

LITERATURA CORRENTE

CURRENT LITERATURE

ASPECTOS SÓCIO ECONÔMICO E PSICOSSOCIAIS

ASNAKE, M.K.; AHMED, M.; GENEBO, T.; DAWIT, M.W.; MEKEBIB, B. Knowledge and attitude of health professionals in relation to the integration of leprosy control into the general health service in Ethiopia. *Int. J. Leprosy*, v.68, n.3, p.299-306, September, 2000.

Since the introduction of multidrug therapy for leprosy patients, the integration of leprosy control in the general health service (GHS) system has been an issue of debate. In Ethiopia, the present policy stresses integrated management of diseases. In spite of the policy, however, leprosy control was a vertical program until 1998 in most parts of the country. A descriptive cross-section study was conducted in the southern region of Ethiopia from October 1996 to March 1997 to determine the levels of involvement of the GHS staff and to identify obstacles to their involvement in the management of leprosy patients. Through a written questionnaire, data were collected from 240 GHS staff, including doctors, nurses and health assistants. It was found that 6% of the GHS staff was involved in leprosy control activities, mainly case finding and health education. Negative attitudes toward leprosy workers were held by 13% of the GHS staff while 40% had intermediate attitudes and the remaining 47% had positive attitudes. Statistically significant differences were found with regard to the level of knowledge among different health professionals, type of health institutions and years of service. The levels of involvement, knowledge and attitude of GHS staff showed that lack of integration and training were core problems. Hence, policy makers should give due attention to promoting the involvement of the GHS staff by integrating the program into the GHS system using the approach already in place in certain parts of the country.

FLOYD-RICHARD, M.; GURUNG, S. Stigma reduction through group counselling of persons affected by leprosy—a pilot study. *Leprosy Rev* v.71, n.4, p.499-504, Dec., 2000.

Stigmatization of persons with leprosy causes the emotional harm of social, economic and spiritual deprivation. Individual counselling has benefits in addressing these psychosocial problems but is a slow process and affects few people at any one time. Our

experience of group counselling of stigmatized persons achieved the following: addressing common issues to more than one person at a time, encouraging the unity of sufferers, developing compassion for others, understanding the common effects of stigmatization, and beginning to overcome its harmful effects.

RAO, VP; RAO, I.R.; PALANDE, D.D. Socio-economic rehabilitation programmes of LEPR India—methodology, results and application of needs-based socio-economic evaluation. *Leprosy Rev.*, v.71, n.4, p.466-471, Dec., 2000.

There is now a better understanding of the scope and process of rehabilitation. The approach recognizes the impact of leprosy on the individual, aims to understand the needs and concerns of those affected, their families and community in the rehabilitation process, and that aims to restore the person to normal social life. LEPR India has undertaken socio-economic rehabilitation (SER) activities in its projects in Andhra Pradesh and Orissa States in India with a holistic approach that has been evolutionary, developmental and participatory. A SER Officer (SERO) was posted to each project. A plan was formulated by the SERO with participation of all project staff. The main emphasis of the programme was on active participation of the affected person in the rehabilitation process. A needs-assessment study was conducted in the target population using a semi-structured questionnaire. Information was elicited about social and economic status, before and after the disease, and the current rehabilitation needs of the persons affected. The next step was meeting the needs through interventions by the SER staff. The impact of the programme on restoration of social and economic status of the affected persons was analysed. The paper stresses the importance of assessing the needs of persons affected by leprosy, structuring a rehabilitation programme with the active participation of the affected person and evaluating the impact of the interventions in restoring normal social and economic life.

de STIGTER, D.H.; de GEUS, L.; HEYNDERS, M.L. Leprosy: between acceptance and segregation. Community behaviour towards persons affected by leprosy in eastern Nepal. *Leprosy Rev.*, v.71, n.4, p.492-498, Dec., 2000.

This study describes community behaviour towards persons affected by leprosy in the eastern Terai districts of Nepal. The results show that 95% of the persons affected

by leprosy recognized by the community have visible signs such as wounds, swellings and deformed feet or hands. Persons affected by leprosy still experience negative behaviour. Motives for negative community behaviour are mostly found in the fact that people fear infection by germs, but fear of a curse from God is also mentioned. This study shows that negative community behaviour is still present in eastern Nepal. Leprosy is more than a disease; the disease can nowadays be medically cured, but the sickness of leprosy still remains. Leprosy control programmes should focus on prevention of impairments and disabilities, because it seems that a visible sign is an important trigger for negative community behaviour.

CLÍNICA

BURDICK, A.E.; HENDI, A.; ELGART, G.W.; BARQUIN, L.; SCOLLARD, D.M. Hansen's disease in a patient with a history of sarcoidosis. *Int. J. Leprosy*, v.68, n.3, p.307-311, September, 2000.

We report a rare case of concomitant Hansen's disease (HD) and sarcoidosis. Reticulin staining may be a helpful diagnostic tool in establishing the diagnosis of sarcoidosis in skin lesions. The diagnosis of HD can be established despite negative polymerase chain reaction results for the detection of *Mycobacterium leprae* DNA. Finally, a well-established diagnosis of sarcoidosis does not preclude the development of another granulomatous disorder. Hence, when new lesions developed in a patient with sarcoidosis despite appropriate therapy, other concurrent diagnoses should be pursued.

FEENSTRA, W.; VAN DE VIJVER, S.; BENBOW, C.; AMENU, A.; SAUNDERSON, P. Can people affected by leprosy at risk of developing plantar ulcers be identified? A field study from central Ethiopia. *Leprosy Rev.*, v.72, n.2, p.151-157, June, 2001.

In the ALERT leprosy control programme, 75 people affected by leprosy, in three different geographical areas, were investigated. Each person was documented as having anaesthesia to the 10g monofilament. The study sought to determine why some people developed ulcers whilst others did not. According to the records, 43 had an ulcer during the last 5 years but 32 had never had an ulcer. In order to examine protective sensation on the sole of the foot, various sensory modalities were tested and the functional anatomy of the foot was examined. The results showed, as may be expected, that it is not possible to define a specific threshold for protective sensation that could be applied to all cases. Some people with only slightly diminished sensation developed ulcers, while many others with almost complete anaesthesia remained ulcer-free. In these rural communities, being a farmer reduced the risk of developing an ulcer, but no other

demographic features were significant. Graded monofilaments were found to be the most appropriate test, with loss of sensation at any of five points tested being a 'positive' result. The 10 g filament was the most sensitive, but only 43% of feet identified by this test actually developed an ulcer. As people with partial loss of sensation were excluded from this study, this figure may be lower under programme conditions. The 50 g and 100 g filaments decrease the number of feet identified as at risk, but increase the percentage which actually develop an ulcer, to 46% and 49%, respectively. An appropriate test for selecting those for special programmes which may have a limited capacity, for example the provision of subsidized footwear or involvement in self-care groups, would be a 100 g filament, which would detect 86% of those feet likely to develop an ulcer, while reducing the number of those selected who are not at great risk. Vibrometry was found to be no better than graded filaments and an examination of functional anatomy did not help in identifying those at risk.

GEBRE, S.; SAUNDERSON, P.; MESSELE, T.; BYASS, P. The effect of HIV status on the clinical picture of leprosy: a prospective study in Ethiopia. *Leprosy Rev.*, v.71, n.3, p.338-343, Sep., 2000.

No major interaction between HIV infection and leprosy has been documented. The ALERT MDT Field Evaluation Study (AMFES) has allowed the examination of possible interactions in a prospective manner, although the total number of HIV-positive individuals was not high at 22 (3.8%) of 581 patients tested. There was an excess number of deaths in the HIV-positive group: 27% compared with 5.7% in the HIV-negative group, although the causes of death were not recorded (relative risk 4.8; 95% CI 2.2-10.2). HIV-positive individuals had a higher risk of ENL reactions (relative risk 5.2; 95% CI 1.7-15.9). Reversal reactions and neuritis (both acute and chronic) were not significantly influenced by HIV status, although there was a possible increase in recurrent reversal reactions in HIV-positive cases (relative risk 2.2; 95% CI 0.98-4.7). There was no evidence to suggest an increased risk of developing leprosy or of developing multibacillary rather than paucibacillary disease. There was no association between HIV positivity and the development of impairment.

ILLARRAMENDI, X.; JARDIM, M.R.; SALES, A.M.; NERY, J.A.; SARNO, E.N. ACRO-OSTEOLYSIS PRIOR TO DIAGNOSIS OF LEPROSY. *Leprosy Rev.*, v. 71, n.3, p.382-387, 2000.

Acro-osteolysis (bone resorption) has been observed in a heterogeneous group of congenital and acquired bone disorders. Leprosy is the main cause of peripheral neuropathy leading to acro-osteolysis in endemic countries. Pure neuritic leprosy, a less common form of the disease, is difficult to diagnose. Two unrelated leprosy

patients with acropathy whose disease began as pure neuritic are discussed.

ILLARRAMENDI, X.; CARREGAL, E.; NERY, J.A.; SARNO, E.N. Progression of acral bone resorption in multibacillary leprosy. *Acta Leprol.*, v.12, n.1, p.29-37, 2000-2001.

Although leprosy became a curable disease after implementation of the Global Strategy for the Elimination of Leprosy (WHO), mutilations and deformities are still commonplace in endemic countries. Hence, it remains important to evaluate the prevalence rate and the risk factors of acral bone resorption in the multidrug therapy (MDT) era. A cohort of 105 newly-diagnosed adult multibacillary leprosy patients admitted for treatment between 1990-1992 was surveyed until 1999. Progression of bone resorption (BR) in cured leprosy patients was observed up to 8 years after release from MDT. Twenty three percent of the patients were found to have acral resorption. BR was found to be associated with male sex, grade of disability at diagnosis with other deformities and with the occurrence of four or more lepra reactions. Patient surveillance after release from MDT continues to be a necessary procedure in individuals with disabilities and recurrent or persistent reactions.

KALLA, G.; PUROHIT, S.; WAS, M.C. Histoid, a clinical variant of multibacillary leprosy: report from so-called nonendemic areas. *Int. J. Leprosy*, v.68, n.3, p.267-271, September, 2000.

This is a hospital-based study of 25 biopsy-proven cases of histoid leprosy in the arid, northwest Rajasthan region of India. Over an 11-year span, a total of 893 new cases of leprosy were diagnosed at our institution. These 25 histoid cases thus make up 2.8% of our new patients. Various clinical and laboratory observations are summarized and compared to other published series.

KUMAR, B.; KAUR, I.; RA', R.; MANDAL, S.K.; SHARMA, V.K. INVOLVEMENT OF MALE GENITALIA IN LEPROSY. *Leprosy Rev.*, v.72, n.1 p.70-77, March, 2001.

Four hundred and sixty-seven male patients with leprosy were screened for genital involvement. Genital lesions were observed in 6.6% of all male cases of leprosy. They were seen most frequently in lepromatous leprosy (25.8%), followed by borderline lepromatous (13.3%) and borderline tuberculoid (1.4%) leprosy.

KUNST, H. Predisposing factors for recurrent skin ulcers in leprosy. *Lepr Rev.*, v.71, n.3, p.363-368, Sep., 2000.

This study was designed to determine the factors associated with recurrence of leprosy

ulcers. Between

April and August 1992, 55 consecutive leprosy patients admitted with skin ulcers were studied. Factors predisposing to recurrence, e.g. patient's age, disease duration, ulcer site, ulcer depth and physical deformity (taking into account neuromuscular and skeletal damage) were evaluated. Ulcer recurrence occurred in 40/55 (75%) patients. Recurrent ulceration was associated with location in the lower extremity ($P = 0.02$), where recurrences were more common in the midfoot and heel ($P = 0.01$). Recurrence was also associated with severity of physical deformity ($P = 0.01$), which increased the odds of recurrent ulceration by 4.2 times (95% confidence interval, 1.01-18.3). The severity of physical deformity itself was associated with the age of the patient ($P = 0.04$) and the disease duration ($P = 0.02$). In conclusion, there is a need to focus on identification of risk factors for recurrent leprosy ulceration. Targeted prevention strategies would be required if morbidity associated with recurrent skin ulceration is to be avoided.

LEMASTER, J.W.; SHWE, T.; BUTLIN, C.R.; ROCHE, P.W. Prediction of 'highly skin smear positive' cases among MB leprosy patients using clinical parameters. *Leprosy Rev.*, v.72, n.1, p.23-28, March, 2001.

Although 'highly skin smear positive' MB leprosy cases are known to be at high risk of relapse after release from treatment, and have been recommended to receive 'prolonged duration' MDT, government field-based control programmes without skin smear facilities have no simple alternative method to detect such cases. This study reports a significant prevalence of 'highly smear positive' cases amongst 2374 new multibacillary cases recently surveyed by skin smears in Nepal, and retrospectively analyses 555 newly detected, previously untreated BL and LL cases to identify clinical and laboratory parameters that may be associated with a 'highly positive skin smear'. While some parameters showed high sensitivity in predicting 'highly positive smear' status, none showed both high sensitivity and high specificity simultaneously.

MANJUNATH, R.; KAMATH, K.N.; PAI, G.S.; PINTO, J.; VINOD, V. Modified Active Surveillance System (MASS); a novel clinicopathological evaluation of PB leprosy patients after RFT, in Mangalore, India. *Leprosy Rev.*, v.72, n.1, p.50-56, March, 2001.

The current recommendations for leprosy control programmes include stopping active surveillance in view of the very low relapse rates and a phased integration of leprosy services with the general health services. Passive surveillance may not be adequate, more so because of the introduction of newer, shorter drug regimens. This study is an effort to evolve a modified active surveillance, which is cost-effective, simple and also a novel substitute for the increased workload caused by the dwindling number of PMWS. One thousand one hundred RFT-PB leprosy

review under the Modified Active Surveillance System (MASS), carried out over two phases. Patients were divided into groups as per the mode of response to the mailed postcards: Responders (patients who reported to the OPD in person), Untraceables (patients whose postcards returned back) and non-responders (patients who did not report of the OPD after receiving the mail). At the end of phase I, we had 120 Responders, 480 Untraceables and 500 Non-responders. In phase II, which began 2 months later, the 500 non-responders were dispatched reminders. In this phase, there were 31 responders, 60 untraceables and 409 non-responders. Thus, at the completion of phases I and II, there were 151 responders, 540 untraceables and 409 non-responders. Of the 151 patients examined, 71 had no complaints (category I), 41 had fresh leprosy-related complaints (category IIA), 14 had fresh leprosy-unrelated complaints (category IIB) and 25 had persistence of old complaints (category III). Cumulative PYR of the 151 patients was 1155.42. Forty-one patients had fresh leprosy-related complaints. Skin biopsy was done in the 17 patients with fresh skin patches, of whom four showed histopathological evidence of relapse. Relapse rate in our study was 0.35/100 PYR. Mean duration after RFT at relapse was 4.9 years. Our scepticism towards passive surveillance systems is justified by these 41 patients with fresh leprosy-related complaints, who voluntarily reported only after receiving the postcards. We recommend the introduction of a phase III, wherein the services of PMWs may be used to contact the 409 patients who remained unresponsive at the completion of phases I and II. We also recommend the introduction of a universal format for recording addresses of all new patients, which would be of immense help in patient retrieval in all such surveillance systems in the future.

MARTELLI, C.M.; STEFANI, M.M.; GOMES, M.K.; REBELLO, RE; PENINNI, S.; NARAHASHI, K.; MAROCLO, A.L.; COSTA, M.B.; SILVA, S.A.; SACCHETIM, S.C.; NERY, J.A.; SALLES, A.M.; GILLIS, T.P.; KRAHENBUHL, J.L.; ANDRADE, A.L. Single lesion paucibacillary leprosy: baseline profile of the Brazilian Multicenter Cohort Study. *Int. J. Leprosy*, v.68, n.3, p.247-257, September, 2000.

In Brazil, there is little information about the clinical and epidemiological characteristics of paucibacillary, single skin lesion leprosy patients (SSL-PB). Only recently has the official notification system distinguished leprosy patients with a single lesion as a clinical entity, for whom the single-dose ROM (rifampin, ofloxacin and minocycline) regimen has been recommended. In this paper, we describe the baseline clinical features and the immunological background of a multicenter cohort of SSL-PB leprosy cases enrolled between December 1997-1998. Patients were recruited at health centers located in the following regions: Southeast = Rio de Janeiro; North = Amazon and Rondonia states and Center-West = Goias state. Eligible cases were newly detected, untreated single-lesion leprosy patients without thickened nerve

involvement, and were assessed by clinical, bacilloscopic and histopathological exams. The Mitsuda skin test and anti-PGL-I serology (ELISA) were also performed. Of the 299 SSL-PB leprosy patients, 259 (86.6%) fulfilled the criteria for single-dose ROM intervention. Our results showed that patients recruited from different sites had similar features, considering the clinical and immunological profiles. There was a predominance of adults (mean age 32.4; S.D. = 16.0), and a BCG scar was detected in 76.7% of the children (< or = 15 years old). Only 7 cases were diagnosed as the multibacillary type, representing less than 3% of the patients being misclassified. Our data indicate that in Brazil SSL-PB case ascertainment based on clinical and bacilloscopic criteria can be accurately defined under a routine control program; 75.0% of SSL-PB cases were Mitsuda positive (> or = 5 mm) and seropositivity for anti-PGL-I was detected in 17.3% of the patients. These data are compatible with effective cell-mediated immunity and low bacillary load, suggesting favorable clinical outcomes for most SSL-PB participants of this cohort.

SAUNDERSON, P.; GEBRE, S.; BYASS, P. Reversal reactions in the skin lesions of AMFES patients: incidence and risk factors. *Leprosy Rev.*, v.71, n.3, p.309-317, Sep., 2000.

Reversal reactions affect the skin and/or nerves of leprosy patients. This paper looks at reversal reactions involving the skin in 594 new patients in central Ethiopia, followed for between 6 and 11 years after the start of treatment. The incidence of reversal reaction declines steadily after the start of treatment, but the first episode may occur as long as 5 years after diagnosis in both paucibacillary (PB) and multibacillary (MB) patients. Recurrent episodes occurred up to 6 years after diagnosis. PB patients were at greatest risk for reversal reaction in the first year after diagnosis and MB patients in the first 4 years. The highest incidence rate was 18 episodes per 100 person years in MB patients during the first year after diagnosis. The ratio of the incidence rates for the first 3 years in MB versus PB patients is 2.4 (95% CI 1.6-3.8). This study confirms that starting effective treatment and borderline classification are risk factors for reversal reactions. Pregnancy/delivery in the 6 months prior to diagnosis was a significant risk factor for presenting with a reversal reaction [relative risk (RR) 5.9 (95% CI 2.1-16.5)]¹, but later pregnancies were not associated with an increased risk. Being female was a significant risk factor for the late appearance of the first episode of reversal reaction. Having a reversal reaction in the first year after diagnosis was a highly significant risk factor for the development of later reactions [RR in PB cases 11.9 (95% CI 3.4-41.7); in MB cases 6.4 (95% CI 3.8-10.6)]¹. Being HIV positive was a risk factor for developing recurrent reversal reactions, although only three out of 29 recurrent cases were HIV positive [RR 2.7 (95% CI 1.4-5.1)]¹.

SAUNDERSON, P.; GEBRE, S.; BYASS, P. ENL reactions in the multibacillary cases of the AMFES cohort in central Ethiopia: incidence and risk factors. *Leprosy Rev.*, v.71, n.3, p.318-324, 2000.

Erythema nodosum leprosum (ENL), or type 2 leprosy reactions are an important complication of multibacillary leprosy. The AMFES cohort includes 300 new multibacillary cases that have been followed for up to 10 years from the start of treatment, in central Ethiopia. Sixteen (5.3%) patients had ENL reactions. The incidence of ENL was maximal in the second and third years after the start of treatment, reaching 6.9 episodes per 100 person years at risk. Factors associated with being lepromatous [LL classification and a high bacillary index (BI)] gave an increased risk of developing ENL; in the univariate analysis, LL classification gave a relative risk of 3.6 (95% CI 1.3-10) and a BI of 6 gave a relative risk of 8.6 (95% CI 2.3-32) for the development of ENL. HIV co-infection was found to be a risk factor in this cohort, but as the numbers involved are small (only two HIV positive patients had ENL), this finding must be confirmed in larger studies. Ten of the 16 cases had recurrent episodes and five had at least five episodes occurring over a period of more than 2 years. The management and prognosis of ENL reactions are discussed.

SAUNDERSON, P.; GEBRE, S.; DESTA, K.; BYASS, P. The ALERT MDT Field Evaluation Study (AMFES): a descriptive study of leprosy in Ethiopia. Patients, methods and baseline characteristics. *Leprosy Rev.*, v.71, n.3, p.273-284, Sep., 2000.

The ALERT MDT Field Evaluation Study (AMFES) is a long-term prospective study of 650 patients (594 new cases and 56 relapses after dapsone monotherapy), treated with fixed-duration multiple-drug therapy (MDT), as recommended by WHO. Follow-up has continued for up to 11 years from the start of treatment. This paper presents the methodology of the study and the baseline characteristics of the cohort, while accompanying papers examine the incidence of, and possible risk factors for, the various complications of leprosy, including relapse, reactions and nerve function impairment. The methods of diagnosis, classification and treatment with MDT are described; nerve function was assessed at every visit to the clinic using a standardized methodology, so that reactions and new impairment could be detected early and treated. Eighty-four per cent of new case had at least one thickened nerve, with the ulnar nerve most commonly involved. Seventy-seven per cent of cases completed treatment and only one adverse reaction to the MDT drugs was noted. Twenty-eight per cent of all patients were given steroids at one time or another, almost always for new nerve function impairment, and 3% of these developed significant complications of steroid treatment. Twenty-nine patients (5%) received hospital care, including 14 patients who underwent major surgery. Sixty-

one per cent of the women over 19 years of age had at least one pregnancy, but pregnancies were much less common after leprosy was diagnosed.

SHAW, I.N.; EBENEZER, G.; RAO, G.S.; NATRAJAN, M.M.; BALASUNDARAM, B. Relapse as histoid leprosy after receiving multidrug therapy (MDT); a report of three cases. *Int. J. Leprosy*, v.68, n.3, p.272-276, September, 2000.

The histoid type of leprosy has been described as occurring in lepromatous leprosy patients who relapse after many years of apparently successful dapsone monotherapy. Three patients who had received the World Health Organization-recommended regimens of multidrug therapy (WHO/MDT) relapsed as histoid leprosy 12-15 years after completion of treatment. In one patient, through mouse foot pad studies, the bacilli were found to be sensitive to rifampin and clofazimine and resistant to dapsone. In the other two patients mouse foot pad studies were inconclusive. The patients were re-started on WHO/MDT. Two patients took regular treatment and improved, both clinically and bacteriologically. One patient was irregular in treatment, and 1 year after re-starting WHO/MDT nodules were still present although the bacterial index had fallen slightly.

SOUZA, C.S.; ROSELINO, A.M.; FIGUEIREDO, E; FOSS, N.T. LUCIO'S PHENOMENON: CLINICAL AND THERAPEUTIC ASPECTS. *Int. J. Leprosy*, v.68, n.4, p.417-425, December, 2000.

We report four cases of necrotizing reactions of the Lucio's phenomenon type, an entity rarely observed in Brazil despite the high prevalence of leprosy. Clinical, histopathological and therapeutic aspects are described and compared to those reported in the literature for cases classified as diffuse, non-nodular lepromatous leprosy with Lucio's phenomenon.

EPIDEMIOLOGIA

EBENSO, B.E.; TURETA, S.M.; UDO, S.O. Treatment outcome and impact of leprosy elimination campaign in Sokoto and Zamfara states, Nigeria. *Leprosy Rev.*, v.72, n.2, p.192-198, June, 2001.

A Leprosy Elimination Campaign (LEC) was implemented in 37 districts of Sokoto and Zamfara states, Nigeria from 13 August to 30 November 1998. The campaign utilized intensive community mobilization and training of local health personnel to detect hidden leprosy cases. During 8 weeks of case finding, 160,127 persons were screened; 353 new cases of leprosy were detected and placed on MDT; 236 (67%) of new cases detected were classified as MB, 64 cases (18%) suffered visible deformities and 24 patients (6.8%) were children. Follow-up in December 1999 of patients placed on MDT

revealed 97% PB and 96% MB cure rates, respectively. Detection of cases in communities led some community leaders to ask for repeat surveys in their communities. Repeat surveys continue to yield new cases. The authors recommend that LECs be maintained for 3 years to accelerate leprosy elimination in the region. The cost effectiveness and impact of LEC in Sokoto-Zamfara are discussed.

FERREIRA, J.; MENGUE, S.S.; WAGNER, M.B.; DUNCAN, B.B. Estimating hidden prevalence in Hansen's disease through diagnosis delay and grade of disability at time of diagnosis. *Int. J. Leprosy*, v.68, n.4, p.464-473, December, 2000.

The objective of the present study was to propose a new method for the calculation of estimated hidden prevalence (EHP) in Hansen's disease (HD). We analyzed the records of 4142 HD patients diagnosed in the state of Rio Grande do Sul, Brazil, between 1970 and 1991. Out of these 4142 cases, 3291 patients had their grade of disability (GD) evaluated at the time of diagnosis and provided information about the time elapsed between the appearance of the symptoms and the moment when HD was identified by a physician (diagnosis delay, DD). Mean DD for the sample (in years) was 1.51 for disability grade 0, 2.14 for grade 1, 4.46 for grade 2, and 9.64 for grade 3. EHP was calculated taking into account only two strata of GD using the formula $HP = [(NC-GD\ 0/1) \times 2.0 + (CN-GD\ 2/3) \times 5.0] / (CGE \times PCP)$, where: NC-GD 0/1 = mean annual number of newly detected grades 0 or 1 cases; CN-GD 2/3 = mean annual number of newly detected grades 2 or 3 cases; CGE = proportion of newly detected cases with GD evaluated; PCP = proportion of the population covered by the state HD control program; 2.0 and 5.0 correspond to an approximation of the mean time in years of DD in each respective stratum of GD. Applying this model, we found an EHP of 529 cases which translates to an excess of 0.58 cases/10,000 population. We also conducted a multivariate analysis using a logistic regression model. This analysis revealed that, in addition to DD, other variables such as clinical form, age group, sex and mode of detection were independent risk factors for the presence of disabilities. We also found two significant effect modification factors: DD versus clinical form and DD versus age group. Taking these findings into consideration, a more complex model was used to calculate the EHP with 16 strata (defined by clinical form of the disease, age group, and GD from 0 to 3). An EHP of 502 cases (excess of 0.55/10,000) was obtained with this more complex model. This result differs only 5% from that of the simplified model. Therefore, we conclude that the simplified model is indicated to estimate hidden prevalence of HD in the field.

GINSBERG, A.M. Leprosy research—setting priorities and facilitating collaborations: a personal perspective. *Leprosy Rev.*, v.71, p.S183-S187, 2000.

In recent years, as the prevalence of leprosy has declined and the tuberculosis epidemic has gained increasing attention, leprosy research has generally taken a 'back seat' to research in tuberculosis and other emerging and re-emerging infections. This has resulted as much from perceived differences of scientific opportunities in these fields as from differences of the disease burden. At the United States National Institutes of Health (NIH), research priority setting is typically based on a number of factors. In the case of leprosy research, the technical difficulties associated with this scientific area have clearly lessened enthusiasm for and progress in this field. Today, however, we are confronted by the reality of not having sufficient scientific understanding to explain a stable or increasing number of leprosy cases detected annually in the face of a dramatically decreasing total number of identified cases. We also lack adequate tools for diagnosis and prevention. At the same time, new molecular and cellular approaches and knowledge of the complete sequence of the genome of *Mycobacterium leprae* render leprosy research significantly more tractable than ever before. The combination of these factors has led a number of groups, including the National Institute of Allergy and Infectious Diseases of the NIH, to review the current state of knowledge in leprosy research and draft recommendations for future leprosy research priorities. It is clear that many of the necessary and exciting research activities can best be addressed through collaborations among investigators, with control programmes, and among countries of high and low endemicity.

GRIFFITHS, S.; READY, N. Defaulting patterns in a provincial leprosy control programme in Northern Mozambique. *Leprosy Rev.*, v.72, n.2, p.199-205, June, 2001.

Cohort-based multidrug therapy (MDT) completion rates are used to assess adherence to MDT. However this measure gives no information about when during the treatment period defaulting occurs. Two districts in Cabo Delgado province in Northern Mozambique were selected for evaluation of multibacillary patient defaulter data between 1993 and 1997 to examine when patients default during the treatment period. In all, 548 (59.2%) of 926 MB patients completed treatment and 378 (40.8%) defaulted between 1993 to 1997. The percentage of defaulters fell steadily from 59.8% in 1993 to 23.2% in 1997. Of the 378 defaulters 57.7% defaulted treatment within 6 months and 83.1% within 1 year of starting treatment. It was observed that patients tend to default early rather than late in the treatment period and that this pattern is maintained over time despite a fall in defaulter rates. Patients established early into a treatment routine were more likely to complete treatment. A comprehensive effort to improve and maintain leprosy control services will probably influence adherence more than any single, specific strategy. Shortening MDT treatment from 2 years to 1 year is unlikely to affect the defaulter rate.

HEYNDERS, M.L.; MEIJS, J.J.; ANDERSON, A.M. Towards an understanding of non-compliance. An assessment of risk factors for defaulting from leprosy treatment. *Lepr Rev.*, v.71, n.3, p.369-376, 2000.

Within the Eastern Leprosy Control Project of Nepal, a retrospective case control study looked for simple factors that might be used operationally to predict non-compliant behaviour in patients. Patients with these factors would then become the targets of measures such as intensified health education messages and home visits in order to reduce the risk of defaulting. A study of 1442 patient cards (half defaulters, half treatment completed) revealed occasional small but significant demographic and clinical differences, but none was of a sufficient magnitude to be operationally useful. Review of the attendance of patients in the first few months of treatment suggested that eventual defaulting was strongly associated with irregularity from the commencement of treatment. It is possible that an early indicator based on attendance over the first months can be used to target patients who are in danger of non-completion of treatment.

MILEP2 Study Group. Approaches to studying the transmission of *Mycobacterium leprae*. *Leprosy Rev.*, v.71, p.526-529, December, 2000. Supplement.

A collaborative study has been undertaken to establish the relationship between infection by *Mycobacterium leprae* and the development of immunity in a community in which multidrug therapy (MDT) has been used for more than 10 years, to elucidate the pathogenesis of infection in leprosy, and to develop and test an intervention strategy based on chemotherapy for interruption of transmission of the organism in the community. The first phase of the study included the establishment of laboratory facilities and pilot work in India. In the course of the second phase, the entire populations of three villages in India and one in Ethiopia have been surveyed, nasal swabs were obtained for detection of *M. leprae* DNA by means of the polymerase chain reaction (PCR), specimens of saliva were obtained for measurement of levels of anti-*M. leprae* IgA antibodies, and follow-up surveys have been carried out. A double-blind trial of chemotherapy among subjects whose PCR was positive is proposed, to determine if the course of the infection can be influenced by treatment. The performance of large numbers of PCR tests in endemic countries has required the development of rigorous internal and external quality control procedures. These have shown that many batches (as many as 50%) fail to meet quality control criteria, and must be retested. Despite this, development of these methods, and their application to field studies should provide tools for studying the transmission of *M. leprae*, and direct methods of testing innovative interventions.

NAAFS, B.; SILVA, E.; VILANI-MORENO, E; MARCOS,

E.C.; NOGUEIRA, M.E.; OPROMOLLA, D.V. Factors influencing the development of leprosy: an overview. *Int. J. Leprosy*, v.69, n.1, p.26-33. March, 2001.

The clinical manifestations of leprosy vary, seemingly depending on the host's immune response. Mode and route of infection, such as skin versus nasal mucosa, insect bites, sexual and gastrointestinal transmission, together with genetic factors that may contribute to the outcome of the infection, including HLA, Lewis factor, Nrampl and more subtle inherited alterations, are discussed. It is theorized that a balance between host responses elicited by different routes of infection and size and spacing of inocula is responsible for the clinical and immunological manifestations of the disease. Genetic factors and contact with environmental microorganisms may modulate these responses. The final result, resistance, delayed-type hypersensitivity, tolerance, disease or no disease, spectrum and reactions, is most likely reached via the orchestration of the induced cyto- and chemokines.

RAO, P.V.; BHUSKADE, R.A.; DESIKAN, K.V. Modified leprosy elimination campaign (MLEC) for case detection in a remote tribal area in the State of Orissa, India. *Leprosy Rev.*, v.71, n.3, p.377-381, 2000.

A leprosy project was established in a difficult to reach area under guidelines of Government of India. The leprosy services were provided by Koraput Leprosy Eradication Project (KORALEP) and general health services by Primary Health Care (PHC). Leprosy elimination campaigns (LECs) were suggested by WHO to detect more cases in the community. A modified leprosy elimination campaign (MLEC), carried out utilizing the services of primary health care workers is discussed in this paper. Apart from the trained health workers, Anganwadi workers along with some literate people from the district were also included in the search teams. In all, 1543 cases were shortlisted from the suspects identified and on re-examination 576 cases were confirmed as active cases. Sixty percent of the cases detected were very early cases with two to three skin lesions. This could be achieved with a very brief training of health workers and involving village voluntary workers. MLEC was found to be a useful tool for case finding in such areas.

RAZAFIMALALA, E.C.; RAKOTOMANGA, S.; RAKOTONDRAMARINA, D.B.; RAKOTOMALALA, J.N. Situation de la lèpre dans une région du Sud-Est de Madagascar de 1996 1998. *Acta Leprol.* v.12, n.1, p.7-10, 2000-2001.

Leprosy is endemic in Madagascar. The authors report the results of an epidemiologic study performed between 1996 and 1998 in Farafanguna, localized in the South-Eastern of the country. During this period, 217 new

cases have been diagnosed. Of the 130 cases included in the study, 69.23% were children aged lower than 15 years and 76.91% suffered from a multibacillary form. More than 50% of the cases belonged to a large family (6 persons or more) and at least one family case was found in more than 60% of cases. These results enhance the severity of the disease in the country and show the presence of multiple risk factors (promiscuity, family cases and multibacillary forms).

WEISS, H.A.; HAWKES, S. An overview of the global epidemiology of HIV/AIDS. *Leprosy Rev.*, v.72, n.1, p.92-98, March, 2001.

Over 5 million people continue to be newly infected with HIV every year, despite advances in understanding the factors that drive the epidemics. It is apparent that control of the HIV epidemics has often proved difficult due to the complex web of behavioural, biological, social and structural vulnerabilities to infection. In this paper we discuss the epidemiology and control of HIV in sub-Saharan Africa, and draw parallels with the emerging epidemic in South and South-East Asia. Prevalence of infection in sub-Saharan Africa has continued to increase overall, but a few countries have successfully reduced national infection rates by employing an integrated, multisectoral control strategy. Prevention of similar devastating epidemics in other regions will rely upon an openness in recognizing risk and upon a concerted multisectoral approach to reduction of risk of risk at the individual level and level and vulnerability at the societal and structural levels.

ZODPEY, S.R.; TIWARI, R.R.; SALODKAR, A.D. Gender differentials in the social and family life of leprosy patients. *Leprosy Rev.*, v.71, n.4, p.505-510, 2000.

A study was carried out at the Leprosy Control Unit, Government Medical College, Nagpur, India, to investigate gender differentials in the social and family life of leprosy patients. The study included 486 (268 males and 218 females) leprosy patients, who were diagnosed and registered at least 1 year prior to the data collection. It was observed that leprosy patients were isolated and refrained from various activities in the family. However, the effect of disease on this isolation was significantly greater in females as compared to males. Similarly, although, men and women were both affected in terms of their social life, women suffered more isolation and rejection from the society. The current study describes the gender differentials in the social and family life of leprosy patients in Central India.

VAZ, M.; DIFFEY, B.; JACOB, A.J.;VAZ, M. Should nutritional status evaluation be included in the initial needs assessment of leprosy patients with disability prior to socio-economic. *Leprosy Rev.*, v.72, n.2, p.206-211, June, 2001.

Because of the large numbers of leprosy patients with disability and the limited resources available, it is important that socio-economic rehabilitation (SER) is targeted towards those who are most in need. Towards this purpose, current assessments of leprosy patients prior to initiating SER include the evaluation of income, assets and household possessions. Conspicuously absent is the nutritional assessment of the patient. In the absence of weight loss associated with illness, population studies indicate that undernutrition reflects poor socio-economic conditions. In this study of 151 cured leprosy patients with disability, 57% of the patients were found to be undernourished using body mass index (kg/m²) derived from body weight and height, and 10% of the patients were severely undernourished (grade III). Undernutrition in the patients was poorly though significantly correlated with personal income ($r = 0.18$, $P < 0.05$). Total household income, reported amount of money spent on food and estimated cereal intakes were not correlated with the BMI of the patient, possibly due to reporting bias and other methodological issues. We propose the inclusion of nutritional status evaluation by anthropometry as part of the initial screening of leprosy patients prior to instituting SER. We believe that this simple and objective evaluation can add to the assessment of 'threat' of economic deprivation or actual economic 'dislocation', and thus help in the prioritization of leprosy patients for SER.

HISTOPATOLOGIA E CITOLOGIA

BHAKE, A.S.; DESIKAN, K.V.; JAJOO, U.N. Cytodiagnosis of histoid leprosy. *Leprosy Rev.*, v.72, n.1, p.78-82, March, 2001.

This paper presents cytomorphological features of the histoid variety of lepromatous leprosy. Fine needle aspiration of a lepromatous nodule showed cytological features consistent with those of histoid leprosy. Simultaneously, a biopsy of the nodule was also performed and the case confirmed as histoid leprosy. The advantages of the fine needle aspiration technique are that it is simple, quickly reportable, and less traumatizing. Multiple aspirations from different sites may be obtained, which would add to the value of sampling. The need to differentiate a histoid nodule from a conventional lepromatous nodule is explained.

ISHIKAWA, S.; MIZUSHIMA, M.; FURUTA, M.; ISHIKAWA, A.; KAWAMURA, K. Leydig cell hyperplasia and the maintenance of bone volume: bone histomorphometry and testicular histopathology in 29 male leprosy autopsy cases. *Int. J. Leprosy*, v.68, n.3, p.258-266, September, 2000.

This study was conducted to determine if osteoporosis in male leprosy patients is caused by

testicular atrophy. Bone volume (BV/TV), trabecular number (TbN), trabecular thickness (TbTh), and trabecular separation (TbSp) were measured in two areas in decalcified paraffin sections of lumbar bones from 29 male leprosy and 6 male nonleprosy autopsy cases. We found significant differences in the average BV/TV measurements among the 7 patients with nodular Leydig cell hyperplasia (BV/TV 12.24%) and the 22 patients without hyperplasia (BV/TV 7.35%) and 6 patients without leprosy (BV/TV 12.98%). Bone volume was maintained in patients with nodular Leydig cell hyperplasia, and we determined no clinical factor other than the Leydig cell hyperplasia that reflected the bone volume. The osteoporosis of male leprosy patients was attributed to secondary gonadal dysfunction due to testicular atrophy, and Leydig cell hyperplasia appears to preserve bone volume.

MYSOREKAR, V.V.; DANDEKAR, C.P.; RAO, S.G. Mast cells in leprosy skin lesions. *Leprosy Rev.*, v.72, n.1, p.29-34, March, 2001.

The density and distribution of mast cells was assessed in skin biopsies of 118 untreated leprosy cases and 20 healthy individuals taken as controls. Mast cells were present in only small numbers in the skin biopsies of healthy individuals. Significantly higher mast cell counts were obtained in the skin lesions of indeterminate leprosy ($P < 0.01$). The mast cell count in the tuberculoid group was significantly lower than that in the lepromatous group ($P < 0.05$). The lepromatous group also showed increased mast cell degranulation and altered morphology. The mast cell distribution in the skin biopsies of the two groups was, however, similar. The mast cell count in leprosy is probably determined by the pattern of cytokines released by the T lymphocytes. However, the influence of mast cells on the outcome of the disease needs to be evaluated further.

REA, T.H. Frequency and extent of thickening of the nucleated epidermis in leprosy lesions. *Int. J. Leprosy*, v.68, n.4, p.410-416, December, 2000.

Using 28 specimens of clinically normal skin from lepromatous leprosy subjects as a standard for comparison, the mean thickness of the nucleated epidermis was found to be significantly increased in untreated lesions from 16 borderline tuberculoid, 21 erythema nodosum leprosum (ENL), and 14 reversal reaction patients, but was unchanged in borderline lepromatous and lepromatous patients. Using specimens from 36 untreated lepromatous and borderline lepromatous lesions as the standard for comparison with the lesions of reversal reactions or ENL which these patients eventually developed, there was a significant thickening of the nucleated epidermis in both reactional states. In both comparison groups, there was a greater mean increase and a larger frequency of thickening in the ENL lesions than in those with reversal reactions. In the

borderline tuberculoid and reversal reaction lesions the increase can be understood as secondary to the presence of gamma interferon or interleukin-2. The increase in thickness in the ENL lesions is more difficult to explain, but it is not inconsistent with a role for these same two cytokines.

SUNEETHA, S.; ARUNTHATHI, S.; KURIAN, N.; CHACKO, C.). Histological changes in the nerve, skin and nasal mucosa of patients with primary neuritic leprosy. *Acta Leprol.*, v.12, n.1, p.11-18, 2000-2001.

Primary neuritic leprosy (PNL) presents as a peripheral neuropathy with no visible skin patches and skin smears negative for acid fast bacilli. The pathogenesis of PNL is poorly understood. The aim of the study was to document the histological changes in the nerve, apparently normal skin and nasal mucosa in PNL and to study its significance to the pathogenesis of leprosy lesions. The study is based on a cohort of 208 PNL patients registered at the Schieffelin Leprosy Research and Training Centre, Karigiri. All patients had a nerve biopsy, 196 had a skin biopsy and 39 had a nasal mucosal biopsy. The findings reveal that PNL patients exhibit a spectrum of disease histologically in the nerve ranging from lepromatous to tuberculoid leprosy with a significant proportion (46%) manifesting a multibacillary leprosy histology. Findings in the apparently normal skin and nasal mucosa reveal that there are widespread changes due to leprosy in tissues such as the skin and nasal mucosa even when the disease appears clinically confined to a few nerves. PNL may be an early stage in the pathogenesis of the disease before the appearance of skin lesions. The number of nerves enlarged and lepromin status did not give any clue to the nature of underlying disease.

VIJAIKUMAR, M.; D'SOUZA, M.; KUMAR, S.; BADHE, B. Fine needle aspiration cytology (FNAC) of nerves in leprosy. *Leprosy Rev.*, v.72, n.2, p.171-178, June 2001.

Leprosy is primarily a disease of the peripheral nerves and a technique that is simpler than nerve biopsy is required to evaluate nerve involvement, especially in pure neuritic (PN) leprosy. This study was designed to evaluate the role of FNAC of the nerve in the diagnosis and classification of leprosy. A prospective study was carried out on 25 patients with clinically active leprosy and at least one thickened peripheral sensory nerve. Nerve aspirates were evaluated by May-Grunwald-Giemsa and Fite's staining. Lepromin test, slit skin smears (SSS), skin biopsies (except PN cases) and nerve biopsies were performed and compared with FNAC. FNAC of nerve from 23 cases (92%) yielded diagnostic aspirates. Acid fast bacilli were observed in six cases by FNAC. FNAC and nerve pathology were equally comparable with the other parameters evaluated.

Based on the results, cytological criteria were developed for interpreting nerve aspirates and the cases were classified as paucibacillary (18), BB (2), BL (2), LL (1) and non-diagnostic (2). All PN cases showed diagnostic paucibacillary type cytology. FNAC of the nerve yields diagnostic aspirates in leprosy comparable with nerve pathology and the proposed cytological criteria may be useful in classification of nerve aspirates.

WENG, X.M.; CHEN, S.Y.; RAN, S.P.; ZHANG, C.H.; LI, H.Y. Immuno-histopathology in the diagnosis of early leprosy. *Int. J. Leprosy*, v.68, n.4, p.426-433, December, 2000.

The present study of 45 early leprosy cases in an endemic area in China indicates: a) Sensitivity of acid-fast bacilli (AFB) detection can be significantly improved by examining approximately 30 serial sections. AFB and/or phenolic glycolipid-I (PGL-I) were mostly detected in the infiltrates in the subepidermal zone, intraneurium, perineurium and around blood vessels. b) PGL-I antigen was positive in 10 clinically suspected, single lesion leprosy cases and AFB positive in 7 patients, AFB and/or PGL-I in nerve in 6 patients. c) Nonspecific chronic inflammation in indeterminate leprosy presented as selective perineural and/or intraneural infiltration with lymphocytes predominating. In the infiltrating mass, fragments of neural tissue were demonstrated with anti-S-100 protein staining. d) Except for 3 cases with unknown numbers of lesions, the present positive immunohistopathological findings are in direct correlation with the number of lesions at first diagnosis, namely: 41.6% (10/24) for single lesion, 66.6% (6/9) for 2 lesions, and 88.8% (8/9) for patients with $>$ or $=$ 3 lesions. e) Typical epithelioid or macrophage granuloma formations were not seen in early leprosy with a single lesion. In testing the immunological inclination of these patients with CD68 or tumor necrosis factor-alpha (TNF-alpha) a positive test is likely to be of prognostic value since TNF-alpha is involved in granuloma formation and nerve damage.

IMUNOLOGIA

BRENNAN, P.J. Skin test development in leprosy: progress with first-generation skin test antigens, and an approach to the second generation. *Leprosy Rev.*, v.71, p.S50-S54, December, 2000. Supplement

One of the most urgent needs from leprosy research is a test for infection. The lepromin test is not suitable as a diagnostic test for leprosy, and neither the Rees nor the Convit soluble antigens has appeared sufficiently specific. Because two new antigens, MLSA-LAM and MLCwA, may not fully meet the requirements for specificity, we have embarked upon the preparation of a second generation of skin test antigens. Size-fractionated cryptozoic proteins were prepared from *M. leprae* by electroelution from

preoperative sodium dodecylsulphate-polyacrylamide gel electrophoresis, and individual fractions were probed with polyclonal and monoclonal antibody reagents to identify both known and novel proteins. In addition, immunological responses were assessed in *M. leprae*-sensitized guinea pigs against both crude subcellular fractions (cytosol, membrane, and soluble cell wall proteins) and the size-fractionated cytosolic proteins. A particularly promising subcellular fraction is the membrane fraction of *M. leprae*, which contains many proteins unique to the organism. Clinical trials of the *M. leprae* membrane proteins are now being planned.

CHARLAB, R.; SARNO, E.N.; CHATTERJEE, D.; PESSOLANI, M.C. Effect of unique *Mycobacterium leprae* phenolic glycolipid-I (PGL-I) on tumour necrosis factor production by human mononuclear cells. *Leprosy Rev.*, v.72, n.1, p.63-69, March 2001.

Mycobacterium leprae cell wall-associated components are found in large amounts in the tissues of leprosy patients, particularly those at the lepromatous pole. Among these molecules, the phenolic glycolipid-1 (PGL-I), unique to *M. leprae*, has been involved in the selective anergy observed in the lepromatous patients. Armadillo-derived *M. leprae* retains only a small proportion of the total PGL-I found in infected tissues. Therefore, the addition of PGL-I to *M. leprae* in vitro is important for a better understanding of *M. leprae* effects in vivo. We have studied the influence of PGL-I on TNF production by normal human peripheral blood mononuclear cells (PBMC) and by a human monocytic leukaemia cell line (THP-1) following stimulation with killed *M. leprae*. PGL-I alone did not induce TNF secretion by PBMC, but when associated with a sub-optimal dose of armadillo-derived *M. leprae* increased the release of this cytokine. In agreement with these results, *M. leprae*-exposed THP-1 cells did not secrete detectable levels of TNF unless PGL-I was simultaneously added to the culture. This increase in TNF production suggests that PGL-I plays a role in the induction of TNF during the natural infection. In addition, the modulatory effect of PGL-I on TNF release by THP-1 cells reinforces that monocytes are one of the possible targets of this molecule.

BUHRER-SEKULA, S.; SARNO, E.N.; OSKAM, L.; KOOK S.; WICHERS, I.; NERY, J.A.; VIEIRA, L.M.; DE MATOS, H.J.; FABER, W.R.; KLATSER, P.R. Use of ML dipstick as a tool to classify leprosy patients. *Int. J. Leprosy*, v.68, n.4, p.456-463, Dec., 2000.

Leprosy control services face the problem of leprosy patients being misclassified by the lack of or the poor quality of skinsmear examination services. Misclassification increases the risk of relapse due to insufficient treatment if a multibacillary (MB) patient is classified as paucibacillary (PB), thereby also prolonging

the time that the patient is infectious. The World Health Organization (WHO) recommends at present an alternative classification based on the number of skin lesions. Its reliability, however, has been questioned. Our investigation sought to determine the usefulness of the ML Dipstick, a simple field assay to detect IgM antibodies to phenolic glycolipid-I of *Mycobacterium leprae*, for the classification of leprosy patients in addition to lesion count. In this study, 264 leprosy patients were investigated. Of 130 patients with a positive bacterial index (BI), 19 (14.6%) had less than 6 lesions and would have been classified as PB. Out of 134 patients with a negative BI, 26 (19.4%) had 6 or more lesions and would have been classified as MB patients if the lesion counting system would apply. Thus, the classification based on the number of lesions only was found to be 85% sensitive and 81% specific (using the BI as the gold standard) at detecting MB cases among the studied population. Sensitivity would have increased if patients would have been classified according to a combination of the number of lesions and the dipstick result. In that case patients are classified as MB when they are either dipstick positive (N = 16), have more than 6 lesions (N = 43), or both (N = 94). Patients negative for both dipstick and number of lesions would have been classified as PB (N = 111). The classification based on the number of lesions alone left 19 BI-positive cases classified as PB, while the combination method of the ML Dipstick and number of lesions left only 8 BI-positive cases classified as PB (5 borderline, 2 borderline lepromatous and 1 tuberculoid), thus preventing undertreatment. The combination method of the ML Dipstick and lesion counting was found to be 94% sensitive and 77% specific, which is an improvement of 9% (chi-squared test, $p = 0.025$) in sensitivity compared to lesion counting only. The results of this study indicate that testing all patients initially classified by lesion counting as PB (48% in our study population) with the dipstick can significantly contribute to improved classification of leprosy patients for treatment purposes.

DOCKRELL, H.M.; BLACK, G.E.; WEIR, R.E.; FINE, R.E. Whole blood assays for interferon-gamma: practicalities and potential for use as diagnostic tests in the field. *Leprosy Rev.*, v.71, p.S60-S62, December, 2000. Supplement.

Recent years have seen the introduction of a number of whole-blood assays, in which unseparated heparinized blood is stimulated with antigen either overnight or for as long as 6 days, and cytokine production is measured in the plasma or supernatant. These assays have potential for use in the field as immunodiagnostic assays, as they require only a small blood sample and basic laboratory facilities. Use of these assays in a large study of the immunological effects of BCG vaccination in Malawi has shown that the diluted blood, 6-day whole-blood assays is robust, and can be used to assess T-cell responses to both crude and recombinant antigens. If used with antigens specific to *Mycobacterium leprae*, these assays could be used to

measure exposure of *M. leprae* within communities or populations, or to aid the early diagnosis of leprosy.

DOCKRELL, H.M.; BRAHMBHATT, S.; ROBERTSON, B.D.; BRITTON, S.; FRUTH, U.; GEBRE, N.; HUNEGNAW, M.; HUSSAIN, R.; MANADHAR, R.; MURRILLO, L.; PESSOLANI, M.C.; ROCHE, P.; SALGADO, J.L.; SAMPAIO, E.; SHAHID, E.; THOLE, J.E.; YOUNG, D.B. Diagnostic assays for leprosy based on T-cell epitopes. *Leprosy Rev.*, v.7, p.555-S59, December, 2000. Supplement.

To date, only a limited number of antigens have been described as specific for *Mycobacterium leprae*, and in many cases, homologues have subsequently been shown to exist in mycobacteria such as *M. avium* and *M. intracellulare*. A Leprosy Synthetic Peptide Skin Test Initiative was established by the Steering Committee on the Immunology of Mycobacteria of the UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases, to investigate the potential of synthetic peptides that encode T-cell epitopes as diagnostic tools, which could be used to develop a skin-test reagent specific for leprosy. Such *M. leprae*-specific peptides should have unique amino acid sequences, or significant sequence-dissimilarity from those in other mycobacteria. Synthetic peptides, 15 amino acids long, were synthesised from 33 genes or open reading frames within the *M. leprae* genome. Tuberculoid leprosy patients from four leprosy-endemic countries, Brazil, Ethiopia, Nepal and Pakistan, were tested as subjects known to have been infected with *M. leprae*, and to make good T-cell responses to antigens of *M. leprae*; UK blood donors were used as non-exposed or non-infected subjects. Peptides inducing potentially specific responses in leprosy patients and not in UK controls, and those inducing cross-reaction responses, present in both leprosy patients and non-exposed, non-infected controls, were identified. A difference from the equivalent *M. tuberculosis* sequence of five or more amino acid residues did not, by itself, identify peptides that were *M. leprae*-specific, suggesting that many of these peptides may have homologues in environmental mycobacteria. To date, this approach has identified a number of peptides with greater than 90% specificity and 19-47% sensitivity, which are undergoing further specificity-testing. Such peptides would have great potential as T-cell reagents with which to monitor exposure to *M. leprae* within communities, formulated either as skin-test reagents, or as antigens for tests in vitro.

GORMUS, B.J.; BASKIN, G.B.; XU, K.; RATTERREE, M.S.; MARTIN, L.N.; MACK, P.A.; BOHM, R.P. JR.; MEYERS, W.M.; WALSH, G.P. Antileprosy protective vaccination of sooty mangabey monkeys with BCG or BCG plus heat-killed *Mycobacterium leprae*: immunologic observations. *Int. J. Leprosy*, v.68, n.4, p.434-443, December, 2000.

Groups of sooty mangabey monkeys (SMM) were vaccinated and boosted with *Mycobacterium bovis* bacillus Ca(mette-Guerin (BCG), or BCG + low-dose (LD) or high-dose (HD) heat-killed *M. leprae* (HKML), or were unvaccinated. Prior to and following vaccination-boosting and subsequent *M. leprae* (ML) challenge, these and unvaccinated, unchallenged control monkeys were immunologically observed longitudinally for approximately 3 years. SMM [multibacillary (MB) leprosy-prone as a species] were not protected clinically by BCG or BCG + HKML, although the disease progress was slowed by vaccination with BCG alone. The longitudinal immune response profiles to BCG or BCG + HKML in SMM showed that: 1) vaccination with BCG or BCG + HKML initially stimulated significant *in vitro* blood mononuclear cell blastogenic responses to ML antigens, which returned to baseline post-boosting and post-live ML challenge; 2) BCG + LD HKML-vaccinated groups gave the largest blastogenic response (SI = 23) followed by the BCG + HD HKML group (SI = 14.5) and by the BCG-only vaccinated group (SI = 3.6); 3) significantly diminished numbers of blood CD4+ (helper) and CD4+CD29+ (helper-inducer) T-cell subsets were observed longitudinally in all ML-challenged groups compared to controls regardless of whether they had been vaccinated or not; 4) CD8+ (suppressor) T-cell numbers remained longitudinally constant, on average, in all ML-challenged groups (vaccinated or not) compared to controls; 5) there was a significant decrease in the CD4+:CD8+ ratio over time in all ML-challenged groups (vaccinated or not); 6) vaccination with BCG or BCG + LD or HD HKML resulted in significantly increased numbers of CD4+CD45RA+ (suppressor-inducer) T cells longitudinally compared to the unvaccinated, ML-challenged control group; and 7) over time, vaccination with BCG + HKML followed by live ML-challenge produced higher IGM: IgG antiphospholipid-I (PGL-I) serum antibody response ratios than BCG-only vaccinated, ML-challenged monkeys or unvaccinated, ML-challenged SMM, consistent with prior observations that IgG anti-PGL-I responses correlate with resistance to and protection from clinical leprosy and IgM anti-PGL-I responses correlate with increased susceptibility.

KRAHENBUHL, J.; ADAMS, L.B. Exploitation of gene knockout mice models to study the pathogenesis of leprosy. *Leprosy Rev.*, v.71, p.S170-S175, December, 2000.

Shepard's technique for growth of *Mycobacterium leprae* in the mouse footpad, described in 1960, and more recent studies in thymectomized-irradiated mice and rats, athymic nude mice, nude rats and severe combined immunodeficiency (SCID) mice have defined the role of T-cell mediated immunity (CMI) in leprosy. However, the normal mouse and the immunocompromised mouse and rat represent only elements of polar tuberculoid disease and polar lepromatous leprosy, respectively. Transgenic, knockout (KO) mice may be employed to study the roles

of individual genes in the ability of the host to mount an effective immune response to pathogens, and may also allow development of mouse models for the immunologically unstable borderline areas of the spectrum. We are exploiting certain KO mice to improve our understanding of CMI to *M. leprae*, and to study the role of the microenvironment of the leprosy granuloma in pathogenesis. CGD (chronic granulomatous disease) mice and iNOS-KO mice lack the ability to produce reactive oxygen intermediates (ROI) and reactive nitrogen intermediates (RNI), respectively, whereas the T cells of GKO mice are unable to produce interferon-gamma (IFN gamma). iNOS-KO mice exhibit an enhanced capacity to form granulomas, and the histopathology of the infected footpad tissues of this strain share many elements of borderline tuberculoid disease. The macrophages of CGD mouse kill or inhibit multiplication of *M. leprae*, although they lack ROI. Multiplication of the organisms in the footpad is enhanced in GKO mice, although these mice retain some host resistance. In addition, we have been investigating supplementary, conditional approaches to KO mouse models. For example, the down-regulatory effects of local prostaglandin production can be controlled with essential fatty acid deficient diets or indomethacin, RNI can be blocked in CGD and GKO mice by treatment with aminoguanidine, NG monomethyl arginine or N6-(1-iminoethyl)-L-lysine, and local elaboration of TNF alpha can be neutralized by anti TNF alpha antibody or excess TNF alpha receptor. Other cytokines can be neutralized by antibody as well, broadening the range of conditional knockout models.

NAKAMURA M.; MATSUOKA, M. Limited ATP generation in cells of *Mycobacterium leprae* Thai-53 strain in enriched Kirchner liquid medium containing adenosine. *Int. J. Leprosy*, v.69, n.1, p.13-20, March, 2001.

The ATP generation in cells of *Mycobacterium leprae* Thai-53 strain takes place *in vitro* when the cells are cultivated in Kirchner liquid medium, pH 7.0, enriched with egg-yolk solution, pyruvate, transferrin, and adenosine at 30 degrees C. Among the supplements, adenosine was key and critical for the ATP generation. The optimal concentration of adenosine was 50 micrograms/ml of the medium. ATP generation, however, was limited; the rates of increase in ATP content extracted from the cells were approximately two- to threefold compared to that of the starting samples, and the increase reached a maximum at 4 or 6 weeks after incubation. No significant ATP generation in *M. leprae* cells was demonstrated in medium at pH 6.2 or pH 6.6, in the original Kirchner medium with or without adenosine, or when cultured at 37 degrees C, or when containing an antileprosy drug. No detectable increase in the number of *M. leprae* cells was observed with the increase in intracellular ATP content and DNA replication. No effect

was seen with renewal of the cultured medium by freshly prepared medium at 6 weeks' cultivation on the progressive ATP generation in *M. leprae*.

NATH, I.; VEMURI, N.; REDDI, A.L.; BHARADWAJ, M.; BROOKS, P.; COLSTON, M.J.; MISRA, R.S.; RAMESH, V Dysregulation of IL-4 expression in lepromatous leprosy patients with and without erythema nodosum leprosum. *Leprosy Rev.*, v.71, p.S130-S137, December, 2000. Supplement.

In order to increase our understanding of the immunological basis of erythema nodosum leprosum (ENL), we studied Th-like cytokine profiles in 130 leprosy patients, employing both the conventional and a novel, real-time, fluorogenic reverse transcriptase-based PCR (RT-PCR). The concomitant expression of both Th-like cytokines, interferon-gamma and IL-4, and the regulatory cytokines, IL-10 and IL-12, was studied in the peripheral blood cells of leprosy patients with and without ENL. In the conventional RT-PCR, varied cytokine profiles were observed in individual patients of all clinical types. Fifty-three percent of lepromatous patients without ENL and 59% of tuberculoid leprosy patients showed co-expression of IFN gamma and IL-4, indicating a non-polarized Th 0 pattern. Of the 36 patients with ENL, 58% demonstrated a polarized Th 1 pattern, with only 30% expressing both cytokines. Semiquantitative RT-PCR indicated a lower expression of IL-4 compared to that of IFN gamma in the lepromatous patients without ENL; the difference was even greater among those with ENL. The sensitive, real-time PCR confirmed the down-regulation of IL-4 and IL-10, with absence of IL-4 in half of the patients, resulting in skewing of the cytokine response toward a Th 1-like profile.

PARK, E.; LEVIS, W.R.; QUINN, M.R.; PARK, S.Y.; SCHULLER-LEVIS, G.B. Regulation of nitric oxide induced by mycobacterial lipoarabinomannan in murine macrophages: effects of interferon-beta and taurine-chloramine. *Int. J. Leprosy*, v.68, n.4, p.444-451, December, 2000.

We examined the effects of interferon beta (IFN-beta) on the production of lipopolysaccharide (LPS)-induced nitric oxide (NO) in peritoneal macrophages from low-responder and high-responder (C3H/HeJ and C3H/OuJ) mice. NO was produced in a dose response when induced by lipo-polysaccharide (LPS) or LAM plus interferon gamma (IFN-gamma) or IFN-beta in both high- and low-responder mice. In contrast to IFN-gamma, both high- and low-responder mice failed to induce nitrite production when IFN-beta was added, except at a high concentration of IFN-beta. Tau-CI (0.5 mM) inhibited NO production about 50% in the high-responder strain when cells were activated with LPS or LAM in combination with either IFN-beta or IFN-gamma, and almost abolished NO production at 1.0 mM. In the low-responder strain, Tau-CI

(0.5 mM) significantly inhibited NO production when cells were activated with IFN-gamma or IFN-beta in addition to LPS or LAM, but did not completely inhibit NO production at 1.0 mM. Tau-CI appears to play a potent role in regulating inflammatory reaction-induced bacterial or mycobacterial organisms. These data indicate a pivotal role for IFN-gamma and IFN-beta for the production of LPS and LAM initiated NO in peritoneal macrophages from low-responder (C3H/HeJ) mice.

SENGUPTA, U. Experience and lessons from the use of lepromin and *Mycobacterium leprae*-specific serology. *Leprosy Rev.*, v.71, p.S63-S66, December, 2000. Supplement.

Skin testing with lepromin, which produces a delayed-type hypersensitivity reaction, has been used in the classification of leprosy, and a good correlation has been found between immunological status and the reaction to lepromin. In addition, the prognostic value of the lepromin test has been demonstrated. More recently, skin testing with two soluble antigens of *Mycobacterium leprae* showed no difference of the mean size of the reaction between household contacts and non-contacts, indicating that these antigens are not useful for the diagnosis of leprosy. This and other evidence points to the need for a better skin test antigen capable of detecting infection of individuals by *M. leprae*. Whereas serological assays for antibodies against both PGL-1 and the 35 kDa antigen of *M. leprae* have been found to yield positive results in 90-100% of patients with lepromatous (BULL) leprosy, these assays fail to identify 40-60% of patients with tuberculoid (BT/TT) leprosy, because of the presence of only an insignificant level of antibody against components of *M. leprae* in these patients' serum, although, in many BT patients, antibody signal could be detected in the local lesions. These data indicate that there remains a need for a specific diagnostic test for leprosy.

TRUMAN, R.W.; KRAHENBUHL, J.L. Viable *M. leprae* as a research reagent. *Int. J. Leprosy*; v.69, n.1, p.1-12, march, 2001.

Mycobacterium leprae remain a rare research resource. They cannot be cultivated on artificial media, and the only established means to quantify viability of *M. leprae* has been by its relative growth in the foot pads of conventional mice (MEP). The MFP method is technically difficult and requires several months to yield results. More effective methods are needed. We examined the association between *M. leprae*'s ability to oxidize 14C-palmitate in axenic culture and the MFP growth results of a large number of suspensions. Oxidative activity was assessed by radiorespirometry (RR) using the Buddemeyer-type biphasic culture vessels containing 7H12 liquid medium and 14C-palmitate, or with commercially prepared BACTEC 12B vessels containing

the same medium. The RR results were highly correlated ($r = 0.71$) with the growth level that each *M. leprae* suspension achieved by the MFP technique. In using this technique to examine the effects that many common laboratory practices have on *M. leprae* viability, we found that viability varies markedly between bacillary suspensions derived from different hosts and tissues. The highest viabilities were obtained with bacilli from moderately enlarged nude MFP (< 1 g). Viability tended to be lower among very large nude MFP or long-duration infections and from armadillo tissues. After their harvest from host tissues, leprosy bacilli lost viability quickly. Suspensions stored in 7H12 liquid medium retained < 1% of their viability within 3 weeks of harvest, and freezing bacillary preparations or incubating them at 37 degrees C resulted in nearly an immediate equivalent loss in metabolic activity and viability. *M. leprae* viability is maintained best when bacilli are stored for only short periods of time at 4 degrees C-33 degrees C. Palmitate oxidation is a rapid, reliable and objective means by which to estimate the viability of *M. leprae* and can be used effectively as a surrogate for the conventional MFP technique in many studies.

ZUMARRAGA, M.J.; RESOAGLI, E.H.; CICUTA, M.E.; MARTINEZ, A.R.; ORITIZ DE ROTT, M.I.; DE MILLAN, S.G.; CAIMI, K.; GIOFFRE, A.; ALITO, A.; BIGI, E.; CATALDI, A.A.; ROMANO, M.I. PCR-restriction fragment length polymorphism analysis (PRA) of *Mycobacterium leprae* from human lepromas and from a natural case of an armadillo of Corrientes, Argentina. *Int. J. Leprosy*, v.69, n.1, p.21-25, march, 2001.

Polymerase chain reaction (PCR)-restriction fragment length polymorphism analysis (PRA) which relies on the amplification of a 439-bp portion of the hsp65 gene present in all mycobacteria, followed by two distinct digestions (with BstEII and HaeIII of the PCR product, offers a rapid and easy alternative that allows identification of the species without the need for specialized equipment. Wild leprosy in the nine-banded armadillo (*Dasypus novemcinctus*) is characterized by the presence of multiple bacilli in internal organs such as lymph nodes, spleen and liver, as well as in nerves and skin. We could observe this in 9 out of 132 animals captured in Corrientes, Argentina, an area endemic for leprosy in humans. *Mycobacterium leprae* were recognized in those naturally infected animals through different techniques. Three samples of extracted DNA of the mycobacteria present in the spleen, liver and popliteal lymph node of a naturally infected animal during the Experimental Program in Armadillo (PEA) and three samples of human lepromas were processed by PRA. The patterns of the six samples analyzed were identical and were characteristic of *M. leprae*. These studies, made for the first time in Argentina, corroborate the initial discoveries in South America made by our investigative group on the detection of armadillos

naturally infected with the Hansen bacillus.

NOORDEEN, S.K. Leprosy research and elimination. *Leprosy Rev*, v.71, p.S12-S14, December, 2000. Supplement.

The contribution of leprosy research to the progress being made toward elimination of leprosy has been critical. A major development in the promotion of leprosy research during the last 25 years has been the initiative taken by the WHO Special Programme for Research and Training in Tropical Diseases (TDR) through two of its scientific working groups, one on the immunology of leprosy (IMMLEP) and the other on the chemotherapy of leprosy (THELEP), which were set up in 1974 and 1976, respectively. IMMLEP and THELEP have greatly facilitated inputs from scientists not usually active in leprosy research. The coordinated efforts of IMMLEP and THELEP also facilitated goal-oriented research toward high-priority target areas such as an anti-leprosy vaccine and newer and better drug-combinations for the treatment of leprosy. Whereas the prospects for a leprosy vaccine appeared very promising in the early years, the first vaccine produced did not meet expectations for several reasons. Moreover, the possibility of using a vaccine in leprosy is not bright, because of both the technical problems as well as the reduced relevance of a vaccine at a time when leprosy is becoming less and less common. On the other hand, the modest expectations for newer and better drug combinations led to multi-drug therapy (MDT) for the control of leprosy. It is the introduction of MDT that is credited with the current global reduction of leprosy and the progress thus far made toward eliminating the disease as a public health problem. Nevertheless, many areas in leprosy, such as nerve damage, remain that require major research inputs in the future.

NEUROLOGIA

BIRKE, J.A.; BRANDSMA, J.W.; SCHREUDERS, T.A.; PIEFER, A. Sensory testing with monofilaments in Hansen's disease and normal control subjects. *Int. J. Leprosy*, v.68, n.3, p.291-298, September, 2000.

Sensory testing with Semmes-Weinstein filaments was conducted on: 112 normal subjects to determine the effects of age, gender and occupation on threshold perception, 27 Hansen's disease (HD) patients to determine inter-observer and intra-observer reliability of testing, and 101 patients with HD and a history of hand and/or foot ulceration to identify thresholds for injury risk. Filament thresholds were found related to age ($p < 0.002$) and occupation ($p < 0.001$) but not gender ($p > 0.1$). Inter-observer and intra-observer reliability was found to be high (intraclass correlation coefficient = 0.88-0.93). The 4.93 (7.0-7.7 g) filament had 97% sensitivity and 100% specificity for identifying a history of foot injuries,

and the 4.17 (1.2-1.6 g) filament had 100% sensitivity and 100% specificity for identifying hand injuries.

BRANDSMA, J.W. Monitoring motor nerve function in leprosy patients. *Leprosy Rev.*, v.71, n.3, p.258-267, Sep., 2000.

Manual muscle strength testing has an important function in the management of leprosy patients. Its importance was first recognized in the 1960s, especially when following patients who were started on steroid treatment to monitor the nerve function and the effect of treatment. In those days, and still in many centres today, many or all muscles were tested that are innervated by the nerves that can be at risk in leprosy. The author argues that not all muscles innervated by the nerves at risk need to be tested and also that many muscles cannot be tested in isolation. A muscle charting form is presented which is suitable for screening purposes, and that also allows for more detail when motor function is impaired.

MITCHELL, P.D. The threshold for protective sensation that prevents neuropathic ulceration on the plantar aspect of the foot: a study of leprosy patients in a rural community in India. *Leprosy Rev.*, v.72, n.2, p.143-150, June, 2001.

The protective sensation threshold is an important concept in the prevention of plantar ulceration in leprosy patients. Previous studies have suggested that skin with sensory nerve damage on the plantar aspect of the foot which can still detect the 5.07 Semmes-Weinstein monofilament (approximately 10 g) is highly unlikely to develop ulceration. While the threshold is thought to be less than the 6.10 filament (approximately 75 g), no work just testing adjacent to current ulcers has been undertaken to assess this more accurately. This is important, as it has been shown that a significant proportion of healthy individuals who wear sandals or go barefoot in India may fail to detect this 5.07 filament in at least some areas of the sole, especially in older age groups, and in certain cases the 5.46 filament (approximately 30 g) is the lightest detected. In an attempt to address this problem, a cross-sectional study on 26 current plantar ulcers in male adults with stable neuropathy due to leprosy was carried out in the rural town of Salur, India. It was confirmed that the ability to detect the 5.07 filament (approximately 10g) did prevent the development of ulceration while in contrast the ability to detect the 5.46 filament (approximately 30 g) did not. This suggests that the threshold for protective sensation lies between these two filaments. An approach is suggested which may help to differentiate feet genuinely at risk of ulceration from those merely unable to detect the 5.07 filament on account of thickened skin callus or advancing age.

RAMADAN, W.; MOURAD, B.; FADEL, W.; GHORABA, E. Clinical, electrophysiological, and immunopa-

thological study of peripheral nerves in Hansen's disease. *Leprosy Rev.*, v.72, n.1, p.35-49, March, 2001.

Hansen's disease is a disease of peripheral nerves. Some patients develop peripheral neuropathy before the diagnosis of the disease, and others develop these complications after starting therapy. Electrophysiological (EP) studies were carried out in Hansen's disease patients. This work studied the neural deficits, electromyography (EMG) and motor nerve conduction (MNC) variables in different types of leprosy and the immunopathology of sural nerve tissue in patients with severe neural deficits. Forty leprosy patients had neurological examinations and EP study. Histopathological and immunopathological study of sural nerve biopsy specimens was performed for 10 patients with severe neural deficits. The results of the neurological study showed that there was involvement of cranial nerves, muscular system, motor reflexes and sensory system and trophic and vasomotor changes. EP study showed significant changes in EMG of abductor digiti minimi in patients as compared to controls. MNC variables of common peroneal nerve were abnormal in 80% of all patients, MNC of median nerve was abnormal in 72.5%, while MNC of ulnar nerve was abnormal in 70% and SNC of ulnar nerve was abnormal in 77.5% of the total. In conclusion, electrophysiological investigations have an important role in the detection of muscle denervation and neuropathic changes in leprosy patients. These investigations are safe, rapid and non-invasive techniques. On the other hand immunopathological study revealed that the degree of immune positivity correlated with the degree of nerve fibrosis.

SARNO, E.N.; SANTOS, A.R.; JARDIM, M.R.; SUFFYS, P.N.; ALMEIDA, A.S.; NERY, J.A.; VIEIRA, L.M.; SAMPAIO, E.P. Pathogenesis of nerve damage in leprosy: genetic polymorphism regulates the production of TNF alpha. *Leprosy Rev.*, v.71, p.S154-S160, December, 2000. Supplement.

Studies carried out over the last decade have strongly suggested that TNF alpha both overtly participates in the cell-mediated immune response against *Mycobacterium leprae*, and is overproduced during reaction. In addition, reactions are intimately related to the onset of nerve damage. Finally, TNF alpha has been implicated in the pathogenesis of many human and experimental autoimmune peripheral neuropathies that, as in leprosy, result in demyelination and axonal lesions. Because of recent findings associating human TNF alpha mutant alleles at the -308 position with increased production of TNF alpha in many immunological and infectious diseases, an investigation of the role of TNF2 in predisposing leprosy patients to reaction has been undertaken. Analysis of 300 patients with leprosy-210 multibacillary and 90 paucibacillary—has shown that the percentage of reactional patients was similar among both

carriers and non-carriers of the TNF2 allele. However, a separate analysis of 57 carriers of TNF2 found that reactions occurred much more frequently among heterozygous than among homozygous patients. Moreover, the frequency of neuritis was somewhat greater among the heterozygous patients than among the non-carriers. Enhanced serum levels of TNF alpha have been noted in both TNF-1 and TNF-2 mutant patients in the course of leprosy reaction. Our observations to date suggest that other factors not related to the presence of the mutant gene may lead to the TNF alpha hyper-responsiveness observed during reaction.

SAUNDERSON, P. The epidemiology of reactions and nerve damage. *Leprosy Rev.*, v.71, p.S106-S110, December, 2000. Supplement.

The ALERT MDT Field Evaluation Study (AMFES) in Ethiopia, which was begun in 1988, involves the follow-up of 594 new patients for as long as 10 years after completion of treatment, including 6-monthly assessments of nerve function. In contrast to similar studies in India and Bangladesh, the Ethiopian cohort presented late, had a high rate of disability at diagnosis (55%), a high rate of multibacillary disease (51%) and a high rate of subsequent neuropathy (43%). Preliminary findings include the following. One-third of the patients never exhibited nerve damage. True acute neuropathy has a very good prognosis when treated with a standard course of steroids; full recovery was observed in 88% of nerves. Chronic and recurrent neuropathy have a worse prognosis; these problems need to be identified early and managed appropriately, employing either new steroid regimens or new drugs. The risk factors identified in this study include, for neuropathy, older age, delay of diagnosis, thickened nerves at diagnosis, and reversal reactions. Risk factors for chronic or recurrent neuropathy include classification, impairment at diagnosis, and reversal and ENL reactions. Those factors associated with a poor outcome include impairment at diagnosis, and chronic or recurrent neuropathy. Various problems faced in research in the area of leprosy reactions and neuropathy are discussed, as are the priorities for research in the future.

SAUNDERSON, P.; GEBRE, S.; DESTA, K.; BYASS, P.; LOCKWOOD, D.N.. The pattern of leprosy-related neuropathy in the AMFES patients in Ethiopia: definitions, incidence, risk factors and outcome. *Leprosy Rev.*, v.71, n.3, p.285-308, Sep., 2000.

The ALERT MDT Field Evaluation Study (AMFES) began in 1988 and followed patients prospectively for up to 10 years after release from treatment (RFT). This paper presents the findings from this cohort with regard to neuropathy and nerve damage. Five hundred and ninety-four new cases of leprosy are included in the study, 300 multibacillary (MB) and 294 paucibacillary (PB) cases. Fifty-five percent of patients had some degree of

impairment at diagnosis and a further 73 (12%) developed new nerve function impairment (NFI) after starting multiple drug therapy (MDT). The overall incidence rate for neuropathy was 39 episodes per 100 PYAR in the first year after diagnosis, gradually declining to 12 episodes per 100 PYAR in the sixth year. In those patients without impairment at diagnosis, the incidence rate of neuropathy was 25 episodes per 100 PYAR for MB cases and 11 per 100 PYAR for PB cases in the first year; in 33% of MB cases whose first episode of neuropathy occurred after diagnosis, that first episode took place after the first year, or after the normal period of treatment with MDT. Seventy-three patients with neuropathy developing after diagnosis are reported more fully: 34 (47%) had only one nerve involved and of these 25 (73%) had a single, acute episode of neuropathy. Nine (27%) had further episodes. Thirty-nine (53%) had more than one nerve involved and of these 16 (41%) had a single, acute episode, while 23 (59%) had further episodes. The terms 'chronic' and 'recurrent' neuropathy are defined and used to describe the pattern of neuropathy in those with repeated attacks. In patients with no impairment at the start of the study, treatment with steroids resulted in full recovery in 88% of nerves with acute neuropathy but only 51% of those with chronic or recurrent neuropathy. The median time to full recovery from acute neuropathy was approximately 6 months, but in a few cases recovery occurred gradually over 2-3 years. Severe neuropathy was less likely to be followed by a complete recovery than mild or moderate neuropathy. Forty-two percent of nerves with acute neuropathy that were not treated with steroids also fully recovered. In the group of patients who were thought to have old, permanent impairments at diagnosis, full recovery of nerve function occurred in 87/374 (23%) of the nerves involved. The overall outcome is illustrated by examining the average EHF score for groups of patients. Patients with no new neuropathy after diagnosis show a gradual improvement in their EHF score, while those with any episodes of neuropathy after diagnosis show a gradual deterioration after completion of MDT. Possible explanations for these findings are discussed. Risk factors for neuropathy, for chronic and recurrent neuropathy, and for a poor outcome 5 years after release from treatment, are examined. Impairment at diagnosis was the main risk factor for a poor outcome, accompanied by the occurrence of chronic/recurrent neuropathy or a reversal reaction.

SMITH, W.C. Review of current research in the prevention of nerve damage in leprosy. *Leprosy Rev.*, v.71, p.S138-S145, December, 2000. Supplement.

Nerve damage and the consequences of nerve damage set 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 resulting from leprosy are, therefore, of the highest priority. Self-care has been demonstrated to be an effective means of preventing secondary tissue damage, and its implementation must now be encouraged within the framework of basic health care. Currently, a comprehensive effort has been made to address all dimensions of impairment of nerve function and its consequences, from prevention of both primary and secondary impairments to interventions in long-term nerve damage. The BANDS prospective study of a cohort of 2664 previously untreated leprosy patients in Bangladesh has provided both a valuable baseline and insight into the epidemiology of nerve damage in leprosy. This work has defined the numbers of patients who present with acute nerve damage, the numbers who are not treated, and the importance of the MB classification, and has described the simple clinical prediction rule. This study also provided the basis for the development of the three TRIPOD randomized clinical trials in Nepal and Bangladesh. Follow-up of the BANDS cohort, which is continuing, will yield more data on the natural history of nerve damage. The encouraging results from the TRIPOD trials of low-dose prophylactic steroids will be followed up, to see whether the effect is sustained over time. The TRIPOD trials are to be completed, a trial of three steroid regimens in reversal reaction is to be completed, and a number of specific research topics within the ILEP programme, INFIR, are to be developed.

SPIERINGS, E.; DE BOER, T.; ZULIANELLO, L.; OTTENHOFF, T.H. The role of Schwann cells, T cells and *Mycobacterium leprae* in the immunopathogenesis of nerve damage in leprosy. *Leprosy Rev.*, v.71, p.5121-5129, December, 2000. Supplement.

Damage to peripheral nerves is the major complication of reversal (type I) reactions in leprosy. The underlying mechanism of nerve damage remains largely unresolved; however, an important role for type-1 T cells has been suggested. *Mycobacterium leprae* has a remarkable tropism for the Schwann cells that surround peripheral axons. Because reversal reactions in leprosy are often accompanied by severe and irreversible nerve destruction, and are associated with increased cellular immune reactivity against *M. leprae*, a likely immunopathogenic mechanism of damage to Schwann cells and peripheral nerves in leprosy is that infected Schwann cells process and present antigens of *M. leprae* to antigen-specific, inflammatory, type-1 T cells, and that these T cells subsequently damage and lyse infected Schwann cells. Previous animal studies with CDB+ T cells revealed evidence for the existence of such a mechanism. A similar role has been suggested for CD4+ T cells. These latter cells may be more important in causing nerve damage in vivo, given the predilection of *M. leprae* for Schwann cells, and the dominant role of CD4+, serine esterase+ Th1 cells in the lesions of leprosy. Antagonism

of the molecular interactions among *M. leprae*, Schwann cells and inflammatory T cells may therefore provide a rational strategy for prevention of damage of Schwann cell and nerves in leprosy.

Van BRAKEL, W.H. Peripheral neuropathy in leprosy and its consequences. *Leprosy Rev.*, v.71, p.S146-S153, December, 2000. Supplement.

Leprosy causes a 'mononeuritis multiplex' of immunological origin that results in autonomic, sensory and motor neuropathy. When detected and treated early, primary impairments may be reversible. However, 11-51% of patients do not recover. In addition, 33-56% of newly registered patients already have clinically detectable impairments, often no longer amenable to drug treatment. Among new patients, 6-27% present with secondary impairments, such as wounds, contractures and shortening of digits. All patients with impairments should be taught methods to prevent further impairment and subsequent disability (POID). As the result of impairments, many people experience limitation of activities of daily living, which can be partially overcome with the help of assistive devices, training, and surgery. As a result of these limitations, because of visible impairments, or simply because of the diagnosis 'leprosy', many people are restricted in their participation in society. Many overcome activity limitations and participation restrictions without assistance, despite residual impairments. However, some require intervention, such as physical or occupational therapy, reconstructive surgery or temporary socioeconomic assistance. Information on these issues is not collected routinely, and the few tools that exist to measure the severity or extent of impairment have not been widely used, nor have they been used to generate cohort-based statistics. There are no agreed indicators for monitoring POID activities or rehabilitation interventions. Work in the general field of rehabilitation has resulted in the ICIDH-2, which provides a conceptual framework for rehabilitation and the entire area of 'consequences of health conditions'. Although experience to date is very limited, the conceptual framework appears appropriate to leprosy. Data on the prevalence and incidence of primary and secondary impairments have been reported from several countries, the link between impairments and activity limitations has been investigated, and a few studies of the magnitude of the need for rehabilitation have been reported. Research priorities include studies of methods to improve detection of autonomic, sensory and motor neuropathy; trials of alternative drugs or regimens for treating neuropathy; studies of the use of various POID-monitoring systems that may be derived from these; studies of the design and use of instruments to assess limitations of activities and restrictions on participation; assessments of needs for rehabilitation and the development of methods to do these; studies of the efficacy of various types of rehabilitation interventions for particular conditions; and studies of the cost-effectiveness

of such interventions.

REABILITAÇÃO

BROEKHUIS, S.M.; MEIMA, A.; KOELEWIJN, L.F.; RICHARDUS, J.H.; BENBOW, C.; SAUNDERSON, P.R. The hand-foot impairment score as a tool for evaluating prevention of disability activities in leprosy: an exploration in patients treated with corticosteroids. *Leprosy Rev.*, v.71, n.3, p.344-354, Sep., 2000.

The hand-foot (HF) impairment score in leprosy patients is the sum of the WHO disability grades for hands and feet. This retrospective study explored the possibility of using the HF score for evaluation of the effectiveness of corticosteroid treatment programmes for nerve function impairment (NH). Changes in the score were compared with changes in sensory testing (ST) and voluntary muscle testing (VMT) for 42 leprosy patients who received corticosteroid treatment. The WHO grade did not change in 30/60 (50%) of extremities gaining, and in 4/10 (40%) extremities losing sensation and/or muscle strength. However, 18/24 (75%) patients with a definite gain in function improved in HF score, while the HF score remained unchanged in 10/11 (91%) patients with no change in nerve function. Five patients with impairment in multiple extremities showed both gain and loss of sensation and/or muscle strength in the same or different extremities. Overall, improvement, deterioration and absence of change in NFI, as indicated by changes in ST and VMT were reflected correctly by the HF score in 28 (76%) of the remaining 37 patients. It was also shown that the HF score does not give appropriate information on the extent of the effect of corticosteroid treatment. This study illustrates that the HF score can not be used to support management of corticosteroid treatment of individual patients, but indicates this score to be a promising device for the evaluation of the effectiveness of corticosteroid treatment programmes. This study used the HF score because information on (changes in) eye impairment was not considered reliable. However, in principle, we consider the EHF score, which is the sum of the WHO disability grades for hands, feet and eyes, preferable for evaluation purposes. We strongly recommend further validation of the EHF score as a tool for evaluation of corticosteroid treatment programmes for patient groups with different distributions of NFI through prospective studies.

CORNIELJE, H.; NICHOLLS, P.C.; VELEMA, J. Making sense of rehabilitation projects: classification by objectives. *Leprosy Rev.*, v.71, n.4, p.472-485, Dec., 2000.

Rehabilitation of disabled persons can take many different forms according to the sociocultural and political context in which it is undertaken. Some approaches have emphasized the restoration of the

physical function of the client, while others have looked beyond to psychological and social well-being. Some have built on the expertise of professionals while others have emphasized the caring capacity available in the family and the community and sought to reinforce it. Besides providing a wide range of possible services to disabled persons, rehabilitation seeks to change the attitudes that prevail in society as a whole and promote the integration of disabled people into society with equal rights and opportunities. This paper reviews a range of models and approaches which have been put forward in the international debate on rehabilitation. Furthermore, four dimensions are described which can be used to characterize and define classes of rehabilitation projects based on the objectives that are defined for them. Thus types of rehabilitation projects can be distinguished. Management, evaluation and technical support for rehabilitation projects need to take these essential characteristics into account.

FEENSTRA, W.; Van de VIJVER, S.; BENBOW, C.; AMENU, A.; SAUNDERSON, P. Can people affected by leprosy at risk of developing plantar ulcers be identified? A field study from central Ethiopia. *Leprosy Rev.*, v.72, n.2, p.151-157, June, 2001.

In the ALERT leprosy control programme, 75 people affected by leprosy, in three different geographical areas, were investigated. Each person was documented as having anaesthesia to the 10g monofilament. The study sought to determine why some people developed ulcers whilst others did not. According to the records, 43 had an ulcer during the last 5 years but 32 had never had an ulcer. In order to examine protective sensation on the sole of the foot, various sensory modalities were tested and the functional anatomy of the foot was examined. The results showed, as may be expected, that it is not possible to define a specific threshold for protective sensation that could be applied to all cases. Some people with only slightly diminished sensation developed ulcers, while many others with almost complete anaesthesia remained ulcer-free. In these rural communities, being a farmer reduced the risk of developing an ulcer, but no other demographic features were significant. Graded monofilaments were found to be the most appropriate test, with loss of sensation at any of five points tested being a 'positive' result. The 10 g filament was the most sensitive, but only 43% of feet identified by this test actually developed an ulcer. As people with partial loss of sensation were excluded from this study, this figure may be lower under programme conditions. The 50 g and 100 g filaments decrease the number of feet identified as at risk, but increase the percentage which actually develop an ulcer, to 46% and 49%, respectively. An appropriate test for selecting those for special programmes which may have a limited capacity, for example the provision of subsidized footwear or involvement in self-care groups, would be a 100 g filament, which would detect 86% of

those feet likely to develop an ulcer, while, reducing the number of those selected who are not at great risk. Vibrometry was found to be no better than graded filaments and an examination of functional anatomy did not help in identifying those at risk.

MEIMA, A.; SAUNDERSON, PR.; GEBRE, S.; DESTA, K.; HABBEMA, J.D. Dynamics of impairment during and after treatment: the AMFES cohort. *Leprosy Rev.*, v. 72, n.2, p.158-170, June, 2001.

This study investigates the dynamics of impairment during and after multidrug therapy treatment for the patient cohort of the prospective ALERT MDT Field Evaluation Study (AMFES). The impairment status was compared at intake, at release from treatment (rft), and at the time of the latest survey between 24 and 48 months after release from treatment (follow-up). The eye-hand-foot impairment score (EHF score), which is the sum of the WHO impairment grades of the eyes, hands, and feet, was used as tool for comparison. In all, 433 out of the 592 patients (224 PB and 209 MB) completed treatment in time and were assessed at release from treatment. The risk of getting impaired was 4% for the 113 PB and 21% for the 91 MB patients who were initially free from impairment. Out of the 111 initially impaired PB patients, 41% recovered or improved and 13% worsened in EHF score. For the 118 initially impaired MB patients, these figures were: recovery or improvement 43% and worsening 13%. Three hundred and twenty-three out of the 433 patients (158 PB and 165 MB) had a follow-up examination in between the next 24-48 months after rft. The risks of impairment at follow-up were 6% for the 79 PB and 18% for the 77 MB patients without impairment at rft. Out of the 79 PB patients with impairment at rft, 35% recovered or improved and 28% worsened. For the 88 impaired MB patients, these figures were: recovery or improvement 26% and worsening 27%. Patients showed a tendency to compensate EHF score improvement before rft by worsening after rft and vice versa. The first main conclusion is that the impairment status at intake was by far the most important determinant for future impairment. The second one is that the dynamics of impairment were less favourable after rft than before. Little is known about the long-term fate of leprosy patients with irreversible nerve damage and the associated risk of developing severe secondary impairment. Especially in this era of the leprosy elimination goal, we should give this accumulating patient group due attention in research and health policy agendas.

RAO, V.P.; RAO, I.R.; PALANDE, D.D. Socio-economic rehabilitation programmes of LEPRO India—methodology, results and application of needs-based socio-economic evaluation. *Leprosy Rev.*, v.71, n.4, p.466-471, Dec., 2000.

There is now a better understanding of the scope and process of rehabilitation. The approach recognizes the impact of leprosy on the individual, aims to

understand the needs and concerns of those affected, their families and community in the rehabilitation process, and that aims to restore the person to normal social life. LEPRO India has undertaken socio-economic rehabilitation (SER) activities in its projects in Andhra Pradesh and Orissa States in India with a holistic approach that has been evolutionary, developmental and participatory. A SER Officer (SERO) was posted to each project. A plan was formulated by the SERO with participation of all project staff. The main emphasis of the programme was on active participation of the affected person in the rehabilitation process. A needs-assessment study was conducted in the target population using a semi-structured questionnaire. Information was elicited about social and economic status, before and after the disease, and the current rehabilitation needs of the persons affected. The next step was meeting the needs through interventions by the SER staff. The impact of the programme on restoration of social and economic status of the affected persons was analysed. The paper stresses the importance of assessing the needs of persons affected by leprosy, structuring a rehabilitation programme with the active participation of the affected person and evaluating the impact of the interventions in restoring normal social and economic life.

RAZAFIMALALA, EC.; RAKOTOMANGA, S.; RAKOTONDRAJAO, J.; RAKOTOMALALA, J.N. Situation de la lèpre dans une région du Sud-Est de Madagascar de 1996 à 1998. *Acta Leprol.* v.12, n.1, p.7-10, 2000-2001.

Leprosy is endemic in Madagascar. The authors report the results of an epidemiologic study performed between 1996 and 1998 in Farafanguna, localized in the South-Eastern of the country. During this period, 217 new cases have been diagnosed. Of the 130 cases included in the study, 69.23% were children aged lower than 15 years and 76.91% suffered from a multibacillary form. More than 50% of the cases belonged to a large family (6 persons or more) and at least one family case was found in more than 60% of cases. These results enhance the severity of the disease in the country and show the presence of multiple risk factors (promiscuity, family cases and multibacillary forms).

SANLORENZO, M.; RAKOTONDRAJAO, J.; CALDERA, D.; BELLATO, C. La chirurgie de la lèpre dans un Hôpital de brousse en Afrique: expérience à Madagascar. *Acta Leprol.*, v.12, n.1, p.19-24, 2000-2001.

We report our experience of leprosy surgery in terms of feasibility and efficacy in a small hospital of bush in Madagascar during the period of September 1989 to January 1993. Operations of neurolysis, corrections of claw hands by the techniques of Lasso-Zancolli or Van Droogenbroeck, arthrodesis, resections and amputations

have been performed. Our results suggest that at least a part of these surgical procedures may be performed by a non specialized medical team, taught on the premises. Thus, the cost of treatment will be low and accessible to more leprosy patients.

VAZ, M.; DIFFEY B.; JACOB, A.J...; VAZ, M. Should nutritional status evaluation be included in the initial needs assessment of leprosy patients with disability prior to socio-economic. *Leprosy Rev.*, v.72, n.2, p.206-211, June, 2001.

Because of the large numbers of leprosy patients with disability and the limited resources available, it is important that socio-economic rehabilitation (SER) is targeted towards those who are most in need. Towards this purpose, current assessments of leprosy patients prior to initiating SER include the evaluation of income, assets and household possessions. Conspicuously absent is the nutritional assessment of the patient. In the absence of weight loss associated with illness, population studies indicate that undernutrition reflects poor socio-economic conditions. In this study of 151 cured leprosy patients with disability, 57% of the patients were found to be undernourished using body mass index (kg/m²) derived from body weight and height, and 10% of the patients were severely undernourished (grade III). Undernutrition in the patients was poorly though significantly correlated with personal income ($r = 0.18$, $P < 0.05$). Total household income, reported amount of money spent on food and estimated cereal intakes were not correlated with the BMI of the patient, possibly due to reporting bias and other methodological issues. We propose the inclusion of nutritional status evaluation by anthropometry as part of the initial screening of leprosy patients prior to instituting SER. We believe that this simple and objective evaluation can add to the assessment of 'threat' of economic deprivation or actual economic 'dislocation', and thus help in the prioritization of leprosy patients for SER.

REAÇÕES À DROGA

NAMISATO, M.; OGAWA, H Serious side effects of rifampin on the course of WHO/MDT: a case report. *Int. J. Leprosy*, v.68, n.3, p.277-282, September, 2000.

A male born in 1935 was diagnosed as having lepromatous leprosy when he was 17 years old. In addition to dapsone (DDS) monotherapy, he had been treated with rifampin (RMP) for 2 terms: first with 450 mg a day for 2 years when he was 39 years old; second with 150 mg a day for 2 months after a 1-year interval from the first regimen. During these entire courses with RMIP, no complication was noted. When he was 64 years old in 1999, a diagnosis of relapsed borderline tuberculoid (BT) leprosy was made, and he was started on the multibacillary (MB) regimen of the World Health

Organization multidrug therapy (WHO/MDT). After the third dose of monthly RMP, he developed a flu-like syndrome and went into shock. A few hours later, intravascular hemolysis occurred followed by acute renal failure. He was placed on hemodialysis for 7 series and recovered almost completely about 2 months later. The immune complexes with anti-RMP antibody followed by complement binding may have accounted for these symptoms. Twenty-four reported cases of leprosy who had developed side effects of RMP under an intermittent regimen were analyzed; 9 of the cases had had prior treatment with RMP but 15 had not. Adverse effects were more likely to occur in MB cases and were more frequent during the first 6 doses of intermittent regimens. The cases with prior treatment with RMP had had a higher incidence of serious complications such as marked hypotension, hemolysis and acute renal failure. However, many exceptions were also found, and we could not verify any fully dependable factor(s) to predict the side effects of RMP. More field investigation is desirable, and monthly administration of RMP must be conducted under direct observation through the course of WHO/MDT

RAO, RN.; LAKSHMI, T.S. Increase in the incidence of dapsone hypersensitivity syndrome—an appraisal. *Leprosy Rev.*, v.72, n.1, p.57-62, March, 2001.

There has been an increase in the reports of dapsone hypersensitivity syndrome (DHS) in the past few years, coinciding with the introduction of multidrug therapy (MDT) for leprosy world-wide. The exact cause of this phenomenon is not clear. We report four cases of DHS observed among 252 leprosy patients on MDT and one case of DHS in a patient taking dapsone for nodulocystic acne in the Dermatology Department of the Osmania General Hospital, Hyderabad, India, between June 1997 and January 1999 with few unusual features. In two of these five patients maculopapular rash was severe and progressed to erythroderma. Introduction of MDT in 1982 has not only decreased the prevalence of leprosy but also brought about a positive change in the attitude of people which increased the voluntary reporting of leprosy patients. This, coupled with improvements in organization of leprosy control and awareness among medical personnel of DHS, are probably the most important reasons for the increased reporting of DHS in recent years.

TERAPÊUTICA

AMENU, A. et al. The pattern of decline in bacillary index after 2 years of WHO recommended multiple drug therapy: the AMFES cohort. *Leprosy Rev.*, v.71 p.332-337, 2000.

With effective antibiotic treatment, the bacillary index (BI) in multibacillary leprosy patients declines over number of years. This can be quantified as a rate of decline in log-units per year or as the time until smear

negativity is reached. In the AMFES cohort 220 cases had data on the changes in their BI over time, while 170 cases are documented until smear negativity. The average BI at the start was 3.3 (SD 1.5; range 0.3-5.5) and the mean rate of decline was 0.85 units per year (median 0.7 units per year); in the first 2 years after diagnosis, the mean rate of decline was 1.15 units per year. The rate of decline was not related to any clinical features of the disease except delay in diagnosis: patients presenting for treatment early had a significantly faster rate of clearing the bacilli (adjusted relative risk 2.3; 95% CI 1.0-5.1). Fifty-eight percent of cases took longer than 3 years to reach smear negativity, but this time interval is largely determined by the initial BI and classification, making it a less useful indicator of bacterial clearance. More severe impairment at the start of treatment was associated with a faster return to smear negativity, for which no obvious explanation can be given. Reversal reactions, which occurred in 25% of the cases reviewed, are not associated with a more rapid clearance of bacilli.

BRITTON, W.J.; MARTIN, E.; KAMATH, A.T.; NEUPANE, K.D.; ROCHE, P.W. Immunoprophylaxis against *Mycobacterium leprae* infection with subunit vaccines. *Leprosy Rev.*, v.71, p.S176-S181, December, 2000. Supplement.

We have investigated the effect of subunit vaccines against infection with *Mycobacterium leprae*, employing DNA plasmids as the vaccine vectors, and the immunodominant 35 kDa protein of *M. leprae* as the candidate antigen. A DNA vaccine that expresses the *M. leprae* 35 kDa protein both stimulated interferon-gamma (IFN gamma)-secreting T cells in mice, and demonstrated protection against *M. leprae*-infection of mice.

DILETTO, C.; BLANC, L.; LEVY, L. Leprosy chemoprophylaxis in Micronesia. *Leprosy Rev.*, v.71, p.521-523, December, 2000. Supplement.

A programme of chemoprophylaxis was introduced as a component of the leprosy control programme in the Federated States of Micronesia (FSM), beginning in 1996. The entire population of the country was to be screened, and a single dose of 600 mg rifampicin, 400 mg ofloxacin and 100 mg minocycline (ROM) was to be administered to the entire population. Two rounds of screening the entire population were carried out, approximately 1 year apart, and chemoprophylaxis was administered at the time of each screening. Ninety percent of the population were screened at least once, and 55% were screened in both rounds; 87% of the population received at least one dose, and 54% received two doses. In the course of the first round, 322 new cases were detected, whereas only 80 new cases were detected during the second round, of whom only 12 had received chemoprophylaxis in the course of the first round. A third round of screening, confined to a small number of villages in both Chuuk and

Pohnpei, in which states leprosy endemicity was high, was carried out approximately 2 years after the second. Only 16 new cases were detected during the third round of screening, whereas 102 new cases had been detected in this same population during the first round of screening, and 32 new cases during the second. Six of the 16 newly detected cases stated that they had been administered chemoprophylaxis at least once; however, this information may not be reliable.

GEBRE, S.; SAUNDERSON, P.; BYASS, P. Relapses after fixed duration multiple drug therapy: the AMFES cohort. *Leprosy Rev.*, v.71, n.3, p.325-331, Sep., 2000.

Relapse rates after multiple-drug therapy (MDT) have been low, although there remains a concern about the possibility of late relapse in those with an initially high bacterial load. In all, 502 patients in the AMFES cohort completed fixed-duration MDT and are included in this report. There have been no confirmed relapses in the AMFES cohort, in a follow-up period of up to 8 years after completion of treatment, even in the 57 cases with an initial average bacillary index of $>$ or $=$ 4.0, 20 of whom have been followed for more than 5 years after ceasing MDT. Methods of diagnosing a relapse are discussed.

GILLIS, T.P.; WILLIAMS, D.L. Dapsone resistance in *Mycobacterium leprae*. *Leprosy Rev.*, v.71, p. S591-5595, December, 2000. Supplement.

The fo1P1 gene of *Mycobacterium leprae*, which encodes dihydropteroate synthase (DHPS), was studied for the presence of mutations associated with resistance to dapsone (DDS). When the fo1P1 of several DDS-resistant clinical isolates of *M. leprae* were sequenced, two missense mutations were identified. One mutation occurred at codon 53, substituting isoleucine for threonine in DHPS-1, and a second mutation occurred in codon 55, substituting arginine for proline. DNA sequencing of strains of *M. leprae* resistant to 0.01g% DDS in the mouse diet revealed that 13 of 14 strains contained either the 53 or 55 fo1P1 mutation. None of the susceptible strains and only one of five strains resistant to 0.001 g% DDS revealed a mutation in fo1P1, suggesting that only high-level DDS resistance is associated with the mutations identified in fo1P1. Development and application of simple molecular tests to assess drug-related mutations in *M. leprae* could establish current levels of drug resistance in leprosy as a reference point for future monitoring of drug resistance at the global level.

GORMUS, B.J.; BASKIN, G.B.; XU, K. et al. Antileprosy protective vaccination of sooty mangabey monkeys with BCG or BCG plus heat-killed *Mycobacterium leprae*: immunologic observation. *Int. J. Leprosy*, v.68, n.4, p.434-443, December, 2000.

Groups of sooty mangabey monkeys (SMM) were

vaccinated and boosted with *Mycobacterium bovis* bacillus Calmette-Guerin (BCG), or BCG + low-dose (LD) or high-dose (HD) heat-killed *M. leprae* (HKML), or were unvaccinated. Prior to and following vaccination-boosting and subsequent *M. leprae* (ML) challenge, these and unvaccinated, unchallenged control monkeys were immunologically observed longitudinally for approximately 3 years SMM [multibacillary (MB) leprosy-prone as a species] were not protected clinically by BCG or BCG + HKML, although the disease progress was slowed by vaccination with BCG alone. The longitudinal immune response profiles to BCG or BCG + HKML in SMM showed that: 1) vaccination with BCG or BCG + HKML initially stimulated significant in vitro blood mononuclear cell blastogenic responses to ML antigens, which returned to baseline post-boosting and post-live ML challenge; 2) BCG + LD HKML-vaccinated groups gave the largest blastogenic response (S1=23) followed by the BCG + HD HKML group (S1=14.5) and by the BCG-only vaccinated group (S1=3.6); 3) significantly diminished numbers of blood CD4+ (helper) and CD4+CD29+ (helper-inducer) T-cell subsets were observed longitudinally in all ML-challenged groups compared to controls regardless of whether they had been vaccinated or not; 4) CD8+ (suppressor) T-cell numbers remained longitudinally constant, on average, in all ML-challenged groups (vaccinated or not) compared to controls; 5) there was a significant decrease in the CD4+:CD8+ ratio over time in all ML-challenged groups (vaccinated or not); 6) vaccination with BCG or BCG + LD or HD HKML resulted in significantly increased numbers of CD4+CD45RA+ (suppressor-inducer) T cells longitudinally compared to the unvaccinated, ML-challenged control group; and 7) over time vaccination with BCG + HKML followed by live ML-challenge produced higher IGM:IgG antiphospholipid-I (PGL-I) serum antibody response ratios than BCG-only vaccinated, ML-challenged monkeys or unvaccinated, ML-challenged SMM, consistent with prior observations that IgM anti-PGL-I responses correlate with resistance to and protection from clinical leprosy and IgM anti-PGL-I responses correlate with increased susceptibility.

GRIFFITHS, S. ; READY, N. Defaulting patterns in a provincial leprosy control programme in Northern Mozambique. *Leprosy Rev.*, v.72, n.2, p.199-205, June, 2001.

Cohort-based multidrug therapy (MDT) completion rates are used to assess adherence to MDT. However this measure gives no information about when during the treatment period defaulting occurs. Two districts in Cabo Delgado province in Northern Mozambique were selected for evaluation of multibacillary patient defaulter data between 1993 and 1997 to examine when patients default during the treatment period. In all, 548 (59.2%) of 926 MB patients completed treatment and 378 (40.8%) defaulted between 1993 to 1997. The percentage of

defaulters fell steadily from 59.8% in 1993 to 23.2% in 1997. Of the 378 defaulters 57.7% defaulted treatment within 6 months and 83.1% within 1 year of starting treatment. It was observed that patients tend to default early rather than late in the treatment period and that this pattern is maintained over time despite a fall in defaulter rates. Patients established early into a treatment routine were more likely to complete treatment. A comprehensive effort to improve and maintain leprosy control services will probably influence adherence more than any single, specific strategy. Shortening MDT treatment from 2 years to 1 year is unlikely to affect the defaulter rate.

GROSSET, J. The new challenges for chemotherapy research. *Leprosy Rev.*, v.71, p.S100-S104, December, 2000. Supplement.

Scientific knowledge is constantly expanding, and needs are changing; therefore, efforts must be made to adapt the treatment of leprosy and the manner in which it is implemented to the newly identified needs. Because an effective vaccine against leprosy remains to be identified, multidrug therapy (MDT) is the only tool available for leprosy control. At present, therefore, the priority is to make MDT available in all endemic countries for all patients, even those living in difficult-to-access areas. The remaining important issues in chemotherapy research are to improve the quality of leprosy case-finding, improve the quality of MDT, identify the areas in which leprosy patients are not receiving proper MDT, and find the means necessary to ensure delivery to all of appropriate MDT. The MDT regimens recommended by the World Health Organization are of too long duration, require correct classification of the patients as PB or MB, and rely upon the daily self-administration of dapsone and clofazimine to prevent selection of rifampicin resistant mutants among MB patients. Thus, research leading to the development of new drug regimens should be directed toward overcoming the shortcomings of the presently recommended regimens. The drugs required to permit use of regimens of shorter duration, that may be employed among both PB and MB patients, and that enable fully supervised drug administration may be already in hand, and the necessary clinical trials to confirm efficacy and acceptability should be carried out.

JI, B.; GROSSET, J. Combination of rifapentine-moxifloxacin-minocycline (PMM) for the treatment of leprosy. *Leprosy Rev.*, v.71, p.S581-S587, December, 2000. Supplement.

To further the development of a multidrug regimen for treatment of leprosy that is suitable for monthly administration and fully supervisable, the bactericidal activities against *Mycobacterium leprae* of HMR 3647 (HMR), moxifloxacin (MXFX) and rifapentine (RPT) were measured by the proportional bactericide technique in the mouse footpad system, and compared with those of

the established antileprosy drugs clarithromycin (CLARI), ofloxacin (OFLO) and rifampicin (RMP). Administered in five daily doses of 100 mg per kg body weight, HMR appeared slightly more bactericidal than CLARI, but the difference did not attain statistical significance. Administered as single doses, MXFX in a dosage of 150 mg per kg was more active than OFLO in the same dosage, and displayed the same level of activity as RMP in a dosage of 10 mg per kg; the combination MXFX-minocycline (MINO) (MM) was more bactericidal than the combination OFLO-MINO (OM); RPT in a dosage of 10 mg per kg was more bactericidal than RMP administered in the same dosage, and even more active than the combination RMP-OFLO-MINO (ROM); the combination RPT-MXFX-MINO (PMM) killed 99.9% of viable *M. leprae*, and was slightly more bactericidal than was RPT alone, indicating that the combination PMM showed an additive effect against *M. leprae*. These promising results justify a clinical trial among lepromatous patients, in which MM is being compared with OM, and PMM with ROM, in terms of efficacy and tolerance.

LOCKWOOD, D.N.J. Steroids in leprosy type 1 (reversal) reactions: mechanisms of action and effectiveness. *Leprosy Rev.*, v.71, p.S111-S114, December, 2000. Supplement.

Steroids are widely used for the treatment of leprosy reactions. The effectiveness of steroid treatment is variable, with only 60% of patients regaining nerve function. Sequential skin biopsy specimens, obtained from 15 patients with type 1 (reversal) reactions, have been studied to document the cytokine profile and cellularity of the lesions. All of the patients were placed on a standard course of steroids after the first biopsy. Subsequent biopsies were performed seven, 28 and 180 days later. The specimens were stained for interferon- γ (IFN γ), interleukin-12 (IL-12) and inducible nitric oxide synthase (iNOS). After the first biopsy, all patients were placed on a standard reducing course of steroids beginning at 30 mg daily. By day 7, treatment with prednisolone showed little effect on the cellularity and cytokine profiles. However, by day 28, significant decreases of IFN- γ , IL-12 and iNOS were found for most patients. Some patients maintained cytokine production at day 28 and even at day 180. These data illustrate the strong Th1 profile of type 1 reactional lesions, the relatively slow response to therapy, and the continuing activity after treatment with steroids for 180 days. The variation of individual responses emphasizes their importance. Additional prospective studies will be required to determine whether patients with high intra-lesional levels of cytokine are at risk of recurrent reactions. The need for studies both of different glucocorticoids and of other non-steroidal immunosuppressants for the treatment of reactions is discussed.

MAJUMDER, V.; SAHA, B.; HAJRA, S.K.; BISWAS, S.K.;

SAHA, K. Efficacy of single-dose ROM therapy plus low-dose convit vaccine as an adjuvant for treatment of paucibacillary leprosy patients with a single skin lesion. *Int. J. Leprosy*, v.68, n.3, p.283-290, September, 2000.

The recent World Health Organization multicentric field study on the treatment of paucibacillary (PB) leprosy patients with single skin lesion (SSL) and a single dose of rifampin-ofloxacin-minocycline (ROM) brought new hope to those who are engaged in the eradication of leprosy from India. Being encouraged by the WHO report, we undertook the present hospital-based study and found that PB leprosy patients with SSL were morphologically and histopathologically heterogeneous. The histological spectrum of SSL ranged from indeterminate through tuberculoid (TT) to borderline tuberculoid (BT) leprosy, and most patients had active BT leprosy. Ninety new, untreated PB leprosy patients with SSL were included in the present study for comparative assessment of the efficacies of ROM and ROM plus Convit vaccine therapies. Children, pregnant women, lactating mothers and patients with any thickening of nerves were excluded. All patients were bacteriologically negative (skin-smear test) but lepromin reactive. The patients were divided into two groups after proper matching for morphological and histological status of SSL: a) The test group included 60 patients and the control group included 30 patients. The test group was given a single dose of ROM initially and two injections of low-dose Convit vaccine, one initially and the other at the end of 3 months. b) The control group was given only a single dose of ROM initially. Both groups were followed clinically every 2 weeks for 6 months and retested for histological, bacteriological and lepromin status at the end of 6 months. Thereafter, they were followed clinically every month for another 6 months. In the test group, the SSL resolved in 33.3%, regressed in 48.3%, and remained active in 18.3% of the patients, while the granuloma disappeared in 70% of the cases. Only one patient developed neuritis, and in another patient the disease relapsed on the eighth month. On the other hand, the SSL in the control patients resolved, regressed and remained active in 13.3%, 63.3% and 23.3% of the cases, respectively, while the granuloma disappeared in 53.3% of the cases. In the seven patients who remained active, the disease course was progressive, and two of them developed neuritis. The clinical outcome of the patients treated with ROM plus low-dose Convit vaccine was statistically superior to those treated with single-dose ROM therapy alone.

MATSUOKA, M.; KASHIWABARA, Y.; NAMISATO, M. A *Mycobacterium leprae* isolate resistant to dapsone, rifampin, ofloxacin and sparfloxacin. *Int. J. Leprosy*, v.68, n.4, p.452-455, December, 2000.

Mycobacterium leprae were isolated from a

Japanese patient, and susceptibility to antileprosy drugs was examined by the mouse foot pad method. The isolate was susceptible to clofazimine and clarithromycin, and resistant to dapsone, rifampin, ofloxacin and sparfoxacin. Mutations were identified in the genes associated with resistance to these drugs. The risk of the emergence of leprosy with multidrug resistance is emphasized.

MEIMA, A. et al. Dynamics of impairment during and after treatment: the AMFES cohort. *Leprosy Rev.*, v.72, n.2, p.158-170, June, 2001.

This study investigates the dynamics of impairment during and after multidrug therapy treatment for the patient cohort of the prospective ALERT MDT Field Evaluation Study (AMFES). The impairment status was compared at intake, at release from treatment (rft), and at the time of the latest survey between 24 and 48 months after release from treatment (follow-up). The eye-hand-foot impairment score (EHF score), which is the sum of the WHO impairment grades of the eyes, hands, and feet, was used as tool for comparison. In all, 433 out of the 592 patients (224 PB and 209 MB) completed treatment in time and were assessed at release from treatment. The risk of Benign impaired was 4% for the 113 PB and 21% for the 91 MB patients who were initially free from impairment. Out of the 111 initially impaired PB patients, 41% recovered or improved and 13% worsened in EHF score. For the 118 initially impaired MB patients, these figures were: recovery or improvement 43% and worsening 13%. Three hundred and twenty-three out of the 433 patients (158 PB and 165 MB) had a follow-up examination in between the next 24-48 months after rft. The risks of impairment at follow-up were 6% for the 79 PB and 18% for the 77 MB patients without impairment at rft. Out of the 79 PB patients with impairment at rft 35% recovered or improved and 28% worsened. For the 88 impaired MB patients, these figures were: recovery or improvement 26% and worsening 27%. Patients showed a tendency to compensate EHF score improvement before rft by worsening after rft and vice versa. The first main conclusion is that the impairment status at intake was by far the most important determinant for future impairment. The second one is that the dynamics of impairment were less favourable after rft than before. Little is known about the long-term fate of leprosy patients with irreversible nerve damage and the associated risk of developing severe secondary impairment. Especially in this era of the leprosy elimination goal, we should give this accumulating patient group due attention in research and health policy agendas.

NAMISATO, M.; OGAWA, H. Serious side effects of rifampin on the course of WHO/MDT: a case report. *Int. J. Leprosy*, v.68, n.3, p.277-282, September, 2000.

A male born in 1935 was diagnosed as having

lepromatous leprosy when he was 17 years old. In addition to dapsone (DDS) monotherapy, he had been treated with rifampin (RMP) for 2 terms: first with 450 mg a day for 2 years when he was 39 years old; second with 150 mg a day for 2 months after a 1-year interval from the first regimen. During these entire courses with RMP, no complication was noted. When he was 64 years old in 1999, a diagnosis of relapsed borderline tuberculoid (BT) leprosy was made, and he was started on the multibacillary (MB) regimen of the World Health Organization multidrug therapy (WHO/MDT). After the third dose of monthly RMP, he developed a flu-like syndrome and went into shock. A few hours later, intravascular hemolysis occurred followed by acute renal failure. He was placed on hemodialysis for 7 series and recovered almost completely about 2 months later. The immune complexes with anti-RMP antibody followed by complement binding may have accounted for these symptoms. Twenty-four reported cases of leprosy who had developed side effects of RMP under an intermittent regimen were analyzed; 9 of the cases had had prior treatment with RMP but 15 had not. Adverse effects were more likely to occur in MB cases and were more frequent during the first 6 doses of intermittent regimens. The cases with prior treatment with RMP had had a higher incidence of serious complications such as marked hypotension, hemolysis and acute renal failure. However, many exceptions were also found, and we could not verify any fully dependable factor(s) to predict the side effects of RMP. More field investigation is desirable, and monthly administration of RMP must be conducted under direct observation through the course of WHO/MDT.

NGUYEN, L.N. ; CARTEL, J.L. ; GROSSET, J.H. Chemoprophylaxis of leprosy in the Southern Marquesas with a single 25 mg/Kg dose of rifampicin. Results after 10 years. *Leprosy Rev.*, v.71, p.S553-S536, December, 2000. Supplement.

In 1988, a programme of leprosy chemoprophylaxis, employing a supervised, single 25 mg/kg dose of rifampicin, was implemented in the Southern Marquesas Islands. Of the 2786 inhabitants, 2751 (98.7%) were treated. In addition, 3144 South Marquesans living elsewhere in French Polynesia were administered the same chemoprophylaxis. During the following 10 years, seven leprosy patients were detected among those who had been administered chemoprophylaxis. Of these, two were very likely missed cases of leprosy, and cannot be considered a failure of chemoprophylaxis. The epidemiometric projection model, based on cases of leprosy observed in the Southern Marquesas during the 20 years preceding implementation of the programme, predicted that 17 leprosy cases could be expected in the South Marquesan population if no chemoprophylaxis were given. In fact, only five cases were detected in the treated population, a number significantly smaller than 17, suggesting that the chemoprophylaxis was 70%

effective, assuming that no change of detection rate would have occurred without chemoprophylaxis. However, during the 10 years following implementation of the chemoprophylaxis programme, the detection rate in the Polynesian population that was not administered chemoprophylaxis declined by about 50%. Therefore, the effectiveness of the chemoprophylaxis was only 35-40%.

NOORDEEN, S.K. Prophylaxis—scope and limitations. *Leprosy Rev.*, v.71, p.S16-S19, December, 2000. Supplement.

Attempts to prevent leprosy by one or another prophylactic method began with the use of dapsone as a chemoprophylaxis. Following early, small-scale studies, which were promising, large-scale studies with dapsone and acedapsonone, both among contacts and in the general population, demonstrated that it is possible to prevent the occurrence of leprosy to a modest extent. With regard to immunoprophylaxis, BCG had long been considered a possibility, particularly in view of its potential to convert the skin test reaction to lepromin. Over the years, major, large-scale field trials of BCG had been carried out in Uganda, Burma, Papua New Guinea and India. All of the studies demonstrated that BCG was capable of preventing leprosy. However, protective efficacy varied from around 20% to greater than 80%. Killed *Mycobacterium leprae* mixed with BCG has also given varying results. Other vaccines based on cultivable mycobacteria have also been tried, and at least one of them appears promising. An approach to prophylaxis must take into account (a) the level of risk addressed and the perception of risk by the community; (b) the level of efficacy of the method of prophylaxis; (c) the possibility of easily identifying high-risk groups; (d) the operational feasibility; and (e) the focus of the prophylaxis, whether the individual or the community, or both. However, in view of the enormous progress being made towards elimination of leprosy by the widespread application of MDT, prophylaxis is becoming less and less relevant and less and less cost-effective, except in very special situations.

RAO, P.N.; LAKSHMI, T.S. Increase in the incidence of dapsone hypersensitivity syndrome—an appraisal. *Leprosy Rev.*, v.72, n.1, p.57-62, March, 2001.

There has been an increase in the reports of dapsone hypersensitivity syndrome (DHS) in the past few years, coinciding with the introduction of multidrug therapy (MDT) for leprosy world-wide. The exact cause of this phenomenon is not clear. We report four cases of DHS observed among 252 leprosy patients on MDT and one case of DHS in a patient taking dapsone for nodulocystic acne in the Dermatology Department of the Osmania General Hospital, Hyderabad, India, between June 1997 and January 1999 with few unusual features. In two of these five patients maculopapular rash was severe and progressed to erythroderma. Introduction of MDT in

1982 has not only decreased the prevalence of leprosy but also brought about a positive change in the attitude of people which increased the voluntary reporting of leprosy patients. This, coupled with improvements in organization of leprosy control and awareness among medical personnel of DHS, are probably the most important reasons for the increased reporting of DHS in recent years.

ROBERTSON, L.M.; NICHOLLS, P.G.; BUTLIN, R. Delay in presentation and start of treatment in leprosy: experience in an out-patient clinic in Nepal. *Leprosy Rev.*, v.71, n.4, p.511-516, Sep., 2000.

Delayed presentation is a recognized risk factor for disability in leprosy but is the result of complex interactions between physical, social, economic and psychological factors. The present study is a response to the situation in an outpatient clinic in Nepal where the wide variation in delay in presentation was a cause for concern. A purpose-written questionnaire was used to collect information on 166 consecutive outpatient admissions. The data included demographics, the first symptom of leprosy, first actions, initial help-seeking behaviour, the reasons for finally seeking treatment and experience with professional health services. Initial analysis found a relationship between delay in presentation and age, rural environment, leprosy classification, walking time, housing not shared with another person affected by leprosy, and an inappropriate first action. The relationship with lack of education and total travel time just failed to reach significance. Further analysis identified that for the study population initial lack of awareness of leprosy and an inappropriate first action were the primary contributors to delay. Extensive and effective health education is needed to address this situation.

SAUNDERSON, P; GEBRE, S.; BYASS, P. ENL reactions in the multibacillary cases of the AMFES cohort in central Ethiopia: incidence and risk factors. *Leprosy Rev.*, v.71, n.3, p.318-324, 2000.

Erythema nodosum leprosum (ENL), or type 2 leprosy reactions are an important complication of multibacillary leprosy. The AMFES cohort includes 300 new multibacillary cases that have been followed for up to 10 years from the start of treatment, in central Ethiopia. Sixteen (5.3%) patients had ENL reactions. The incidence of ENL was maximal in the second and third years after the start of treatment, reaching 6.9 episodes per 100 person years at risk. Factors associated with being lepromatous [LL classification and a high bacillary index (BI)] gave an increased risk of developing ENL; in the univariate analysis, LL classification gave a relative risk of 3.6 (95% CI 1.3-10) and a BI of 6 gave a relative risk of 8.6 (95% CI 2.3-32) for the development of ENL. HIV co-infection was found to be a risk factor in this cohort, but as the numbers involved are small (only two HIV positive

patients had ENL), this finding must be confirmed in larger studies. Ten of the 16 cases had recurrent episodes and five had at least five episodes occurring over a period of more than 2 years. The management and prognosis of ENL reactions are discussed.

SHAW, I.N.; NATRAJAN, M.M.; RAO, G.S.; JESUDASAN, K.; CHRISTIAN, M.; KAVITHA, M. Long-term follow up of multibacillary leprosy patients with high BI treated with WHO/MDT regimen for a fixed duration of two years. *Int. J. Leprosy*, v.68, n.4, p.405-409, December, 2000.

Forty-six, newly detected, previously untreated multibacillary (MB) patients with a bacterial index (BI) of $>$ or $= 3+$ who had received WHO/MDT for 2 years were followed up for a total duration of 424 person-years and a mean duration of 9.26 ± 2.98 years per patient. The BIs of the patients continued to fall, and all of the patients, except one, reached skin-smear negativity. WHO/MDT was well accepted and well tolerated. Relapse, which was defined as an increase in the BI of $1+$ or more with or without clinical evidence of activity, was observed in only one patient, giving a relapse rate of 2.2% or 0.23 per 100 person-years in patients with a BI of $>$ or $= 3+$ after long-term follow up. This patient was started on a second course of WHO/MDT to which he responded favorably. WHO/MDT for a fixed duration of 2 years for MB patients as recommended by the WHO is vindicated.

SCHON, T. et al. High dose prednisolone treatment of leprosy patients undergoing reaction in associated with a rapid decrease in urinary nitric oxide metabolites and clinical improvement. *Leprosy Rev.*, v.71, p.355-362, 2000.

Evidence is accumulating that nitric oxide (NO) produced by macrophages has a role in the pathogenesis of reactions in leprosy. We followed the urinary levels of the metabolites of NO [nitrite (NO₂) and nitrate (NO₃)] and the clinical response to prednisolone treatment in leprosy patients ($n=9$) admitted to ALERT leprosy hospital Addis Ababa, Ethiopia, because of reversal reaction (RR) or erythema nodosum leprosum (ENL). In untreated reactional leprosy patients, the levels of urinary NO metabolites (1645 ± 454 mM, $n=9$, ENL=4, RR=5) decreased significantly 2 weeks after high dose prednisolone treatment (1075 ± 414 mM, $P<0.05$), and remained stable 4 (895 ± 385 mM, $P<0.02$) and 6 weeks following treatment initiation (1048 ± 452 mM, $P<0.02$). This decrease was also present when the reactional patients were subdivided according to the type of reaction (ENL, RR) and coincided with a clinical improvement. In patients showing a poor clinical response to steroids, no or minor effects on the urinary NO metabolite levels were observed. We conclude that there is a correlation between the decrease in urinary NO metabolites and a favourable clinical response after high dose prednisolone treatment of reactional leprosy patients.

VIJAYAKUMARAN, P. et al. Chemoprophylaxis against leprosy: expectations and methodology of a trial. *Leprosy Rev.*, v.71, p. S537-5541, December. Supplement.

Because of the great efficacy of multidrug therapy (MDT), it had been hoped that the widespread use of MDT would bring about a rapid decrease of the incidence of leprosy. To the present, a decrease of incidence has not been observed, possibly because of the long incubation period of the disease, and because general implementation of MDT is still recent. Other reasons, such as environmental sources of infection or the role of healthy carriers in transmitting *Mycobacterium leprae*, cannot be excluded. Therefore, one must seek alternative or supplementary strategies, such as chemoprophylaxis. Household contacts of leprosy patients are at greater risk of developing leprosy than is the general population. Therefore, a randomized, controlled trial of chemoprophylaxis, using a single 10 mg/kg dose of rifampicin, or a placebo, is planned in nine projects in India, among the household contacts of newly detected leprosy patients. Based upon assumptions of a protective efficacy of the chemoprophylaxis of 50%, an annual incidence of 2 per 1000 contacts, a desired power of the study of 90%, and a level of significance of 95%, 15,000 household contacts will be allocated randomly by household to each arm of the study, and followed for 5 years. Considered as household contacts will be all persons living in the same household as an index case and sharing the same kitchen. Pregnant women and infants will be excluded. To be certain that transmission of the organisms from the index case cannot occur once the prophylaxis is administered, rifampicin will be administered 2 months after diagnosis of the index case. Diagnosis of leprosy will be clinical, and confirmed independently. Although household contacts usually constitute only a small proportion of the new patients detected in a control programme, their high-risk status makes them particularly appropriate for a study of the potential effect of chemoprophylaxis. Following the trial, one could evaluate the usefulness and feasibility of using the same strategy in other population-groups, based on the number of persons necessary to treat to prevent one case.

WAKHLU, A. et al. Response of *Mycobacterium habana* vaccine in patients with lepromatous leprosy and their household contacts. A pilot clinical study. *Leprosy Rev*, v.72, n.2, p. 179-191, June, 2001.

Single dose vaccination was carried out with *Mycobacterium habana* vaccine, 31 lepromatous leprosy cases receiving 1.5mg (1.5mg=6.2' x 10' bacilli) and 36 household contacts randomly receiving 1.5, 2.0, 2.5 mg vaccine intradermally. Duration of study was 18 weeks.

Vaccination induced lepromin conversion in 100% of lepromatous leprosy cases and lepromin negative household contacts and augmentation of lepromin reactivity in 100% of lepromin positive household contacts, which was stable for the 15 weeks duration of follow-up. The maximum augmentation in lepromin reactivity was obtained with 1.5mg of vaccine, which is probably the supramaximal dose. Overall, post-vaccination, those without prior BCG vaccination scars showed higher mean values of lepromin augmentation. Local vaccination site changes included induration, ulceration, itching, pain and uncomplicated regional lymphadenopathy, all of which remitted spontaneously by 15 weeks. Systemic side-effects noted were pyrexia, ENL

and jaundice, and were seen with no greater frequency than that reported in other vaccine trials. Overall, systemic side-effects were easily controlled and were not accompanied by clinically detectable nerve or ocular damage. The safety profile investigations revealed an increase in the mean values of Hb%, RBC count and PCV in household contacts and of PCV in lepromatous patients, post-vaccination. Alterations in the liver function tests were also observed in patients of lepromatous leprosy. Thus, *M. habana* vaccine appears to be useful in stimulating specific CMI against *M. leprae* as evidenced by increased lepromin reactivity.