Leprosy Hospital is presented in this thesis. In seven out of eleven patients in whom cytological aspiration of the affected nerve was done, multiple acid-fast bacilli were found, thus strongly supporting the diagnosis of pure neural leprosy.

Chapter six describes a new method for the early detection of intrinsic muscle function loss in the foot. Plantar intrinsic foot muscles provide structure to the foot during walking and thus regulate foot sole stresses. In leprosy, unlike with the intrinsic muscle testing of the hand, little attention is paid to the early and regular examination of plantar intrinsic muscle activity. In the prevention of impairment and deformity of the foot most attention goes to the loss of protective sensation. In our view it is therefore not amazing that in spite of the prescription of protective footwear, there is too high a recurrence rate of foot ulcers and that these remain the main indication for admission in hospitals specialized in leprosy. Intrinsic muscle function loss in the foot equals intrinsic muscle function loss in the hand in causing soft tissue damage. In order to assess the intrinsic muscles of the foot we developed and tested a new, simple and non-invasive method called “the Paper Grip Test (PGT)”. As a result of an intrinsic muscle function loss in the foot, as demonstrated by the PGT, often a “Failing forefoot syndrome” (clawing of the toes, flattening of the transverse arch, undue stress under the MTP-1 and MTP-2 joints) can be observed and this may explain why most (recurrent) ulcers can be found in this area. Therapeutic advices to prevent ulceration are discussed of which the most important one is the protection of the forefoot during the push-off phase of walking.
Chapter seven starts with the observation that type-1 or reversal reactions are the major cause of nerve damage and disability in leprosy. The Anandaban Mycobacterium Research Laboratory detected that seropositivity for IgM antiphenolic-glycolipid-1 (PGLA) antibodies, but not IgG anti-lipoarabinomannan or anti-Mycobacterium leprae 35 kDa protein antibodies, was significantly associated with subsequent manifestation of a type-1 reaction (p<0.001). The concentration of IgM anti-PGL-1 antibodies in serum was significantly higher in patients in whom a type-1 reaction developed, and this risk was independent of leprosy class, skin smear positivity, and the presence of other anti-\textit{M leprae} antibodies. It was concluded that anti-PGL-1 positivity and lepromin reactivity are significant independent risk factors for subsequent reaction and patients with these risk factors should be carefully monitored during the first two years after commencing anti-microbial treatment. This monitoring may result in the earlier initiation of anti-inflammatory treatment and so the minimising of impairment and disability.

In chapter eight it is discussed how the contribution of type-1 reactions to sensory and motor function loss in 297 borderline leprosy patients was measured and the efficacy of treatment with prednisone assessed. Of the 297 borderline patients 157 (53%) experienced a type-1 reaction during an average follow-up time of 30.7 months (range 6-74 months). No significant differences were found between BT, BB or BL patients, neither between left and right hands, feet or eyes. A decline in sensation (21%) and muscle strength (13%) in non-reactional patients indicated a silent neuritis of which 71% of the episodes will occur in the first year of MDT.

Of the 157 patients with a type-1 reaction treated with prednisone, in 65 (41%) patients there was an improvement in the cumulative sensory test score, in 39 (25%) patients there was a worsening while in 53 (34%) patients the score remained unchanged. In this same group the cumulative VMT scores improved with prednisone in 56 (36%) patients, worsened in 20 (13%) patients and remained unchanged in 81 (51%) patients. These data point to a need to find better regimens for the treatment of nerve damage in type-1 reaction. Patients who were treated as inpatients during their reaction improved significantly more than those treated as outpatients. The difference may be largely explained by the fact that about 20%-30% of the outpatients failed to collect their full course of steroids. The reasons for the non-compliance with this form of treatment are unknown.

Therefore, in chapter nine we try to identify factors that are causing non-compliance. As mentioned earlier the primary concern of those affected by leprosy lies not in the eradication of the \textit{M. leprae} in the body, but merely in how to hide the visible symptoms and to prevent social, physical and economic disablement. The resulting mental stress relates directly to the process of non-compliance with treatment and defaulting. For the identification of factors contributing to mental stress in leprosy patients the WHO Self-Reporting Questionnaire was used, and to this test we added a number of separate questions on socio-economic factors. This test was already validated in Nepal and was designed to measure non-psychotic psychiatric morbidity by scoring twenty questions. We feel with other authors that
a positive score may not necessarily imply “hard” psychiatric morbidity but rather that a patient is experiencing undue mental stress which needs further assessment. In the general Nepali population and when using this test, the prevalence of “psychiatric morbidity” is around 10%. In 1990/1 in the first survey among 411 leprosy patients from the Eastern, Central and Western Regions of Nepal, “psychiatric morbidity” was found in 16.3%. This figure rose significantly in the follow-up survey of 2000/1 to a prevalence of 31.5%. Women, older patients, and those with a visible disability scored significantly higher than males, younger patients, and those without disability. The patient’s own outlook on their disease and their future was also associated with a high risk of psychiatric morbidity. This latter association persisted after adjustment by other factors, suggesting a causal link as well as a logical association as a product of psychiatric morbidity. Among the strongest “protective factors” was education and literacy. Patients with families whom they reported as treating them well and with a belief in their own eventual cure were at significantly lower risk of developing psychiatric morbidity; this effect however was removed after adjusted Odds ratios were calculated. Comparison of the two cohorts showed in 2000/1 suggested that social circumstances seemed to have improved with a higher proportion of patients telling their families about their disease and living with their own families; this implies less social rejection than the patients of the 1990/1 experienced. Nevertheless there were also more patients who stated that their families avoided them and that they faced difficulties in going to the shops. In 2000/1 more patients gave “germs” as the cause of their disease. Importantly, fewer patients in 2000 believed that they would be cured than in 1990. The knowledge gained by these surveys is helpful in monitoring mental stress and thus in the timely offering of assistance. Ultimately, one can expect that this will be reflected in an enhanced quality of leprosy care.

For those affected by leprosy the magnitude of their problems is mostly beyond the limited reach of the surgeon’s scalpel and their burden is not relieved by sterile statistics. In order to be of any real assistance, we are all challenged to involve ourselves in the leprosy patients’ personal world in its widest sense. A small part of this endeavour is reflected in this thesis.