Our study suggests that emphasis must still be placed on instituting adequate measures for early detection of ocular complications of leprosy, particularly where there is, or has been, a high prevalence of multibacillary leprosy. Continuing care of treated patients is required to prevent blinding complications of established ocular impairments such as corneal anaesthesia and inadequate eyelid closure. Other epidemiological factors which may contribute to the high prevalence of blindness in the Jhalda study group will be discussed.

This study provides evidence that in leprosy, particularly of multibacillary type, blindness remains a significant risk which requires to be addressed in all leprosy control and treatment programmes.

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MECHANISM OF NERVE DAMAGE IN LEPROSY

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Nerve damage leading to impairment and permanent disability is still the major problem in the course of a leprosy infection. This nerve damage may occur before, during and after anti-mycobacterial treatment, especially during so called reactional episodes. Two types of nerve damaging immunological reactions are recognised, the reversal reaction (RR) or type-1 reaction and the erythema nodosum leprosum (ENL) or type-2 reaction. The immunological and pathophysiological mechanisms behind the reaction will be discussed. This will include recognition of M.leprae antigenic determinants on bacilli and self antigens, cytokines among which TNF-alfa and adlhesion molecules like N-Cam. Silent neuritis (nerve damage) will be included.

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IMMUNOLOGICAL STUDIES IN LEPROUS NEURITIS

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Immune complexes were found raised in a sequential study both in B.T and LL groups of patients with reduced complement mediated solubilization (Ramanathan et al, 1998)· Since painful neuritis is an important problem in leprosy, a histoimmunological study on 30 nerve biopsies of patients with neuritis was carried out (Ramanathan et al, 1989) Immunoglobulins and complement were detected in a proportion of cases and mycobacterial antigen even in the absence of intact bacilli. In an ongoing study, 103 leprosy patients and 14 healthy normal individuals were investigated for serum anticeramide IgM and IgG antibodies. The patients belonged to three groups, namely A. patients with painful neuritis, B. patients who had been treated for neuritis, C. patients without painful neuritis.

Antibodies to ceramides were significantly raised in all groups of patients. IgG antibodies were raised in large number of A and B groups. IgG antibodies are involved in autoimmune disorders. A number of investigators have suggested that auto-immunity may have a role in Leprous neuropathy which our studies also indicate.

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ALTERATIONS IN AXONAL NEUROFILAMENT PROTEIN AND SILENT NERVE DAMAGE IN LEPROSY

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Through morpholopjcal studies it was firmly established that a reduction in axonal caliber (atrophy) precede demyelination leading to conduction block and is the manner in which silent nerve damage occur in leprosy. We have sought to study the biochemical basis of atrophic changes in leprous nerves. The study was planned with following 4 objectives based on the assumption that the axonal caliber is governed by the carboxy terminal phosphoylation of high molecular weight neurofilament protein (NFH).

1. Study through immunocytochemistry the state of NF phorphorylation in the affected peripheral nerves in leprosy.

2. To correlate the morphological and immunocytochemical changes.

3. To demonstrate the presence of altered phosphorylated form of NFH.

4. Biochemical correlates of NF phosphorylation by quantifying the enzyme(s) which regulate the phosphorylation on carboxy terminal region.

The study was carried out in a total of 22 leprous and 4 normal human peripheral nerves and in the experimental mouse sciatic nerve model for leprosy. The results

explicitly demonstrate both morphological and biochemical evidence of alteration in NFs. There was hypophosphorylation of NFs, priorer to atrophy, was demonstrated using SMI-31 antibody, that specifically binds to phosphorylated - COOH terminal of NFH and NFM. Antigens of

M.leprae seem to play a crucial and specific role in the sequence of events. However there was no CDK5 activity detected in both normal and leprous peripheral nerve supernates, indicating that, other kinases may be involved.

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RETROSPECTIVE STUDY ON DAMAGE OF THE LOWER EXTREMETES NERVES AND THEIR BRANCHES IN LEPROSY

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Objective : To study the incidence and clinical feature of n.tibialis, n.peroneus communis and their branches damage in leprosy.

Methods : Examine 275 cured patients carefully including 63 hospitalized cases and 212 cases living in communities.

Results : The damage incidence of the lower-limb nerves was 65.45%(180/275) in cases or

53.09% (292/550) in nerves. The tibial nerve damage incidence was 54.18% (149/275) or 43.64% (240/550). The damage incidence of tibial nerve branches were in muscularis popliteal fossa and leg of 1.82% (5/275) or 1.09% (6/550) , n.cutancous surae medialis of 22.18% (61/275) or 17.09% (94/550) , n.calcanealis of 38.91% (107/275) or 30.55% (168/550), n.plantaris medialis of 44% (121/275) or 35.27% (194/550) and n.plantaris lateralis of 45.82% (126/275) or 36.91% (203/550) respectively. The damage incidence of n.peroneus communis was 59.27% (1631275) or

46.18% (254/550) and its branches were n.cutaneous surae lateralis 41.45% (114/ 275) or 30.55% (168/550), n.peroneus superficialis of 52.36% (144/275) or 39.64% (218/550) and n.peroneus profuntus 44.36% (122/275) or 33.45% (184/550) respectively. The damage of lower limb nerves is related to leprosy type and diseased duration, which characterized with more sense impairment and motor impairment secondly.

Conclusion : The damage of lower limb nerves was most frequent and useful to diagnosis, classification and finding risk nerve through its clinical symptoms. Authors considered that the early case-finding, early diagnosis and early treatment be the most important measures to control disability.

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TRIPOD TRIAL - PROPHYLACTIC USE OF PREDNISOLONE, RESULTS AT 4 & 6 MONTHS

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The TRIPOD trial is a double blind, placebo controlled, multi-centre trial of the use of Prednisolone in three aspects of leprosy treatment - prophylactic use for the prevention of nerve function impairment, treatment of early sensory nerve function impairment and treatment of longstanding nerve function impairment. First results are available for the part of the trial looking at prophylactic use of Prednisolone.

DESIGN - Six centres in two countries (Bangladesh and Nepal) recruited over 600 newly diagnosed MB patients to the trial. Patients had either no detectable nerve function impairment or pre-existing nerve function impairment of duration greater than six months. Other entry restrictions also applied. Half received Prednisolone and half an identical placebo tablet. All centre staff- including prescribing paramedics, physiotechnicians monitoring patients and the supervising medical staff were blind to the type of tablet used for each patient. Informed consent was received for each patient entering the trial.

PROTOCOL - Prednisolone/placebo was given as a 20 mg daily dose for 3 months, with a tapering dose in the 4th month.

FOLLOW UP - Patients returned, or were traced, for follow up at 1,2,3,4,6,9,&12 months. A late follow up at 24 months will assess the incidence of TB in the two groups.

OUTCOME MEASURES - At each follow up, the patients were assessed for nerve function impairment by sensory testing with graded ono-filaments, voluntary muscle testing and assessment of nerve tenderness. Fixed criteria were applied for the diagnosis of nerve function impairment and removal of a patient from the trial. Potential side effects were checked according to a fixed protocol. Presence of severe side effects also resulted in exit from the trial.

RESULTS - Results are available for patients at 4

months (the time of cessation of prophylactic treatment) and at 6 months.

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SENSIBLE MANUAL MUSCLE STRENGTH TESTING TO EVALUATE MOTOR FUNCTION

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Manual muscle strength testing is an established assessment technique to evaluate and monitor motor nerve function impairment (NFI). There is little consensus about important aspects that relate to motor function assessment. Knowledge of these may lead to uniformity in assessment and recording. Uniformity in assessment and recording will facilitate comparison and analysis of data. These aspects will be discussed under 4 headings: Why nerve function assessment, when, by whom and what detail?

Furthermore. information about the reliability of motor function assessment will be given and areas for further research will be indicated.

It is now an established practice to assess nerve function of all suspected and new patients to evaluate if, and to what extent, nerve function may be impaired. Nerve function should be assessed at the time of diagnosis, monthly thereafter. and every time a patient complains about nerve discomfort (pain), and (new) weakness or numbness. Assessment frequency should be increased when there is acute nerve function loss. Each person involved in the diagnosis and treatment of nerve function loss should know how to assess nerve function.

Detail of assessment needed depends on the preliminary findings of motor assessment, the possibility to isolate muscles, biomechanics of the hand and espertise of the examiner.

Few studies have reported about the reliability of muscle testing in leprosy. (Inter) tester reliability is influenced by skill of examiners and availability of, and adherence to. muscle testing protocol. It is also influenced by the number of tests and detail of grading.

More research is needed into the (inter)reliabilitv of manual muscle testing. Additional research is needed to establish to what extent other manual muscle strength testing techniques can be of value in assessing and monitoring motor nerve function in leprosy patients.

A chart to assess and evaluate motor function that allows for simple and detailed assessment and recording will be presented.

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A SIMPLE RULE TO PREDICT NERVE FUNCTION IMPAIRMENT

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Background : Nerve-function impairment (NFI) commonly occurs during or after chemotherapy in leprosy. The data arising from the Bangladesh Acute Nerve Damage Study, a prospective study based on the DBLM project in Nilphamari, Bangladesh, have allowed us to describe the development of NFI and to develop a simple clinical prediction rule for estimating the risk of NFI occurrence.

Methods : New leprosy cases (MBs and PBs) were recruited and followed up for 2 years in a field setting. We used multivariable regression analysis by Cox s proportional hazards model to identify predictive variables for NFI. Discriminative ability was measured by a concordance statistic. Internal validity was assessed with bootstrap re-sampling techniques.

Findings : Amongst 2510 patients, 166 developed new or further NFI during the first 2 years of follow-up. A simple model was developed with leprosy group (either paucibacillary leprosy [PB] or multibaciliary leprosy [MB] and the presence of any nerve-function loss at registration as predictive variables. Patients with PB leprosy and no nerve-function loss had a

1.3% (95% CI 0.8-1.8%) risk of developing NFI within 2 years of registration; patients with PB leprosy and nerve-function loss, or patients with MB leprosy and no nerve-function loss had a 16.0% (12-20%) risk; and patients with MB leprosy with nerve-function loss had a 65% (56-73%) risk.

Interpretation : Our prediction rule can be used to plan surveillance of new leprosy patients. Patients at low risk of NFI may need no follow-up beyond their course of chemotherapy (6 months); patients with intermediate risk need a minimum of 1 year of surveillance; and patients with high risk should have at least 2 years of surveillance for new NFI. Current recommendations for surveillance of patients with leprosy (for the duration of chemotherapy only) exclude an important group of patients who are at risk of developing NFl after completion of treatment.

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PREVENTING NERVE DAMAGE - A STRATEGIC REVIEW Smith W.C.S.

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Introduction : Nerve damage, and the consequences of nerve damage, sets leprosy apart from other diseases. The irreversible motor and sensory impairments caused by leprosy lead to increasing secondary impairments long after the disease process has been arrested. Interventions that prevent, reverse or limit the impairments due to leprosy are therefore of the greatest priority. This review addresses the question of priorities for both research and service provision given limited resources.

Methods : The current research efforts are reviewed in terms of their likelihood of delivering significant health gain in the short and long term. Interventions to prevent nerve damage are reviewed in terms of the effectiveness, feasibility in primary care settings and cost.

Results : The majority of nerve damage occurs prior to diagnosis and efforts to improve early diagnosis and treatment have great potential for preventing nerve damage. Prophylaxis using steroids may be cost effective when targeted to groups at highest risk. Simple means of identifying those at high risk are important. Treatment of acute episodes of nerve damage and reactions is less than satisfactory since not all cases present for treatment and treatment is not always successful. Self-care has been demonstrated to be an effective means of preventing secondary tissue damage but now needs to be developed for implementation within basic health care. Although the benefit may be limited, it may, along with re-constructive surgery, be one of the few approaches open for those who have completed MDT.

Conclusions : Early case detection and MDT treatment is the most cost effective means of preventing nerve damage and the size of the potential benefit is large - this is a priority for research and interventions. Treatment of acute reactions remains a challenge while steroid prophylaxis, if effective, may offer considerable benefit when targeted to those most at risk. Self care has been shown to be effective and may, along with re-constructive surgery, be one of the few approaches available for those who have completed MDT.

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CAN RISK FACTORS IN LEPROSY BE IDENTIFIED BEFORE THEY BECOME OPERATIVE?

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Risk factors in leprosy are defined as factors responsible for reversible and irreversible nerve function impairment (NFI) leading to disability and deformity. 87 patients were inducted into a double blind clinical trial of prednisolone therapy in Type 1 reactions. It was observed that some patients developed recurrence of reactions and hence required an additional course of steroids. Inflation observed in skin lesions may indicate simultaneous sub-clinical inflammation in the nerves endangering their functional integrity. In addition, episodes of nerve inflammation can occur without skin manifestations. Identifying these phenomena through other parameters can help to selectively give higher dose or longer duration of steroids in this special group of patients. In this study, patients needing additional steroids were identified and compared with those not requiring additional steroids using a pre-determined clinical scoring method, scores being allotted to each known risk factor. Some of the known risk factors suggested for the development of Type 1 reaction and /or NFI include face patch, extent of disease, duration of disease, borderline type of disease, nerve involvement, history of reaction, duration of treatment and bacteriological positivity. Despite all the available information, there is as yet no simple test available to predict risk factor responsible for NFI. If risk factors are identified and recognised at the start of chemotherapy, adding a suitable dose of steroids along with MDT would prevent nerve damage/protect the nerve. We describe here a simple and reliable clinical scoring method to estimate the risk of development of NFI before starting chemotherapy. In this paper we recommend the use of a clinical scoring model to predict early NFI which can be used to assign patients into high risk group and plan active intervention and follow up.

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MALARIA, LEPROSY AND MULTI-DRUG THERAPY CONTAINING DAILY 100 MG DAPSONE

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Sulphonamides and sulphones are known to have antimalarial activity. To test this, we carried out serological as well as parasitaemia assessments on 322 lepromatous leprosy patients receiving 100 mg. dapsone daily and 669 healthy subjects, living in three different districts of India, endemic for leprosy as well as malaria. Blood smears fiom 124 lepromatous patients with fever and 379 afebrile control subjects showed that the prevalence of malaria parasitaemia in both the groups was similar and varied from 25% to 30%.