

RESUMOS/ABSTRACTS

Indian Journal of Leprosy International Journal of Leprosy Leprosy Review

PERÍODO CONSIDERADO:

Janeiro de 1990 a dezembro 1992

CLÍNICA

ABRAHAM, A. et. al. Assessment of testicular volume in bacilliferous leprosy: correlation with clinical parameters. *Int. J. Lepr.*, 62(3), p. 310-315, 1990.

Testicular involvement in leprosy was studied in 30 multi-bacillary (BULL) patients. Ten (33.3%) gave past history of type II reactions, of whom nine (30%) gave history of testicular pain and/or swelling. Decreased libido was a common complaint (63.3%). Gynaecomastia was noted in 3 patients (10%) and altered hair pattern in 11 patients (36.7%). Testicular sensation was impaired in 10 (33.3%). Testicular volume was assessed objectively using the Prader orchidometer and found to be reduced in nine (30%) patients. Reduction in testicular volume correlated with longer duration of disease and a past history of type II reaction.

ABRAHAM, A. et. al. Acid-Fast Bacilli in Semen; Correlation with Bacterial Index. *Int. J. Lepr.*, 58(3), p. 466-468, 1990.

Thirty multibacillary patients (12 LL, 18 BL) were historically reviewed and clinically assessed for evidence of testicular involvement. The bacterial index (BI) of the patients ranged from 1+ to 6+; the morphological index (MI), from 0% to 3%. Nine (30%) patients has oligospermia.

while acid-fast bacilli (AFB) were demonstrable in the semen of 3 (10%) patients (2 LL, 1 BL). There was a significant correlation between the BI and the demonstration of AFB in semen ($p < 0.01$).

AGARWAL, U.S. et. al. Hypopigmented lesions in early leprosy - a clinical and histological study. *Int. J. Lepr.*, 62(4), p. 416-421, 1990.

26 Patients of leprosy presenting with hypopigmented lesions were divided on morphological grounds into 3 Sub groups, Group I (9 patients) with well-defined single patch with moderate to complete sensory loss; Group II (8 patients) with single ill-defined lesion having partial sensory loss; and Group III (9 patients) having multiple hypo-pigmented patches with mild to moderate sensory loss. Epidermal atrophy was a conspicuous histological finding in all groups. Only patients in Group I showed epithelioid cells in dermal infiltrate with erosion of epidermis in one case. This group may be labelled as maculoanesthetic leprosy. Patients in Group II and III showed mononuclear cell infiltrate in dermis, around neurovascular bundles and appendages. They were histologically consistent with indeterminate leprosy. Follow-up biopsy after six to eight months of treatment showed healing of the lesion of reduction in the infiltrate in most cases.

BERHE, D. et. al. Epidemiological pattern of leprosy in Ethiopia: a review of the control programmes. *Leprosy Review*, 61(3), p. 258-266. 1990.

Leprosy control started in a limited area of Ethiopia in 1956. Extended coverage of the country was achieved in the early seventies. Review of the data from the control projects since 1976 revealed that leprosy is a disease of the Ethiopian highlands where prevalence rates as high as 7 per thousand have been recorded in some provinces, while the cumulative national average for the last 13 years was 2-6 per thousand. The paucibacillary form was predominant. However, unlike other African countries, a relatively high proportion of multibacillary leprosy was found in Ethiopia. The male-to-female ratio was 2:1 with the highest prevalence in the 15-44 years age bracket. Detection rates for new cases have shown a gradual decline since 1982, a year before multiple drug therapy (MDT) was introduced into the country. For the last 5 years the number of new case has stabilized at 4700/year. These trends probably reflect a general reduction in the prevalence of leprosy in the country, while the conspicuous decline in 1982 is most likely related to discharge of cases during screening before MDT. The new villagization policy of Ethiopia with its effective reorganization of the populations is believed to make control programmes and supervision of MDT easier and presumably more effective. Similarly, more reliable prevalence and incidence studies could be undertaken with success.

BHATIA, V.N. et. al. Sub-clinical infection with *Mycobacterium leprae* in household contacts of leprosy. *Ind. J. Lepr.*, 62(3), p. 296-304, 1990.

870 household contacts of leprosy patients were examined for sub-clinical infection with *M. Leprae* by smear (skin and nasal), lepromin and FLA-ABS tests. 0.6%, 3.3%, 71.5% and 14.4% of the contacts were found to be positive for skin smear, nasal smear, lepromin and FLA-ABS tests respectively. An analysis of the results revealed that 4% of the lepromin positive contacts and

3.6% of the lepromin negative contacts were positive to booth FLA-ABS and skin or nasal smear.

BRANDT, F. et. al. The pathology of the eye in armadillos experimentally infected with *Mycobacterium leprae*. *Leprosy Review*, 61(2), p. 112-131, 1990.

One hundred and twenty-seven from 66 *Mycobacterium leprae* inoculated armadillos were studied histologically and some ultrastructurally.

Inflammatory reactions were found in the following extraocular tissues: the eyelid, including the orbicularis muscle and the third eyelid, extraocular muscles, tear gland and Harder's gland.

The early and slight changes of the intraocular tissues, small amounts of lymphocytes, plasma cells and macrophage infiltrations were confined to the area around the anterior angle specifically within the trabeculae and the adjacent ciliary body, the root of the iris and the limbus region of the cornea.

But in the cases with severe lesions the whole uvea was densely infiltrated with large, foamy macrophages intermingled with small amounts of lymphocytes, plasma cells and frequently, neutrophils. No specific necrosis of the granulomas was seen. No explanation for the neutrophil infiltrations was given.

The lesions in the cornea were significantly less severe than those in the uvea. Retinal lesions comprised of macrophage infiltrations were all obvious extensions of the adjacent uvea lesions. Acid-fast bacilla (AFB) were found within all tissues. The infection of the intraocular tissues in the armadillo eyes seemed to be mainly, if not solely, haematogenous.

BRIGHTMER, M.I. New cases of leprosy in the Cross River Region, Nigeria. *Leprosy Review*, 61(3), p. 273-281, 1990.

Rates of leprosy cases newly reporting during 1986 are examined for a region of south-eastern Nigeria. Figures reveal that in the part of

the region which was designated in 1987 as a new state, half of the administrative units had new case reporting rates higher than in adjacent areas, while the other half had very few cases reporting in 1986. Possible explanations are offered and the implications of the pattern for leprosy control in the new state are examined.

CREE, I.A. et. al. A Quantitative Study of the Relationship Between Systemic and Histological Parameters of Immunity in Individual Leprosy Patients. *Int. J. Lepr.*, 58(2), p. 347-352, 1990.

A group of 52 untreated leprosy patients were examined to determine the relationship between local and systemic immunological parameters across the clinico-pathological spectrum. The Ridley-Jopling classification, bacterial index (BI), and granuloma fractionation (GF) were assessed in biopsies from 40 cases. The densities of apoptoses, mitoses, and plasma cells were also measured. Systemic immunity to mycobacteria was assessed by skin tests with leprosin A and PPD, and by measurement of the serum antibody responses to *Mycobacterium leprae*, *M. tuberculosis*, and *M. scrofulaceum*. The serum responses to phenolic glycolipid-I (PGL-I) of *M. leprae* was assessed using a glycoconjugate which mimics an immunodominant epitope.

The serum antibody levels and skin test results showed the expected inverse relationship. The BI within lesions showed an inverse correlation with the skin test results, but none of the other histological parameters studied showed a significant relationship with the other measurements of systemic immunity. Our findings suggest that the inverse relationship between delayed type hypersensitivity and humoral immunity in leprosy patients, which is strong in groups of patients across the leprosy spectrum, is less strong in individual patients than is often thought. The lack of correlation of many histological and systemic parameters suggests that local factors modulate systemic immunity in the pathogenesis of leprosy lesions.

DESAI, R.G. An unusual Case of Hansen's Dis-

ease (Lepromatous Leprosy) with Circulating Anticoagulant and Macroglobulinemia. *Int. J. Lepr.* 58(3), p. 462-465, 1990.

A 42-year-old Mexican migrant laborer with a previous history of neurofibromatosis presented with a stuffy nose and chronic ulceration of his soft palate. Multiple subcutaneous nodules were found on his skin, and laboratory investigation revealed an elevated activated partial thromboplastin time (APTT). Further laboratory evaluation showed a lupus-like circulating anticoagulant deemed IgM by quantitative immunoglobulin studies. Although coagulation defects in lepromatous leprosy are rare, the preoperative preparation of a patient with leprosy may require a screening prothrombin time (PT), APTT and platelet count. Abnormalities in these values may indicate the need for specific factor assays and a search for circulating anticoagulant.

ESQUENAZI, D.A. et al. Effect of treatment on immune responsiveness in lepromatous patients. *Leprosy Review*, 61(3), p. 251-257, 1990.

This study was performed in order to analyse whether the immune unresponsiveness to *Mycobacterium leprae*, largely seen in lepromatous patients, persisted after discharge from treatment. Lymphoproliferation and skin tests were performed using two mycobacterial antigens (*M. leprae* and BCG) in three groups of lepromatous patients grouped by treatment status. Forty-seven per cent of the lepromatous patients tested acquired reactivity to *M. leprae* after long-term treatment.

FURUTA, M. et. al. Leprosy and Malignancy: Autopsy Findings of 252 Leprosy Patients. *Int. J. Lepr.*, 58(4), p. 697-703, 1990.

The occurrence of malignant tumors in leprosy patients was studied in 252 autopsied cases. Malignant tumors were found in 33 out of 110 autopsy cases from 1962 to 1971, and in 51 out of 141 autopsy cases from 1977 to 1989 (until

July). In 1974, a lepromatous case with Kaposi's sarcoma was autopsied. The incidence of malignant tumors in our 252 cases were 33.7% (85 out of 252). Carcinoma of the alimentary system was most common: stomach, liver and large intestine, in that order. There was an increased number of hepatocellular carcinoma closely related to liver cirrhosis. Carcinoma of the lung has increased remarkably in leprosy patients quite recently. Malignant lymphoma was the most common of the nonepithelial malignant tumors, and four of these cases were seen in lepromatous leprosy patients. Eight cases showed double or triple cancers; seven of these were autopsied during 1977 to 1989.

Further studies should be done to ascertain which types of leprosy showed the highest incidence, and which sex showed more frequent malignant tumors.

GARG, S.P. et. al. Conjunctival Microbial Flora in Leprosy. *Int. J. Lepr. (Falta número da revista)*, p. 39-44, 1990.

Conjunctival sacs of Seventy-one leprosy patients, paramedical and medical personnel working in a Leprosy Home were cultured. None of these eyes had any pathology of the outer eye. Surprisingly, 46.2% of the culturally positive eyes, carried accepted pathogens, *Staphylococcus aureus* being the commonest. Determining the preoperative bacterial flora and their elimination before undertaking intraocular surgery is recommended.

GEORGE, K. et. ai. The role of intrahousehold contact in the transmission of leprosy. *Leprosy Review* 61(1), p. 60-63, 1990.

This study examines the role of intrahousehold contact in the transmission of leprosy using the case control methodology. The study was done in the leprosy control area of the Community Health and Development (CHAD) Programme of the Christian Medical College. Three age, sex and village matched controls were selected for each case. This study shows that

persons with intrahousehold contact with leprosy have a higher risk of acquiring leprosy compared with those who did not (RR 2.509; 95% confidence limits 1.23 5.109).

GILL, H.K. et. al. *Mycobacterium leprae* reactive T cell clones from lepromatous leprosy patients after prolonged dapsone chemotherapy. *Leprosy Review*, 61(1), p. 25-31, 1990.

The proliferative responses of peripheral blood mononuclear cells (PBMC) to *Mycobacterium leprae* and BCG were studied in two groups of leprosy patients: a group of 8 lepromatous patients who had been on treatment for more than 20 years (TLL) and a group of 8 untreated lepromatous leprosy patients (ULL). The mean response to *M. leprae* of the TLL group was 6195 cpm with 5 of the 8 patients responding positively. The mean response to *M. leprae* of the ULL group was 617 cpm, with only 1 patient showing a positive response. The corresponding proliferative responses to BCG were 19,908 cpm in the TLL group and 7908 in the ULL group.

Thirteen *M. Leprae* reactive clones were established from 2 TLL patients and 5 *M. leprae* reactive clones were established from 2 tuberculoid leprosy patients. Seven of these clones, 4 from the TLL patients and 3 from the tuberculoid (TT) patients could be studied further. Three of the TLL clones responded specifically to *M leprae*, while one of the clones exhibited a broad cross-reactivity to other mycobacteria. All of these clones were of the CD4+CD8 - phenotype.

Our findings suggest that responsiveness to *M. leprae* can be detected in vitro in a proportion of LL patients who have undergone prolonged chemotherapy, and that this response involves *M. leprae* reactive CD8+CD8-T cells, of which some appear to be specific to *M. leprae*.

GIRDHAR, A. et. al. Histoid lesion in nerve of a lepromatous patients. *Leprosy Review*, 61(3), p. 237-241, 1990.

This report pertains to a patient who had

untreated diffuse lepromatous disease of 8 - to 10 - years' duration. Two peripheral nerves were beaded, which on biopsy showed histoid features. Because of its rarity, the case is reported.

GONZALEZ-ABREU, E. et. al. Serodiagnosis of leprosy in patients' contacts by enzyme-linked immunosorbent assay. *Leprosy Review*, 61(2), p. 145-150, 1990.

Serum samples from 3336 contacts of leprosy patients were tested for antiphenolic glycolipid I antibodies by enzyme-linked immunosorbent assay with the albumin coupled synthetic disaccharide antigen. The overall positivity rate was 9.3%. No significant differences were seen between a group of household contacts of lepromatous patients and those of the other types of the disease. The proportion of ELISA positives was slightly higher in the relatives as compared to workplace contacts and neighbours but significantly different only between the two former ($p < 0.05$). Among those contacts with absorbance values higher than 0.100, 5 new leprosy patients were diagnosed, 2 of them with positive skin smears. A sixth contact was detected with a very high absorbance value in whom no single skin lesion was found but whose lepromin reaction was 0 mm and the skin smear showed a bacteriological index of 3+.

GROENENE, G. et al. A Longitudinal Study of the Incidence of Leprosy in a Hyperendemic Area in Zaire, with Special Reference to PGL-Antibody Results. *Int. J. Lepr.*, 58(4), p. 641-650, 1990.

Between 1984 and 1988 yearly surveys for leprosy were done among the 1500 people living in a previous leprosy segregation village in Zaire. In 1984 lepromin tests and phenolic glycolipid (PGL) antibody tests were done in a significant part of the population. The prevalence of the disease at that time was 16.1%, the proportion of multibacillary cases was 11.3% overall and 22% among active cases. Prior to 1984, 23% of paucibacillary cases and 56% of multibacillary

cases had presented themselves spontaneously to the Leprosy Service. The exposure to the infection is uniform, but there is a suggestion of family clustering of cases. In spite of a rapidly bactericidal treatment of all known cases in 1984 and thereafter, the annual incidence of 0.34% did not decrease during the 4 years of the study. The PGL antibody test did not contribute to the diagnosis, classification or prognosis of the disease.

GUPTE, M.D. et al. Experiences with *Mycobacterium leprae* soluble antigens in a leprosy endemic population. *Leprosy Review*, 61(2), p. 132-144, 1990.

Rees and Convit antigens prepared from armadillo-derived *Mycobacterium leprae* were used for skin testing in two leprosy endemic villages to understand their use in the epidemiology of leprosy. In all, 2602 individuals comprising 202 patients with leprosy detected in a prevalence survey, 476 household contacts and 1924 persons residing in non-case households were tested with two antigens. There was a strong and positive correlation ($r = 0.85$) between reactions to the Rees and Convit antigens. The distribution of reactions was bimodal and considering reactions of 12 mm or more as 'positive', the positivity rate steeply increased with the increase in age. However, the distributions of reactions to these antigens in patients with leprosy, their household contacts and persons living in non-case households were very similar.

These results indicate that Rees and Convit antigens are not useful in the identification of *M. leprae* infection or in the confirmation of leprosy diagnosis in a leprosy endemic population with a high prevalence of nonspecific sensitivity.

GUPTE, M.D. et. al. Inter-observer agreement and clinical diagnosis of leprosy for prophylaxis studies. *Ind. J. Lepr.*, 62(3), p. 281-295, 1990.

Clinical diagnosis is still the most useful tool for detecting early cases of leprosy in field

research. In prophylaxis studies accuracy of clinical diagnosis of leprosy is important during intake as well as for measuring efficacy of the intervention. This paper reports our observations regarding the extent of inter-observer variations in clinical diagnosis of leprosy and its implications for a prophylaxis study. Information on 225 suspects and cases of leprosy, each examined independently by three senior workers after initial standardization, was used for this purpose. Agreement among the examiners regarding the presence of skin patch, thickened nerve trunk and sensory deficit was fairly high ($Kappa=0.7$). Agreement on the presence of infiltration in a skin patch was not satisfactory ($Kappa=0.4-0.5$). It was observed that in clinical diagnosis of leprosy, presence of skin patch and sensory deficit, as well as thickened nerve trunk and related anaesthesia were correlated observations. The influence of inter-observer variations on defining leprosy problem in the community can be quite large. The paper suggests some ways of overcoming the problem.

HEYING, W. et. al. Preliminary observations on experimental leprosy in tupaia (Tupaia belangeriyunalis). *Lepr. Rev.*, 61(1), p.1218, 1990.

The *Tupaia belangeri yunalis* (tree shrew) is one of the primitive primates. They were inoculated subcutaneously in the footpad or intravenously with *Mycobacterium leprae* from a patient with multibacillary leprosy. As controls, the footpads of CFW mice were inoculated with the same suspension of *M. leprae*. The results showed growth of acid-fast bacilli (AFB) in the footpads of locally inoculated CFW mice and in the footpads of both locally and intravenously inoculated tupaia. Whereas the numbers of AFB declined in the footpads of CFW mice after 12 months, they increased in the tupaia footpads, up to 2.44×10^9 AFB/g of tissue. The footpads of one tupaia were swollen, which on section revealed a granulomatous infiltration, including foamy and heavily infected macrophages. *M. leprae* were also seen in the branches of cutaneous nerves. Also AFB occurred in some viscera. Preliminary studies indicate that the AFB multiplying in tupaia

are *M. leprae*.

HIRATA, T. Low-magnification electron micrography of leproma in human skin based on semithin and ultrathin sectioning. *Leprosy Review*, 61(3), p. 227-236, 1990.

Low-magnification electron micrography of leprosy lesions is described. The various cell types in the lesions, the relationships to leprosy bacilli and the distribution of bacilli in the lesions of lepromatous leprosy, are neatly demonstrated in the low-magnified pictures.

IBRAHIM, M.A. et. al. Leprosy in Saudi Arabia, 1986-89. *Leprosy Review*, 61(4), p. 379-385, 1990.

This study on leprosy includes information obtained from the Ibn Sina Hospital, a specialized centre established 27 years ago for treatment and management of the disease in Saudi Arabia. A total of 792 patients with leprosy were reported during the period of the study (1986-89). A steady decline was observed in the number of patients reported: 432(54.55%) were non-Saudi and 360 (45.45%) were Saudi. Patients were reported from a total of 22 different countries. The majority of the non-Saudi patients were from the Yemen, 286 (36.11%). The male-to-female ratio was 3.83: 1. The age groups comprised: 133(16.79%), 51 to 80; 575(72.60%), 21 to 50; and 84 (10.61%), under 20 years of age. The disease was classified into five categories (Ridley and Jopling classification): 295(37.25%), lepromatous type, 238 (30.05%), tuberculoid type; 146 (18.43%), borderline-tuberculoid type; 29 (3.66%), borderline type; and 84 (10.61%), borderline-lepromatous type.

Although the number of registered patients is decreasing, this trend does not suggest an overall decline in the disease in the country. It is recommended, therefore, that the services being provided to patients with leprosy must be integrated with the nationwide network of the Primary Health Care Centres to implement effective control and prevention, including health edu-

cation for the general population. Furthermore, mutual agreements must be developed with adjacent countries to study the geographic distribution of the disease.

IRGENS, L.M. et. al. Leprosy in Portugal 1946-80: epidemiologic patterns observed during declining incidence rates. *Leprosy Review*, 61(1), p. 32-49, 1990.

Compulsory notification of leprosy in Portugal formed the basis for the establishment of a national patient registry used in an epidemiological study. Highest incidence rates were observed in the coastal counties in the middle of Portugal and particularly in the municipalities with a high annual rainfall. Peak incidence rate in male was observed at the age of 25-29 years against 50-59 in females. A continuous and increasing decline in incidence rates was observed throughout the observation period, 1946-80. Towards the end of the period the slopes of the incidence curves seemed to be identical with those observed in other countries where leprosy has previously been eradicated. This is consistent with the notion that towards the end of an endemic situation no new transmission of the disease occurs, and the incidence curve takes the shape of the right part of the distribution of incubation periods which apparently is uniform in leprosy, irrespective of time and place. The pattern observed in other areas during declining incidence rates, of an increase in age at onset by year of onset together. Portuguese data, also consistent with a break in the transmission of the disease a long time before the final termination of the endemic situation.

KARTIKEYAN, S. et. al. The sociocultural dimension in leprosy vaccine trials. *Leprosy Review*, 61(1), p. 50-59, 1990.

This paper briefly describes organizational, operational, and sociocultural aspects of the phase-III clinical trials of the ICRC anti-leprosy vaccine in Maharashtra, India. Our experience is that vaccine trials can be launched quickly and

more cost effectively by using the services of health personnel from the existing public health infrastructure. That is why the trials could be launched in just 4 months after receiving the financial grant from the Indian Council of Medical Research, New Delhi (India). At the community level, a person-to-person approach in Health Education scores over audio-visual aids and the mass media. The compliance in target groups is increased when preventive programmes are backed-up by curative services and when their privacy and daily routine are not disturbed.

KLENERMAN, P. et. al. Vibration sense and tarsal Disintegration. *Ind. J. Lepr.*, 62(4), p. 422-428, 1990.

The extent of loss of vibration and pressure sensations was assessed in 21 leprosy patients with disintegration of the tarsus. Feet which had and did not have tarsal desintegration both showed severe impairment of pressure sensation, but the loss of vibration sense was more severe in feet which had undergone the destructive process. It appears that loss of deep sensation is an important factor in the process of tarsal disintegration in feet which are already anaesthetic. Measurement of vibration sense using a biothesiometer may be a valuable clinical test in investigation and follow-up of the patient with the insensitive foot to identify those at risk of developing tarsal disintegration.

LAMBA, P.A. & ROHATGI, J. Leprotic Keratopathy in India. *Ind. J. Lepr.*, 62(2), p. 186-192, 1990.

Corneal affections cause severe ocular morbidity in leprosy. Poor nutrition and low socioeconomic status make the eyes prone to repeated secondary Infections which makes the pattern of corneal disease in this country different from that reported in western literature. A study of 250 patients shows that leprotic keratopathy has 4 different patterns. Primary leprosy keratitis was seen in 56.5% of cases, while secondary leprosy keratitis (groups B, C & ID) constituted 57.7%. In

the latter group the ocular morbidity could be prevented by controlling infection and prevention of concomitant diseases. Cases of lepromatous leprosy showed a consistently higher incidence of different types of corneal involvement than tuberculoid cases.

LEWALLEN, S. et. al. Intraocular Pressure and Iris Denervation in Hansen's Disease. *Int. J. Lepr.*, 58(1), p. 39-43, 1990.

We retrospectively analyzed 255 Hansen's disease patients and found low intraocular pressure (< 7 mm Hg) in 12% of them. We showed a correlation between low intraocular pressure and avascular keratitis and iritis. We also found that patients with low intraocular pressures had abnormally large postural changes in intraocular pressure. We speculate that abnormalities in the autonomic innervation of the anterior segment of the eye may be related to the intraocular pressure abnormalities. Further investigations along this line may increase our understanding not only of the pathophysiology of Hansen's disease but also of the mechanisms regulating homeostasis of intraocular pressure.

MALATY, R. et. al. Ocular Leprosy in Nine-banded Armadillos Following Intrastromal Inoculation. *Int. J. Lepr.* 58(3), p.554-559, 1990.

Leprosy shows a higher percentage of ocular involvement than any other systemic infection. In humans, the cornea is the first ocular tissue affected. Our previous studies in armadillos with naturally acquired and experimental disseminated leprosy showed that 44% had corneal infection. *Mycobacterium leprae* is found in armadillo burrows in Louisiana, U.S.A., and ocular abrasions may be the portal of entry for these organisms in wild armadillos. To test the cornea as a route of infection, we injected eight armadillos intrastromally with 2×10^6 *M. Leprae* in 1 ul. Two and 4 months later, the armadillos were sacrificed and their eyes processed for light and electron-microscopy. After 2 months, *M. leprae* were found in histiocytes mainly in the corneal

limbus, sclera and bulbar conjunctiva. At 4 months, however, there was a visible corneal leproma in one animal. Microscopically, it was found to be a histiocytic granuloma with heavy *M. leprae* invasion. In addition, cells were seen in the anterior chamber. Leprosy is endemic in regions where other corneal infections which compromise the epithelial barrier property are prevalent and where leprosy bacilli are found in the environment. The entry of leprosy bacilli into the cornea may produce lesions which spread posteriorly in the eye.

PAVITHRAN, K. Non-pruritic eczemas as presenting manifestation of leprosy. *Ind. J. Lepr.*, 62(2), p. 202-207. 1990.

Three patients who presented with eczemas as manifestation of leprosy are described. One of them having lepromatous leprosy had extensive areas of acquired ichthyosis. He developed asteatotic eczema on the legs. The pathophysiologic mechanisms for the development of ichthyosis and asteatotic eczema in this patient are briefly discussed. The second patient, with tuberculoid leprosy, presented with allergic contact eczema due to neomycin which he had applied over the plaque for scaling and crusting. The third patient, also with tuberculoid leprosy, presented with features of nummular eczema. Dryness of the skin that resulted from leprosy had led to the development of nummular eczema in this case. One peculiarity noted in all these eczemas was that they were non-pruritic.

PONNIGHAUS, I.M. et. al. Disabilities in leprosy patients ascertained in a total population survey in Karonga District, Northern Malawi. *Leprosy Review*, 61(4), p. 366-374, 1990.

This paper describes the pattern of disability among 1654 leprosy patients ascertained between 1973 and 1987 in Karonga District, Northern Malawi. Approximately 20% of patients identified prior to 1980 had some disability at registration, but this percentage fell to approximately 10% with the introduction of total popula-

tion surveys in the Lepra Evaluation Project, The proportion of patients with disabilities at registration increased with age, was higher among males than females, was higher among borderline and lepromatous than tuberculoid patients, and was higher for passively than for actively detected patients. The risk of developing disabilities among patients without any disabilities at registration was approximately 5 per 1000 person years, and appeared to be slightly higher after the completion of treatment than during treatment.

PONNIGHAUS, J.M. et. al., The anatomical distribution in an African population, and its implications for the pathogenesis of leprosy. *Leprosy Review*, 61(3), p. 242-250, 1990.

Data on the anatomical sites of single leprosy lesions found in 635 newly diagnosed and biopsy-confirmed leprosy patients are presented. These patients were found during total population surveys carried out by the Lepra Evaluation Project, a prospective longitudinal study of the epidemiology of leprosy in Karonga District, Northern Malawi. There was a striking excess of single lesions on the face and the back of the arms, compared to the distribution of skin surface area, and a deficit on the legs, regardless of age. There is some evidence for a sex difference in lesion distribution among adults, with facial and arm lesions being relatively more common in females and back lesions being more common in males. The excess of lesions on the face compared to the lower limbs is similar to data from Uganda, but very unlike data from Burma and elsewhere in Asia. Overall, the distribution of lesions does not suggest a pattern reflecting entry of *Mycobacterium leprae*, nor does it suggest an association with anatomical distribution of the nervous or vascular system. It is argued that the distribution reflects the influence of some 'local' environmental or behavioural factors.

SAHA, K. et. al. Sexually Transmitted Diseases in Leprosy Patients in North and Northeastern India. A Futile Search for Human Immunodeficiency Virus Antibody. *Mt. J.*

Lepr., 58(4), p. 660-665, 1990.

Three-hundred-eighty-four leprosy patients were clinically examined for sexually transmitted diseases (STD) in north and northeastern India, revealing a high incidence (5.2%) of STD among them. Eighteen males, one female, and one eunuch were found to have chancroid ulcer, gonococcal urethritis, lymphogranuloma inguinale, and primary chancre. Of these patients, only 100, selected randomly, could be screened serologically for STD due to *Treponema pallidum*, herpes simplex (type 1 and 2), *Entamoeba histolytica*, hepatitis-associated virus, cytomegalovirus, *Chlamydia trachomatis* and human immunodeficiency virus (HIV); 100 control sera were included for comparison. In addition, sera from another 133 normal subjects and another 176 lepromatous patients were also screened for HIV antibody. Thus, a total of 233 normal sera and 276 leprosy sera were tested for HIV antibody. Although our leprosy patients have shown significantly high incidences of clinical STD and also high seropositivity against *T. pallidum*, herpes-simplex viruses types 1 and 2, hepatitis-associated virus, and cytomegalovirus, the search for antibody against HIV was negative. Our clinical and serological data suggest promiscuity in our patient population. The absence of HIV antibody in this high-risk population, however, seems to be an enigma.

SAXENA, U. et. al. Multiple cutaneous nerve abscesses on a healed tuberculoid patch. *Leprosy Review*, 61(2), p. 180-182, 1990.

A case of healed tuberculoid leprosy (TT) with multiple superficial nerve abscesses involving the whole cutaneous network on the patch is reported. To the best of our knowledge multiple cutaneous nerve abscesses involving the entire subcutaneous plexus on a TT patch is a very uncommon observation.

SHAH, P.K.D. et. al. Cardiovascular Dysautonomia in patients with lepromatous leprosy. *Ind. J. Lepr.*, 62(1), p. 91-97, 1990.

Autonomic functions were studied by six standard tests in 65 patients with lepromatous leprosy and 25 healthy controls. Dysautonomia was observed in 22 patients, all having the disease for more than five years. Associated peripheral neuropathy, judged clinically, was present in all, except one patient. Of the 22 dysautonomic patients, 9 each had mild or moderate dysautonomia and 4 had severe dysautonomia as per the scoring schedule devised by us. Syncope, gustatory sweating and impotence were the symptoms suggestive of dysautonomia. But not all affected patients reported these symptoms. Involvement of the sympathetic system was more frequent than that of the parasympathetic system. Statistically significant abnormality was seen with Atropine ratio, standing 30:15 beat ratio, postural hypotension and sustained hand grip test. Sustained hand grip test was the one which consistently gave abnormal results in all the 22 dysautonomic patients.

SHWE, T. et. al. The effect of tetanus toxoid in leprosy patients. *Ind. J. Lepr.*, 62(1), p. 104-108, 1990.

Since cases of lepra reaction following small pox vaccination and BCG vaccination had been reported the effect of tetanus immunisation on leprosy patients (whether it may provoke a lepra reaction or not) was studied. Three doses of purified tetanus toxoid (one ml initially, one ml after six weeks and one ml after six months) were given to 357 leprosy patients and 60 patients living in the same environ were followed as controls. The antibody response following immunisation was followed in six lepromatous leprosy patients using toxin antitoxin neutralisation test at the Lf/1000 level in mice and in three of them the antibody titre of leprosy patients rose to satisfactory level. The number of lepra reactions in these patients was monitored for nine months (two months before vaccination, during the six months period of vaccination and one month after the last

dose of vaccine). There was no significant rise in the number of patients with reaction following the vaccination.

SREEVATSA, G.N.M. et. al. Preliminary observations on myiasis in leprosy patients. *Leprosy Review*, 61(4), p. 375-378, 1990.

Out of 3350 leprosy patients attending the surgical outpatient department for various ulcerative lesions, 18 patients had typical symptoms of myiasis. Maggots were collected in 5 cases from the nose, in 3 cases from ulcers of the hand and in 10 cases from ulcers of the foot. It was possible to rear the maggots into flies in 8 out of 18 cases. The flies were identified as *Sarcophaga ruficomis* and *Chrysomya bezziana*.

VADIEE, A.R. et. al. The evolution of antibody response in armadillos inoculated with *Mycobacterium leprae*. *Leprosy Review*, 61(3), p. 215-226, 1990.

Plasma from 30 armadillos (*Dasypus novemcinctus*) was collected prior to inoculation and at approximately 3-month intervals for a period of 1-3 years. These animals were inoculated intravenously with $6.1 \times 10^8 \pm 2 \times 10^8$ ($x \pm SD$) armadillo-derived *Mycobacterium leprae*. These samples were analysed for antibodies of IgM and IgG class to phenolic glycolipid (PGL-I) and to sonicated *M. leprae* components using ELISA and immunoblotting techniques, respectively. We had previously observed among a group of 11 armadillos, that some animals produced and maintained a high IgG antibody response to PGL-I. In this study, an animal's ability to produce and maintain an elevated IgG anti-PGL-I response was significantly correlated with their ability to delay dissemination of the infection and their ability to survive longer. When the animals were moribund, a significant decrease in the IgG anti PGL-I absorbance value was observed. The detection of PGL-I in the plasma samples collected from moribund armadillos suggested that high concentrations of PGL-I in the plasma may have contributed to a drop in absorbance values by the

formation of non-lattice-type immune complexes in vivo.

As detected by immunoblotting, the IgM and IgG response to antigens derived from sonically disrupted *M. leprae* was directed towards molecules with broad bands of immunoreactivity ranging from 21 - to 45 - kDa. There were no distinguishing features of these antibody responses among amadillos as was evident with the IgG anti-PGL-I responses.

WARNDORFF, D.K. & WARNDORFF, J.A. Leprosy control in Zimbabwe: from a vertical to a horizontal programme. *Leprosy Review*, 61(2), p. 183-187, 1990.

In Zimbabwe leprosy control services were re-established in 1983, following the war of independence. Its main objectives were the nationwide implementation of multiple drug treatment (MDT) and the integration of leprosy control into the general health services.

The MDT regimens have led to a rapid reduction of the prevalence of leprosy. At the beginning of 1989, 357 patients were on treatment and 1299 under follow-up. Six hundred and twenty-seven new cases have detected since 1984, which represents an annual case detection rate of 1.6 per 100.000. This seems a fair reflection of the incidence rate, as the new cases are characterized by a minority of patients under the age of 15 (4%) and a lepromatous percentage of 50%.

As the budget of the programme has remained unchanged integration of leprosy control into the general health services has become imperative. However, this transition is now hindered by a number of obstacles that were not foreseen at the start of the programme, because they are in measure corollaries of the successful implementation of MDT.

Most of the problems that leprosy control is facing in Zimbabwe could have been avoided if instruction in leprosy had been introduced into the curricula of the (para) medical training schools 20 years ago.

WATERS, M.F.R. et. al. Positive Mitsuda lepromin reactions in long-term treated lepromatous leprosy. *Leprosy Review*, 61(4), p. 347-352, 1990.

Twenty-four lepromatous (LL) patients, treated for 22 to 40 years with chemotherapy, including sulphones and with multidrug therapy, were tested with standard Wade Mitsuda lepromin. Thirteen gave weak positive (3-4 mm) Mitsuda reactions, confirmed histologically in the ten whose reactions were biopsied. Six of the eleven negative reactors were partly accounted for by a history of relapse, and two others had probably taken dapsone irregularly. Eleven control LL patients, treated for less than 20 years, were uniformly lepromin negative. Spontaneous lepromin conversion appears to occur around 24 years after commencing successful chemotherapy. The late Mitsuda conversions are attributed to delayed clearance of the reservoir of bacterial antigen, but a poor correlation between Mitsuda and Fernandez positivity is not explained.

WATERS, M.F.R. & RIDLEY, D.S. Tubercloid relapse in lepromatous leprosy. *Leprosy Review*, 61(4), p. 353-365, 1990.

It is commonly accepted that the attainment of bacteriological negativity fails to restore the immune state of leprosy patients who have downgraded to lepromatous. We report six patients who had been lepromatous (LLs), and who, after many years of chemotherapy and bacteriological negativity, were found upon relapse to have upgraded to borderline-tubercloid (BT). Five had become Mitsuda lepromin positive. The relapses could be accounted for by proven or suspected dapsone resistance. The upgrading was associated with minimal signs of reaction, which was attributed to the low level of antigen in the almost resolved lesions. The manner of development of the new high immune lesions resembled the onset of a primary infection, clinically and histologically. The development of a positive Mitsuda reaction in longstanding 1.1. leprosy is not necessarily an indication of cure.

ABBOT, N.C., et. al. Impairment of Fingertip Vasomotor Reflexes in Leprosy Patients and Apparently Healthy Contacts. *Int. J. Lepr.*, 59(4), p. 537-547, 1991.

Fingertip blood-flow velocity and its control by vasomotor reflexes were studied in leprosy patients and in healthy controls with a laser Doppler flowmeter. In newly registered patients, the flow was significantly lower than in the healthy controls, and even lower values were recorded in the longstanding patients with lower limb ulcers and/ or deformity. The newly registered patients showed substantially impaired vasomotor reflex responses in the fingertips to cold challenge of the opposite hand or deep inspiratory gasp. Low blood flow and impairment of vasomotor reflexes were more prominent in those leprosy patients who showed clinical evidence of neuropathy and/or histological evidence of reaction in a punch biopsy of leprosy skin lesions. This aspect of dysautonomia to cold challenge was particularly prominent in apparently healthy, fully treated ex-patients. There was an unexpectedly high prevalence of impairment of vasomotor reflexes in newly registered and apparently healthy, adequately treated leprosy patients. The method is very sensitive, and it remains to be established whether the lesions it detects are nonprogressive residues, or previous nerve damage, or an indication of on-going nerve damage. A minority of leprosy contacts showed impairment of vasomotor reflexes. Those with two or more affected fingers were more likely to have had a higher level of exposure to *Mycobacterium leprae* than those with one or no affected fingers. The cause of this unexpected impairment of fingertip vasomotor reflexes in a minority of leprosy control workers has not yet been determined.

ANNICCHINO-BIZZACCHI, J.M. & MACHADO, T. F.G.S. Leprosy and acquired factor VIII inhibitor a case report. *Leprosy Review*, 62(2), p. 155-157, 1991.

In this report we describe a case of factor VIII inhibitor appearing in a man with leprosy, with comments on the clinical presentation of the disease, laboratory findings and outcome of the

patient.

BHATIA, V.N. Observations on nerve tissue infected with *M. Leprae*. *Ind. J. Lepr.*, 62(4), p. 492-494, 1990.

Nerve tissue from leprosy patients showed (i) small linear pinkish translucent crystalloid bodies, (ii) small round structures in relation to filamentous strands (iii) short pieces of filaments with round spaces within them and (iv) miscellaneous structures like pink granules, brown bodies and dark masses. These structures are being studied for their relationship to leprosy.

DANDAPAT, M.C. et. al. Treatment of leprosy neuritis by neurolysis combined with perineural corticosteroid injection. *Leprosy Review*, 62(1), p. 27-34, 1991.

A study on leprosy neuritis, involving the ulnar nerve, was carried out on 39 patients. The evaluation of nerve function was done before and after treatment by a score chart. Patients were divided into two groups. Group A (21 patients) was subjected to neurolysis only, and group B (18 patients) were given the combined treatment of neurolysis and perineural corticosteroid injection at the same time as neurolysis and subsequently at the end of the second and third weeks. In group B, 83.3% of patients showed 10% or more increase in the post-treatment score in comparison with 57.1% in group A. Improvement was more marked in paucibacillary cases and when the duration of nerve involvement was less than 3 months. Patients with short segments of nerve involvement with minimal thickening had better recovery. This procedure was observed to be simple, easy and well accepted by the patients, with a marked beneficial effect.

FANDINHO, F.C.O. et. al. Mycobacterial Flora of the Skin in Leprosy. *Int. J. Lepr.*, 59(4), p. 569-575, 1991.

The presence of mycobacteria on the

skin of healthy people and in leprosy lesions has been documented previously. The present study observed the mycobacterial flora on the hands (by the hand-washing method) and fingers (by the inoculated culture medium using scraped material obtained during the preparation of slit-skin smears) in 89 untreated leprosy patients. We also evaluated the slit-skin smears from fingers for the diagnosis of leprosy. In 16 patients (17.9%) mycobacteria were cultured from scrapings and hand washings. The frequency of isolates from lepromatous (LL) leprosy cases (52.9%) was significantly higher than from tuberculoid (TT) leprosy cases (5.2%). It was observed that *Mycobacterium avium* and *M. scrofulaceum* were the only opportunistic mycobacteria isolated from multibacillary patients, and two hypotheses are discussed to explain these findings. The slit-skin smears from fingers were as satisfactory as smears from other sites for the diagnosis of leprosy, but they were less satisfactory for estimating the morphological index.

GUPTA, S.C. et. al. A rapid technique for detection of leprosy. *Ind. J. Lepr.*, 62(4), p. 488-491, 1990.

Comparison of prevalence rates of leprosy as assessed by a rapid survey technique, in which only the exposed parts of the body were examined, with that assessed by a routine total body examination in a population of about 700 showed that most cases of leprosy were detected by the former.

HOGEWEG, M. & FABER, W.R. Progression of Eye Lesions in Leprosy: Ten-year Follow-up Study in The Netherlands. *Int. J. Lepr.*, 59(3), p. 392-397, 1991.

Forty-eight leprosy patients in The Netherlands were re-examined 10 years after initial examination. Forty-six of these patients had received a course of multidrug therapy (MDT), according to the World Health Organization recommendation, at the time of their initial examination. Two patients had burned-out disease and had

been merely under observation. Out of 40 patients, who initially did not show eye complications due to leprosy, 37 patients were essentially the same 10 years later. The eyes had changed in 3 multibacillary patients: 1 patient had developed a late type 1 reaction with facial nerve involvement and lagophthalmos; 2 patients had undergone intra-ocular surgery for cataract and acute glaucoma, respectively. Out of 8 patients with pre-existing eye involvement, 1 patient recovered and the lesions in 2 patients remained unaltered. One patient showed progression of pre-existing exposure keratitis. Four patients had undergone cataract extractions; all four patients were lepromatous, with a long history of disease and signs of iris involvement at the first examination. The main progressive lesions were cataracts in lepromatous patients.

HOGEWEG, M. et. al. The significance of facial patches and Type I reaction for the development of facial nerve damage in leprosy. A retrospective study among 1226 paucibacillary leprosy patients. *Leprosy Review*, 62(2), p. 143-149, 1991.

Charts of 1226 paucibacillary leprosy patients, registered between 1982 and 1987 were reviewed for recent facial nerve damage, facial patches and the presence of Type I reaction. Twenty-six (2.1%) patients with recent lagophthalmos were identified. In a great majority (85%) patients with recent lagophthalmos showed significant patches over the malar region or around the eye, at the same side as the nerve damage together with clinical signs of Type I reaction.

This combination of significant patches in certain locations and Type I reaction seems to be a pre-condition for facial nerve damage.

The clinical implication is that a small group of patients may be identified, who are at risk of facial nerve damage. By examining these patients more carefully it will be possible to detect nerve damage early and to prevent permanent damage of the facial nerve by timely treatment with an appropriate steroid regimen.

HUSAIN, S. et. al. Nasal myiasis in leprosy. *Lepr. Rev.*, 62(4), p. 389-394, 1991.

Infestation of the nose with larvae of certain flies can occur in leprosy patients. This results in severe distress and agony and can cause extensive tissue damage. The predisposing factors, clinical presentation and treatment is described.

JHA, P.K. et. al. Localized borderline lepromatous leprosy. *Leprosy Review*, 62(2), p. 212-216, 1991.

A 48-year-old soldier presented with 3 small leprosy lesions localized over the flexor area of the forearm. There was no nerve thickening and clinically the lesions looked like borderline-tuberculoid leprosy. However, these lesions demonstrated bacteriological index (BI) of 4+ while no acid-fast bacilli (AFB) could be demonstrated from any other site of the body. A lepromin test was negative. Histologically evidence of borderline lepromatous leprosy was conspicuous. The case was diagnosed as localized borderline lepromatous-leprosy and treated with multidrug therapy. After 1 year of treatment, the lesions regressed, a lepromin test was positive (5 mm) and the BI from the lesions fell to 1+.

KAUR, G. et. al. A Clinical, Immunological, and Histological Study of Neuritic Leprosy Patients. *Int. J. Lepr.* 59(3), p. 385-391, 1991.

An assessment has been made of 108 neuritic leprosy patients to find out if the number of affected nerves and the clinical presentations of these patients give any indication of the underlying severity (classification) of the disease. Detailed clinical recordings, skin smears, lepromin testing with Dharmendra antigen, and a leukocyte migration inhibition test (LMIT) using sonicated *Mycobacterium leprae* antigens were done these patients. Nerve biopsies of available affected nerves were taken in 39 patients. The results show that neuritic leprosy patients also have a spectrum. However, none of the clinical param-

eters, including the number and distribution of affected nerves, the immune response and the nerve histology, were found to be interrelated. Further, even though all of the patients were skin-smear negative, a significant proportion showed lepromatous histology and nearly two thirds had a moderate-to-heavy bacterial load within the nerves.

KIRAN, K.U. et. al. Treatment of recent facial nerve damage with lagophthalmos, using a semistandardized steroid regimen. *Leprosy Review*, 62(2), p. 150-154, 1991.

Twenty-seven patients with borderline leprosy and facial nerve damage of < 6 months duration (36 eyes) were treated with a semistandardized regimen of steroids (the average starting dose was 25-30 mg, duration 5-6 months) on an outpatient basis. Red and raised reactive patches were usually present in the upper malar area or around the eye(s) in patients with recent lagophthalmos.

The lid gap was measured in millimetres during gentle and strong closure. After completion of the steroid course 75% of the eyes had complete closure or only a slight gap of 5-2 mm on gentle closure.

Steroids were found to be beneficial and safe, in the dosage that we prescribed.

KOHLI, M. et. al. Does Convit vaccine (BCG + *Mycobacterium leprae*) afford protection against biochemical changes in renal brush border membrane in experimental leprosy? *Leprosy Review*, 62(3), p. 269-275, 1991.

Renal functional status in *Mycobacterium leprae* infected mice can be best studied by examining the enzymatic status of brush border membrane vesicles from proximal convoluted tubule. The role of vaccination in modulation of the renal status brought by the disease has been studied using this technique. The characteristic marker enzymes of renal brush border membrane - namely alkaline phosphatase, leucine aminopeptidase and γ -glutamyl transpeptidase decreased significantly ($p < 0.01$) in due course in *M. leprae* infec-

tion over a period of 9 months. The combined vaccine (BCG + *M. leprae*) may have a protective effect on renal abnormalities only in the initial stages of infection as indicated by a significant rise in enzymatic levels. However, no significant ($p < 0.05$) protective effect of vaccine was found in a more advanced disease state after 9 months in infected mice.

MULIYIL, J. et. al. Effect of BCG on the risk of Leprosy in an Endemic Area: A case Control Study. *Int. J. Lepr.*, 59(2), p. 229-236, 1991.

The effect of BCG on the risk of leprosy was measured using a case-control design in area endemic for the disease. In this study, 397 newly diagnosed cases and 669 controls matched for age, sex and locality were selected from a defined population. Information on exposure to BCG, contact with another case of leprosy, and relevant socioeconomic variables were obtained from the subjects. Having infectious (multibacillary) and noninfectious (paucibacillary) contacts in the household increased the risk of disease 11.7 times ($p < 0.001$) and 2.7 times ($p < 0.001$), respectively. Overall, the protection offered by BCG was not significant (odds ratio = 0.8; $p = 0.17$). However, BCG appeared to increase the risk for indeterminate leprosy (adjusted odds ratio=2.7; $p = 0.09$) while protecting against borderline disease (adjusted odds ratio=0.39; $p = 0.03$). It is possible that BCG causes a shift in the overall cell-mediated immune response, thus increasing the risk for milder and transient forms of leprosy while protecting against more serious forms. These findings may have important implications for the design and interpretation of vaccine trials. Namely, trials should be designed to measure the protective efficacy of vaccines.

PEREIRA, J.H. et. al. Mycobacteria in nerve trunks of long-term treated leprosy patients. *Leprosy Review*, 62(2), p. 134-142, 1991.

Mycobacteria were present in 4 out of 8 mixed peripheral nerve trunks from patients (3 BT

and 1 BL) treated with DDS and/or MDT for periods ranging from 21 months to 8 years. Most of the bacilli appeared to be 'whole'. Nerve destruction with areas of granulomatous infiltration appeared more active than expected. Possible reasons for a continued presence of bacilli in treated nerves and its implications in 'relapse' are discussed.

PONNIGHAUS, J.M. et. al. HIV Infection a Risk Factor for Leprosy? *Int. J. Lepr.*, 59(2), p. 221-228, 1991.

A case control study was undertaken during 1988 and 1989 within the framework of the LEPRA Evaluation Project (LEP)/Karonga Prevention Trial (KPT) in Karonga District, northern Malawi, to investigate whether HIV infection is a risk factor for clinical leprosy. Cases were newly ascertained, biopsy-confirmed, incident leprosy patients older than 14 years of age. Controls were selected from the computer data base on over 170,000 people who form the basis of LEP/KPT. They were matched for sex, age, and area of residence. HIV seropositivity rates were 1.8% (2/112) for incident leprosy cases and 2.4% (24/1011) for controls. The Mantel Haenszel odds ratio is 0.6 (95% confidence interval 0.1-3.3). Thus, no evidence for an association between HIV infection and leprosy incidence has been observed in this population. In a parallel investigation, an odds ratio of 7.4 (95% confidence interval 3.3-16.7) was found for 102 microscopy - and/or culture-confirmed, incident pulmonary tuberculosis cases in the same population during 1989, a result similar to those obtained elsewhere in Africa. Among leprosy relapses, 16.7% (2/12) were HIV positive.

RAMESH, V. et. al. Post-kala-azar dermal leishmaniasis: a case report strikingly resembling lepromatous leprosy. *Leprosy Review*, 62(2), p. 217-221, 1991.

An adult man with post-kala-azardermal leishmaniasis who had lesions, distributed in a manner strikingly similar to lepromatous leprosy

is described. He was mistakenly treated with multidrug therapy as recommended by the WHO Expert Committee on leprosy. All investigations including slit-skin smears, histopathology, culture for *Leishmania donovani* and an indirect fluorescent antibody test to confirm post-kala-azar dermal leishmaniasis proved futile. The diagnosis was ultimately based on the previous history of kala-azar, the absence of other disorders which were ruled out by relevant laboratory tests and the good therapeutic response to sodium antimony gluconate. The epidemiological significance of this case and the salient points to distinguish this condition from leprosy are discussed.

RICHARDUS, J.H. & SMITH, T.C. Squamous cell carcinoma in chronic ulcers in leprosy: a review of 38 consecutive cases. *Lepr. Rev.*, 62(4), p. 381-388, 1991.

The histories of 38 consecutive cases of squamous cell carcinoma (SCC) arising in chronic ulcers of leprosy patients treated between 1981 and 1990 at the McKean Rehabilitation Centre, Northern Thailand were analysed retrospectively. The study included 37 individual patients; 29 males and 8 females. The average age was 60 years, the average duration of leprosy was 34 years and the average duration of ulcers was 12 years. Most patients (76%) came from leprosy settlements. Patients with borderline-tuberculoid (BT) leprosy were most commonly affected (63%), followed by lepromatous (LL) leprosy (21%) and borderline lepromatous (BL) leprosy (16%). Four patients (11%) had histories of SCC on other extremities. Metastatic spread was observed in 2 cases (5%), both instances leading to death. The commonest site of involvement of SCC was the foot, but it was seen on the knee in 1 patient and on the hand in 2 others.

The incidence rate of SCC in the group at risk (leprosy patients with disability grading 1 and 2) is calculated as being 0.79:1000 per year. SCC was seen in 1.8% of all cases admitted for ulcer care at the Centre. Treatment is by radical amputation.

SCC in chronic ulcers in leprosy patients cannot be considered rare and emphasizes the

need for an active policy of disability prevention in leprosy programmes.

RAO, P.S. et. al. Is bacteriological examination by skin smear necessary in all paucibacillary leprosy patients in mass control programmes? *Lepr. Rev.*, 62(3), p. 303-309, 1991.

Skin smear bacteriological examination results of 11,255 paucibacillary leprosy patients from 8 leprosy control units under the National Leprosy Eradication Programme (NLEP) in South India and the Outpatient Department (OPD) of the Central Leprosy Teaching & Research Institute (CLT&RI), Chengalpattu, between 1987 and 1989 were collected and analysed. Only 0.05% of the smears from leprosy control units and 2.49% from the OPD of CLT&RI were found to be positive. Not a single smear from indeterminate, tuberculoid and pure neuritic types of leprosy out of 8263 examined was found positive under field conditions. The relevance of carrying out routine bacteriological examination in mass leprosy control programmes is discussed.

SAXENA, Uma. et. al. Persistent reaction in paucibacillary leprosy: case reports. *Leprosy Review*, 62(2), p. 206-211, 1991.

Three patients of histopathologically confirmed borderline-tuberculoid leprosy showing no acid-fast bacilli and with lesions confined to the face, 2 on the cheek and 1 on the forehead, were given multidrug therapy as recommended by the WHO for paucibacillary cases. Within 3 months the lesions showed signs of upgrading (or reversal) reaction which was substantiated by histopathology. In 1 patient the facial nerve was affected leading to facial palsy. The lymphocyte transformation test did not show a significant rise. All 3 patients were given oral prednisolone for periods varying between 5 and 7 months, but the response was poor except in 1 patient in whom the facial palsy responded favourably. Injections of sodium antimony gluconate tried in 1 patient after stoppage of steroids did not control the reaction.

After 18 months of regular follow-up during therapy, the cutaneous reaction in the patient with facial nerve involvement subsided leaving significant atrophy. However, in the other 2 patients the skin lesion persisted with clinical and histopathological evidence of upgrading reaction. The reasons for the unnatural persistence of reaction in these patients is not clear.

SEN, R. et. al. Patterns of erythropoiesis and anaemia in leprosy. *Leprosy Review*, 62(2), p. 158-170, 1991.

A total of 128 leprosy patients were investigated for the morphological type of anaemia the underlying disturbances in iron metabolism and patterns of erythropoiesis and other cytomorphological changes in the bone marrow. The anaemia was a mild to moderate degree in paucibacillary (PB) leprosy, while in multibacillary (MB) leprosy it was of a severe degree. Iron deficiency was observed in only a few patients. Impaired iron utilization as observed in anaemia of a chronic disorder was a common finding in MB leprosy (41.7%) and more so in new cases (50%). Megaloblastic erythropoiesis was also more frequent in MB leprosy (45.2%) as compared to PB leprosy (16%), accounting for the severe degree of anaemia in the former type. In 17.2% of the total patients (MB, 21.4%; PB, 9%) both megaloblastic erythropoiesis and features of impaired iron utilization were observed in bone marrow. Disturbances in iron metabolism and erythropoiesis were also observed but to a lesser degree in patients receiving specific antileprosy treatment. Irrespective of the type of disease and duration of treatment, increasing frequency of acid-fast bacilli (AFB) positivity and granulomas was observed in the bone marrow with an increasing severity of anaemia.

SOEBONO, H. & KLATSER, P.R. A Seroepi-demiological Study of Leprosy in High and Low-endemic Indonesian Villages. *Mt. J. Lepr.*, 59(3), p. 416-425, 1991.

A seroepidemiological study was performed in three different leprosy-endemic areas in

Indonesia, including two isolated villages with high endemicity in South Sulawesi (Kaluarang and Hub) and an area with low endemicity in Java (Jepara). A total of 2430 serum samples were collected from 2672 individuals in these locations. The prevalence of leprosy in these three areas, as determined during this study, was 29/1000, 11/1000, and 7/1000 in Kaluarang, Hub and Jepara respectively.

Two serological assays were employed in this study to detect antibodies against *Mycobacterium leprae*. One is an enzyme-linked immunosorbent assay (ELISA) based on the detection of antibodies to the species-specific epitope of phenolic glycolipid-I (PGL-I) of *M. leprae*. The second test, using inhibition of an ELISA reaction (ELISA-INH) detects antibodies to a species-specific epitope on the 36-kDa protein antigen of *M. leprae*. In comparison with clinical findings, the specificity of both serological tests was calculated to be 91%. The sensitivity of the ELISA was 97.6% for multibacillary (MB) cases and 56.8% for paucibacillary (PB) cases; for the ELISA-INH, it was 97.6% and 81.8% for MB and PB cases, respectively.

Seropositivity rates were shown to be unrelated to sex, to Mitsuda skin-test reactivity, or to BCG vaccination status. The pattern of Seropositivity was, however, clearly age-related, with high seropositivity in the age group 10-19 years and decreasing rates of positivity in the older age groups. Age-standardized seropositivity ratios were not correlated to the prevalence of leprosy when comparing the three areas. Therefore, it is not yet clear whether or not seropositivity reflects infection. If it does, other, as yet unidentified, factors may play a role in the natural history of the disease.

THANKAPPAN, T.P. & SULOCHANA, G. Keratosis spinulosa developing in borderline-tuberculoid lesions during type I lepra reaction: two cases reports. *Leprosy Review*, 62(1), p. 49-52, 1991.

Two cases of borderline-tuberculoid leprosy which developed keratosis spinulosa over the anaesthetic areas alone during type 1 lepra

reactions are described. Both patients only developed spiny papules during the period of reaction and subsided with control of the reaction. The probable mechanism of the peculiar phenomenon might be due to the generation of epidermal growth factors by local T cell activation during the type 1 lepra reaction.

UPLEKAR, M.W. & CASH, R.A. The private GP and leprosy: a study. *Lepr. Rev.*, 62(4), p. 410-419, 1991.

In urban and rural areas alike, people in India tend to prefer private medical care to the existing government health services. Nevertheless, the large private health care sector has hitherto been virtually alienated from activities of public health importance including priority disease control programmes. This study of 106 private general practitioners (GPs), practising in low socioeconomic areas of Bombay, shows a gross lack of knowledge and awareness among private doctors about leprosy and also about the National Leprosy Control Programme. The possible reasons are discussed. Effective involvement of GPs in the National Leprosy Control Programme should facilitate both integration and better implementation of leprosy control activities. The study also highlights some areas for future interventions at both primary and secondary health care levels and the need for a strategy, based on larger studies, to train and make private doctors participate in controlling diseases of major public health concern like leprosy.

BIRKE, J.A. et. al. Healing rates of plantar ulcers in leprosy and diabetes. *Lepr. Rev.*, 63(4), p. 365-374, 1992.

Comparison was made of wound healing time in a consecutive series of leprosy and diabetic patients with plantar ulceration. In the leprosy group, 66 of 70 (94%) ulcers healed in a mean time of 42.7 (\pm 36.1) days, and in the diabetic group 75 of 80 (94%) ulcers healed in a mean time of 39.7 (\pm 32.1) days. Analysis of all healed ulcers using a general linear model found

wound depth ($p < 0.03$), and wound diameter ($p < 0.05$) significantly related to ulcer healing time. Diagnosis, healing devices (cast, splint and cut-out sandal), age and sex were not significant. In diabetic subjects a regression model including depth, diameter and age explained 36% of the variation in healing time. A meaningful regression model was not found in leprosy patients.

COURTRIGHT, P. & LEWALLEN, S. Considerations in the integration of eye care into leprosy care services. *Lepr. Rev.*, 63(1), p. 73-77, 1992.

Little attention has been directed to the development, management and evaluation of eye care programmes for leprosy patients. This paper examines when an eye care programme for leprosy patients is needed, methods for integrating eye care into leprosy control programmes and lists of available ocular leprosy teaching materials.

HAUHNAR, C.Z. et. al. A clinical and radiological study of maxillary antrum in lepromatous leprosy. *Ind. J. Lepr.*, 64(4), P. 487-494, 1992.

Seventy consecutive patients having multibacillary leprosy were questioned about symptoms of nasal involvement and sinusitis. Complete otorhinolaryngeal examination was carried out in all these patients and they were subjected to radiographic examination of paranasal sinuses. Radiological abnormality of maxillary antrum was found in 40 (57%) patients. Radiological changes were unilateral in 25 and bilateral in 15 patients. Localised or generalised mucosal thickening was the most common finding, followed by diffuse opacity. The development of radiological changes in maxillary antrum correlated with high bacterial density (BI 3+ and above), nasal deformity, and disease duration of more than two years.

HAUHNAR, C.Z. et. al. Maxillary Antrum Involvement in Multibacillary Leprosy: A radiologic, Sinusoscopic, and Histologic Assessment. *Int. J. Lepr.*, 60(3), p. 390-395, 1992.

Thirty patients having lepromatous leprosy (22 males, 8 females) and showing radiological involvement of the maxillary antrum were subjected to sinuscopy, biopsy, and histopathological examination. Radiological observations showed diffuse opacity in 33.3% of the sinuses, localized mucosal thickening in 28.6% and generalized thickened mucosa in 38.1%. Sinuscopy revealed inflamed mucosa as the most common finding (40%) followed by ulcerative (26.7%) and granulomatous (10%) lesions of the mucosal lining. The mucosal thickening (localized or generalized) evident on radiology was always associated with granuloma formation and acid-fast bacilli in the histology. The presence of an external nasal deformity indicated a statistically significant chance of encountering mucosal involvement on sinuscopy and histopathology ($p < 0.05$). There was more chance of finding positive sinusoscopic lesions in those patients with a bacterial index above 3+.

JENNEKENS, F.G.I. & JENNEKENS-SCHINKEL,
A. Neurological examination of patients suffering from leprosy: Is it worthwhile? *Leprosy Review*, 63(3), p. 269-276, 1992.

We examined 28 male leprosy patients to discover if a more extensive neurological investigation than usual would be worthwhile in diagnosis and/or management. Our findings were fully compatible with what might be expected from a mononeuritis multiplex, either due to leprosy or other causes. The following observations are noteworthy. Changes of position sense and a decrease of some tendon reflexes were present in a minority of the patients. In soles of the feet, considered to be an - or hypaesthetic, some residual pain sensation could occasionally be detected. Functional testing of at least one muscle group (m. triceps surae) appeared to be more reliable than manual testing according to MRC criteria. We concluded that an extensive neurological examination is probably not required for diagnosis. It

does provide, however, more accurate information on the extent of damage to the peripheral nervous system, which maybe important for management and for assessment of treatment effects. The use of a myometer is advocated.

KUMAR, V. et. al. An ultrastructural study of schwann cells in peripheral nerves of leprosy patients. *Ind. J. Lepr.*, 64(1), p. 81-87, 1992.

An ultrastructural study of peripheral nerves in leprosy patients was carried out of ascertain the changes in Schwann cells containing myelinated and nonmyelinated axons. Axonal multiplication was noticed in nonmyelinated axons in specimens from both tuberculoid and lepromatous leprosy. The Schwann cells in tuberculoid nerves were devoid of M. leprae. In contrast to those in lepromatous nerves in which large number of bacilli were seen. These observations suggest that the Schwann cells containing nonmyelinated axons may be affected more frequently in either type of leprosy.

LIWEN, D. et. al. Diagnostic exploration of enlarged peripheral nerves in suspected cases of leprosy. An analysis of 55 cases. *Leprosy Review*, 63(2), p. 141-144, 1992.

In 55 cases presenting with enlarged peripheral nerves without any skin lesions, a rice grain-sized biopsy of the nerve lesion was taken for histopathological examination. As a result definitive diagnoses could be established leprosy was diagnosed in 32 cases. In 23 cases the cause of nerve enlargement was not leprosy: post-traumatic neuritis 9, cysts 5, hypertrophic neuritis 3, nonspecific 4, neurofibroma 1, and amyloidosis 1. In all of these cases there was a deficit of the nerve function and postoperatively there were no complications. The authors, as a result of this experience, believe that surgical exploration and biopsy is a harmless diagnostic tool for establishing a definitive diagnosis of leprosy in cases presenting with enlarged peripheral nerves without any skin lesions. In 23 out of 55 such cases the nerve

enlargement was proved to be other causes than leprosy.

MAFOYANE, N.A. et. al. Primary neuritic leprosy in a black South African. *Lepr. Rev.*, 63(3), p. 277-281, 1992.

A case of primary neuritic leprosy in a black South African is described, in which the multiple peripheral nerves were affected. The clinical picture and eletrophysiological studies are in keeping with a picture of mononeuritis multiplex. Selective involvement of the facial nerve branches with normal blink reflex latencies was observed. The biopsy of the sural nerve disclosed features most consistent with borderline leprosy.

PALANDE, D.D. & BOWDEN, R.E.M. Early detection of damage to nerves in leprosy. *Lepr. Rev.*, 63(1), p. 60-72, 1992.

Methods of examining and diagnosing damage to nerves commonly involved in leprosy are described. The equipment used is inexpensive, gives reliable and repeatable results and is useful in making objective assessments in terms of function in everyday living.

PATKI, A.H. & MEHTA, J.M. Hyperkeratotic and verrucous skin lesions on lower extremities of leprosy patients. *Ind. Lepr.*, 64(2), p. 183-188, 1992.

Three morphological varieties of hyperkeratotic and verrucous skin lesions on the anterior aspect of ankle joints in patients with leprosy are described: (i) verrucous lesions with thread-like horny projections similar to filiform warts; (ii) irregular compact hyperkeratotic lesions with deep fissures in a between; and (iii) hyperkeratotic lesions with linear fissures corresponding to the transverse creases on the anterior aspect of the ankle. Chemical cautery was useful for the treatment of the first two varieties, and a potent topical corticosteroid with salicylic

acid was useful for the third.

RASOULI, I. & MEHTA, L.N. Reaction of peripheral nerves to vascular and bacterial injuries. *Ind. J. Lepr.*, 64(1), p. 14-27, 1992.

Mouse sciatic nerves were subjected to desvascularization, *M. leprae* inoculation, and combined insult of desvascularization + footpad inoculation (FPI). Changes were seen in FPI nerves only after eight months, but in cases of combined insult, changes were evident in hours. Both the groups showed initial loss of small myelinated fibres. No proliferation of Schwann cells was in FPI nerves, but in combined insult it was maximum after two weeks. Presence of *M. leprae* seems to be arresting Schwann cell activity after two weeks. Blood vessels showed increased endothelial cell cytoplasm, basement membrane proliferation and villi formation. These changes seem to be specific of endoneurial blood vessels of leprosy nerves. Increased number of mast cells seems to be specific of devascularized and FPI nerves, Increased number of macrophages expressed low immunity of devascularized nerves. Eosinophils migrated to endoneurium as a result of leakage of axoplasm.

SONI, N.K. Leprosy of the tongue. *Ind. J. Lepr.*, 64(3), p. 325-330, 1992.

Ten out of the twenty-five lepromatous leprosy patients studied showed clinical evidence of involvement of the tongue, and they presented with various symptoms like loss of taste, stiffness of tongue, bleeding, pain etc. Various rypes of lesions ranging from small nodule to granuloma formation, ulceration, macroglossia and fissured cracked tongue were noted. The tongue lesions were found to be related to the severity of leprosy.

TALWAR, S.; JHA, P.K.; & TIWARI, V.D. Neuritic leprosy: epidemiology and therapeutic responsiveness. *Leprosy Review*, 63(3), p. 263-268, 1992.

We studied epidemiology, progression and therapeutic responsiveness in 62 cases of neuritic leprosy. Numbness was the main presenting symptom. Mononeuritis involving the ulnar nerve, followed by the common peroneal nerve was the commonest presentation. The lepromin test was positive in 34 cases while a slit-skin smear was negative in all cases. We treated 20 of these cases with dapsone monotherapy and 5 cases (25%) developed a skin lesion after an average duration of 3 months'treatment. We treated 42 cases with a combination of dapsone and rifampicin, and 3 cases (7%) developed a skin lesion after an average duration of 2-6 months. The subsequent diagnosis in cases developing skin lesions was borderline-lepromatous in 1 case, borderline-tuberculoid in 4 cases, tuberculoid in 2 cases and indeterminate in 1 case.

VREEBURG, ANNA. Clinical observations on leprosy patients with HIV1-infection in Zambia. *Leprosy Review*, 63(2), p. 134-139, 1992.

The clinical observations carried out on 10 leprosy patients with HIV1-infection, admitted between 1.1.1986 and 1.5.1988 to the Salvation Army Hospital at Chikankata, Mazabuka, Zambia are described. A total of 8 of this group were newly-diagnosed borderline leprosy patients.

Their clinical data were compared with those of 34 newly-diagnosed borderline leprosy patients, admitted in the same period - 50% were men, 50% women.

The clinical presentation, with respect to leprosy, on admission, did not differ very much in both groups. The incidence of neuritis in both groups was 50% (respectively 5 and 17). The outcome of specific therapy of neuritis was worse in the HIV1 patients than in the order group, only partial recovery in 4 out of 5 and no response in 1, compared with a complete recovery in 10 cases, and a partial recovery in 7 cases in the other

group.

A total of 6 patients of the HIV1-group admitted to have had multiple heterosexual contacts, 5 had a history of sexually transmitted disease, 7 had generalized lymphadenopathy and 4 presented with another disease in addition to leprosy.

While in hospital the group of 10 HIV1-infected patients suffered 17 episodes of intercurrent disease against none in the other group, 1 patient (male) died with generalized dermatitis and sepsis: 1 woman died with fulminant hepatitis.

HANSENÍASE EXPERIMENTAL

JOB, C.K. et. al. Early infection with *M. leprae* and antibodies to phenolic glycolipid-I in the nine banded armadillo. *Ind. J. Lepr.*, 62(2), p. 193-201, 1990.

Nine-banded armadillos were intravenously infected with 109M. *leprae*. IgM antibodies to PGL-I were evaluated three times during the six months before and every two months after the infection. A thorough autopsy examination was done on animals that died or were sacrificed at intervals of 3, 4, 6, 12, 15 and 18 months after the infection. Three animals which had acquired the infection in the wild and one experimentally infected animal showed significant increases in antibody levels corresponding to their high bacterial load. In the other five experimentally infected animals, *M. leprae* infection was established in the cells of the reticulo endothelial system (RES) long before the IgM antibody levels to PGL-I became positive. It is possible that in human leprosy also *M. leprae* may enter and multiply in the RES initiating antibody production during the incubation period before clinical disease with neuritis becomes manifest.

BASKIN, G.B. et. al. Experimental Borderline Lepromatous Leprosy with Intraneural *Erythema Nodosum Leprosum* in a Mangabey Monkey (*Cercocebus atys*). *Int. J. Lepr.* 59(4), p. 618-623, 1991.

Asooty mangabey monkey (*Cercocebus atys*) was inoculated with *Mycobacterium leprae* and developed borderline lepromatous leprosy and intraneural erythema nodosum leprosum. Previously studied mangabeys have developed only disseminated lepromatous leprosy without reactions. This case broadens the spectrum of leprosy seen in experimentally inoculated animals and further characterizes the nonhuman primate model of leprosy.

CHACRABARTY, A.N. et. al. Mouse footpad pathogenicity of leprosy derived nocardioform bacteria cultivated in vitro. *Ind. J. Lepr.*, 63(1), p. 43-60, 1991.

In vitro cultures of the nocardioform bacteria from leprosy-infected tissues consisted of granules and bacilli. Inoculation of these granules into mouse footpads (MFP) produced a mild, localised, inflammation for 4-6 weeks. The granules evoked typical granulomatous response in the subcutaneous tissue and showed gradual disintegration. Infiltration of muscles, connective tissue and epithelial cells by bacillary/mycelial masses was seen very frequently, and that of nerve bundles occasionally. Plenty of mycelial tufts emanated from many macrophage globi. By 6-8 months, the granules disintegrated nearly completely releasing a large number of acid-fast bacilli (AFB), single layered rings of AFB, small globi and some residual mycelia. These AFB, harvested from the MFP, were similar to or indistinguishable from the bacillary preparations from the in vitro cultures and from the leprosy bacillus obtained directly from humans or as passaged into the MFP, on the basis of many criteria studied, including the 36k gene positivity.

GORMUS, B.J. et. al. A Serologic Study of Naturally Acquired Leprosy in Chimpanzees. *Int. J. Lepr.*, 59(3), p. 450-457, 1991.

Data from longitudinally obtained serum samples spanning several years has permitted us to identify two chimpanzees with leprosy and to estimate the time of *Mycobacterium leprae* exposure/infection. The results confirm high levels of specific anti-*M. leprae* phenolic glycolipid-I (PGLI) as well as antilipoarabinomannan (anti-LAM) antibodies in both chimpanzees, and identify additional chimpanzees with possible *M. leprae* exposure. The observations are consistent with the hypothesis that leprosy exists in chimpanzees in the U.S.A. and suggest the possibility that *M. leprae* may be transmitted among chimpanzees. The data suggest that monitoring anti-PGL-I and anti-LAM IgG and IgM levels longitudinally in leprosy contacts may be useful in the recognition of preclinical leprosy.

JOB, C.K. et. al. An attempt to produce experimental tuberculoid leprosy in the nine-banded armadillo. *Ind. J. Lepr.*, 63(2), p. 159-165, 1991.

In an attempt to produce experimental tuberculoid leprosy, three nine-banded armadillos, two borderline tuberculoid lepromin reaction, and one with tuberculid lepromin reaction, were chosen. They were injected subcutaneously in a four square centimetre area in the abdominal skin with saline suspension of 6.5×10^7 *M. leprae*. Induration of skin at the injected site appeared in 24 hours and persisted for 6 months in one and for 18 months in the other two animals. Histopathological examination of the infected site at 6 weeks, 18 and 20 months showed progressively decreasing granulomatous inflammation; but the cutaneous nerves were uninvolved. Autopsy examination of the three animals failed to show disseminated disease. Since there was no evidence of nerve involvement, experimental transmission of tuberculoid leprosy to armadillos

could not be established in this study.

ROJAS-ESPINOSA, O. et. al. Inhibition of Complement Activity in Murine Leprosy. *Int.J. Lepr.*, 59(4), p. 605-612, 1991.

NIH mice Infected with *Mycobacterium lepraemurium* (MLM) show a marked depression in their levels of hemolytic complement that is proportional to the degree of infection. The defect affects more the activation of complement through the classical pathway (CPW) than the activation of complement through the alternative pathway. Although this low activity of CPW-complement may be due to different causes (complement consumption by the infecting microorganism, lack of biosynthesis of complement components, or the presence of complement inhibitory factors), our results seem to support the last possibility. The generation of factors in the infected animals that inhibit the autologous activity of complement as the infection goes on reduces the risk of complement-mediated tissue damage and prolongs the survival time of the host, a wise strategy on the part of the MLM, to assure its own survival as a parasite.

ESTRADA-G., I.C.E. et. al. Use of Synthetic Peptides Corresponding to Sequences of *Mycobacterium leprae* Proteins to Study Delayed-Type Hypersensitivity Response in Sensitized Guinea Pigs. *Int.J. Lepr.*, 60(1), p. 18-27, 1992.

In this work we report the synthesis of 10 peptides (P1-P10) corresponding to one or several segments of the amino acid sequence of proteins from *Mycobacterium leprae*: 65 kDa, 28 kDa, 18 kDa, and 28 kDa superoxide dismutase, recently renamed antigens 2L, 9L, 12L, and 14L, respectively. They were assayed in the guinea pig model for the induction of a delayed-and BCG-sensitized animals. To sensitize the animals two

schemes were used: either a single dose of 5×10^8 irradiated or autoclaved whole bacilli, or four weekly intramuscular injections each containing 500 ug of soluble extract of *M. leprae* (MLSE) in incomplete Freund's adjuvant. Because the second scheme used far too much antigen, we decided to use the first scheme for the experiments we report here. DTH reactions of sensitized animals were induced after 30 days with intradermal injections of 5 g of MLSE and with each of the 10 peptides at three different concentrations: 250 g, 100 g, and 0.05 g. All *M. leprae*-sensitized guinea pigs gave indurations of 10 mm or more with MLSE, which indicates that the animals were sensitized. None of them gave DTH indurations with 250 g or 100 g, but some of them had positive DTH reactions with the 0.05 ug doses of the synthetic peptides. This is most likely due to the fact that we have used an outbred strain of guinea pigs. The peptides were also tested at 0.05 ug in animals sensitized with BCG P7 and P10 seem to be nonspecific peptides; the remaining peptides only induces DTH in the *M leprae*-sensitized guinea pigs. P3 (segments 65-85 of the 65-kDa protein) induced a positive DTH in 58% of the tested animals.

In other experiments, guinea pigs were sensitized with a single injection (500g) of each of the synthetic peptides. All animals except those sensitizes with P4 and P8, had positive DTH responses when the homologous peptide was used. Those sensitized with P2, P4, P5, P7, and P8 were able to produce indurations when MLSE was used for the induction of the DTH reaction.

GANGADHARAM, P.R.J. & DHOPLE, A.M.

Utility of beige mouse in leprosy research. *Ind. J. Lepr.*, 64(4), p. 475-482, 1992.

Dissemination of *M. leprae* to visceral organs is seen by four months onwards only in beige (C57BU6/bg'/bgl) but not BALB/c mice followin intravenous or intraperitoneal infections. Inoculation of the beige mouse derived *M. leprae*

showed all the characteristics of *M. leprae*, including growth pattern in the foot-pads of BALB/c mice. *M. leprae* inoculated into foot-pads of beige mice multiplied faster than those in the foot pads BALB/c mice. The possibility of using beige mouse in chemotherapeutic studies in leprosy is discussed.

SHETTY, V.P. et. al. Ultrastructural study of mouse dorsal root ganglion cultures infected long term with *M. leprae*. *Ind J. Lepr.*, 64(3), p. 293-302, 1992.

Ultrastructural changes in the mouse dorsal root ganglion cultures infected long-term with viable *M. leprae* were studied. Subtle cytomorphological changes and loss of neurites noted in the long-term infected cultures were correlated early events in the nerve damage.

IMUNOLOGIA

AMEZCUA, M.E. et. al. Prospective Immunological Follow-up in Household Contacts of Mexican Leprosy Patients. *Int. J. Lepr.*, 58(4), p. 651-659, 1990.

A 6-year prospective study of 79 household contacts of leprosy cases was made in order to correlate the development of the disease with their specific T-cell immunity, measured by the Mitsuda test, and levels of *anti-Mycobacterium leprae* antibodies determined in three consecutive observations with the FLA-ABS test. Overall in the contacts, 71.7% were Mitsuda positive and 93.6% showed seropositivity, without regard to their age, sex, or leprosy type of their index case. Households were divided into lower-risk and higher-risk groups according to either the paucibacillary or multibacillary character of their index case. The lower-risk group consisted of 19 contacts of 2 tuberculoid (TT) and 5 indeterminate cases. The higher-risk group was made up of 60 household contacts of 18 active lepromatous (LL) cases. All but two contacts in the former group had

a positive Mitsuda reaction; the most common antibody titer was 1:160, with tendency to stabilize or decrease over time. In the two Mitsuda-negative contacts, increased antibody levels were observed. In the higher-risk group, 61.6% were Mitsuda positive and showed a humoral profile similar to those Mitsuda positive in the lower-risk group. In most of the Mitsuda-negative LL contacts, the antibody levels remained constant or progressively increased, suggesting a high probability of active subclinical infection. This assumption was partially supported by the finding of a new borderline lepromatous (BL) leprosy case in the Mitsuda-negative LL contact group. Nevertheless, the contribution of the close and extensive contact with a multibacilliferous case as a risk factor was difficult to evaluate because of the small size of the sample studied.

BAGSHAW, A.F. et. al. IgM Serum Antibodies to Phenolic Glycolipid-1 and Clinical Leprosy: Two Year's Observation in a Community with Hyperendemic Leprosy. *Int. J. Lepr.*, 58(1), p. 25-30, 1990.

A village population with hyperendemic leprosy in Papua New Guinea was repeatedly examined for clinical leprosy and for serum IgM antibodies to phenolic glycolipid-I (APGL-1) over 2 years between 1984 and 1986. In 1984, serum APGL-I was elevated in 15% of the subjects without clinical leprosy, and the prevalence of seropositivity was not significantly different in subjects from households with or without leprosy. In 1986, the prevalence of elevated serum APGL-I in leprosy-free subjects had risen to 23%. The incidence of seroconversion from APGL-I negative to APGL-I positive was 9.5% per year (95/ 1000 person years) in 253 subjects tested in 1984 and 1986. During the same period, 27 of 40 (67%) leprosy-free subjects reverted from positive to negative. The positive seroconversion rate in the community was higher than the incidence of clinical leprosy (11.2/1000 person years) over the same period. However, elevated serum APGL-I was not associated with clinical disease and failed to predict the development of disease over 2 years. The significance of persistent

seropositivity found in 14(5%) leprosy-free subjects is uncertain.

CARTEL, J.L. et. al. Assessment of Anti-Phenolic Glycolipid-I IgM Levels Using an ELISA for Detection of *M. leprae* Infection in Populations of the South Pacific Islands. *Mt. J. Lepr.*, 58(3), p. 512-517, 1990.

Anti-phenolic glycolipid-I (PGL-I) IgM levels were determined in 96% of the general population of the Southern Marquesas and Maupiti, remote islands of French Polynesia, where the average annual detection rates of leprosy during the past 30 years have been 57.1 and 4.4 per 100,000 respectively. The seropositivity in these two areas was 4.3% and 4.2%, respectively. No significant difference ($p > 0.05$) was found between either these two figures or between the percentages of persons with high ($z > 0.500$ OD) anti-PGLI IgM levels (9.2% and 5.3%). In the two islands, the age distributions of anti-PGL-I IgM were very similar, the percentage of positive responders was higher in females than in males and higher in adolescents than in adults. These results suggest that the usefulness of the determination of anti-PGL-I IgM levels by ELISA, using the synthetic trisaccharide as antigen, for detecting *Mycobacterium leprae* infection in leprosy control programs is extremely doubtful.

COWLEY, S.A. et. al. Major Histocompatibility Complex Class II Antigen Expression in Nerves in Leprosy; an Immunoelectron microscopical Study. *Int. J. Lepr.*, 58(3), p. 560-565, 1990.

A technique for immunoelectron microscopy has been used to investigate major histocompatibility class II expression in leprosy nerves. In normal nerves, endothelial cells and occasional endoneural cells (not Schwann cells) were constitutively class II positive. In both paucibacillary and multibacillary leprosy nerve biopsies, infiltrating leukocytes were positive but class II-positive Schwann cells were not seen. These observations indicate that Schwann cells

may not be involved in presenting *Mycobacterium leprae* antigens to T cells in leprosy. This conflicts with evidence from in vitro studies, but may be explained by the fact that in vivo Schwann cells are surrounded by basement membranes and are closely associated with axons.

D'SOUZA, D. et. al. Effects of Lepromatous Leprosy (LL) Serum Factor(s) on Normal Blood Lymphocytes. *Mt. J. Lepr* 58(4), p. 666-673, 1990.

To investigate the clastogenic activity of sera from leprosy patients, normal peripheral blood lymphocytes were cultured in both inactivated and noninactivated lepromatous leprosy (LL) sera. An increase in the frequency of chromosome aberrations was observed in normal lymphocyte cultures supplemented with both inactivated (5.2%) and noninactivated (5.0%) LL serum compared to that of cultures supplemented with normal human AB + serum (2.4%). An enhanced frequency of sister chromatid exchanges (SCEs) was also observed in normal lymphocyte cultures supplemented with both inactivated (8.2 ± 3.85) (mean \pm S.D.) and noninactivated (8.3 ± 4.61) LL serum compared to that of controls (6.8 ± 3.45). The normal blood lymphocyte cultures with LL serum have revealed a slow cell-cycle kinetics at a 48-hr incubation period, but a slightly faster proliferation rate was observed at 72 hr compared to cultures, supplemented with normal human AB+ serum, indicating a depressive effect of LL serum on normal blood lymphocyte proliferation. The results obtained from the inactivated LL serum showed that the factor(s) which induce chromosomal damage, depress the mitotic index and the cell proliferation rate were not destroyed at 56°C. These results are the first documentation of cytogenetic effects of LL sera on normal human peripheral blood lymphocytes.

GORMUS, B.J. et. al. Antibodies to Lipoarabinomannan Antigen in Sooty Mangabey Monkeys Experimentally Inoculated with *Mycobacterium leprae*. *Int J. Lepr.*, 58(1), p. 65-72, 1990.

IgG and IgM antibody levels to mycobacterial lipoarabinomannan (LAM) antigen were determined by ELISA in eight sooty mangabey monkeys (*Cercocebus atys*) prior to and at intervals after experimental inoculation with *Mycobacterium leprae*. High levels of anti-LAM IgG were present before inoculation and increase thereafter in the five mangabeys that developed lepromatous (LL) forms of leprosy; lower levels of anti-LAM IgG were observed in two mangabeys that developed indeterminate leprosy and tuberculoid/neuritic leprosy, respectively, and in a mangabey, that was leprosy resistant. IgM anti-LAM levels were near zero before *M. leprae* inoculation in all eight animals, rose significantly in only three LL-leprosy-susceptible animals after inoculation, and returned to near zero in all animals within 3 years.

Anti-LAM antibody levels appear to be potentially valuable as an indicator of leprosy susceptibility, and when measured longitudinally together with antibody levels to *M. leprae*-specific phenolic glycolipid-I antigen, as a means to detect preclinical *M. leprae* infections in high-risk individuals.

HUSSAIN, R. et. al. Quantitation of IgM Antibodies to the *M. leprae* Synthetic Disaccharide Can Predict Early Bacterial Multiplication in Leprosy. *Int J. Lepr.*, 58(3), p. 491-502, 1990.

Quantitative enzyme-linked immunosorbent assays detecting IgM to the soluble *Mycobacterium leprae* crude sonicate (CD75) and the synthetic disaccharide antigen coupled to bovine serum albumin (ND-BSA) were assessed for their ability to determine early infection in families/household contacts of leprosy patients and employers of a leprosy center working in close contact with leprosy patients. Although IgM to both antigens (CD75 and ND-BSA) correlated

with the bacterial index (BI) assessed histologically on skin-biopsy samples, the level of IgM antibodies to ND-BSA was a much more sensitive indicator of low bacterial loads. A 4.4-fold difference in antibody levels was observed between the mean group levels of endemic controls (N=116) and tuberculoid leprosy patients with a BI of 0 (N=88), increasing to sevenfold in tuberculoid leprosy patients with a BI of 1 (N=20). Using a statistical cut off with endemic controls (mean+2S.D), household contacts showed 30% seropositivity (N=180) as compared to staff contacts who showed 17% seropositivity (N=55). Percent seropositivity in family contacts was not related to the type of leprosy of the index case (lepromatous vs. tuberculoid) or the duration of treatment of the index case. Age of the individual in the family contact group had a significant influence on seropositivity. These results support the hypothesis that in this community, factors other than the viable bacterial load of the index case, such as genetic susceptibility, may be influencing the high rate of seropositivity in family contacts. IgM ND-BSA antibodies seem to provide a good indicator of low antigenic loads and could prove to be useful in detecting subclinical infection before the onset of disease. Follow-up studies of these seropositive individuals are in progress to understand the relationship between seropositivity and the progress of clinical disease.

JOB, C.K. et. al. Phagocytosis of *Mycobacterium leprae* by cardiac muscle cells - A Preliminary Report. *Ind. J. Lepr.*, 62(1), p. 55-59, 1990.

Fetal cardiac muscle cells were shown to ingest *M. leprae* easily within 20 minutes of exposure in vitro. This phagocytosis is considered nonspecific and facilitated by the lipid coat of the mycobacteria. The presence of *M. leprae* free in the cytoplasm of the muscle cells did not seriously affect the morphology or rhythmic contractions of the cells. The significance of the presence of *M. leprae* in somatic cells needs further study.

MAKONKAWKEYOON, S. et. al. Immunologic Defects in Leprosy Patients. I. Evidence of Immune Aberration os Suppressor-T Lymphocytes in Lepromatous Leprosy. *Int.J. Lepr.*, 58(2), p. 302-310, 1990.

Immunoregulation in various types of leprosy patients was evaluated in vitro using peripheral blood mononuclear leukocytes (PBML) stimulated with phytohemagglutinin-P (PHA-P) or concanavalin A (ConA) for a cell-mediated immune (CMI) assay or pokeweed mitogen (PWM) for a humoral mediated immune (HMI) assay. The immune responses were evaluated by a lymphocyte transformation test (LTT) and lymphocyte-mediated cytotoxicity (LMC) for the immunoregulation of CMI, and a reverse hemolytic plaque assay for measuring the plaque-forming cells (PFC) and a sandwich ELISA for measuring IgG concentrations for the immunoregulation of HMI.

In LTT with PHA-P or ConA, the mean of the normal controls was not significantly different from the means of the untreated LL, BL, BB, BT, and TT leprosy patients. However, a wide variation of LTT results from BT to LL patients was noted: the LTT results of TT patients and normal controls were less variable. A similar pattern of immune responses was noted when studied by LMC in untreated LL, BL, BB, BT, and TT leprosy patients and normal controls. When the untreated patients and normal controls were studied for PFC, using PBML, stimulated with PWM, a very similar pattern of PFC was obtained with the different types of leprosy patients.

The immuno regulatory role of lymphocytes in leprosy patients was further evaluated by cell mixing cultures. ConA-stimulated PBML from lepromatous leprosy patients were mixed with normal PBML and then stimulated with PHA-P. The immune regulation was then measured by LMC. Untreated BULL patients having a bacterial index (BI) of 3+ or more had significantly less suppressive activity than treated BULL patients having a BI of less than 3+, less than treated TT patients, and less than normal controls.

The activity of suppressor-T lymphocytes from untreated LL patients was further evaluated by the isolation of CD8 + T cells or ConA-sheep erythrocyte (SRBC) rosetted T cells from PBML of

these patients and normal controls. The CD8+ T cells or ConA-SRBC rosetted T cells were cultured in various percentages with normal PBML and then stimulated with PWM. The immunoregulation of these T-cell populations was measured by quantitative determination of the PFC, using a reverse hemolytic plaque assay, or by quantitation of IgG with an ELISA. The CD8+ T cells and Con-A-SRBC rosetted T cells from these LL patients showed significantly less suppressive activities in all of the tested cell concentrations when compared with normal controls.

MAKONKAWKEYOON, S. et. al. Immunologic Defects in Leprosy Patients. II. Interleukin 1, Interleukin 2, and Interferon Production in Leprosy Patients. *Int.J.Lepr.*, 58(2), p. 311-318, 1990.

The capabilities of monocytes and lymphocytes in peripheral blood mononuclear leukocytes (PBML) to produce interleukin-1 (IL- 1), IL-2, and interferon (IFN), respectively, were evaluated in various types and treatments of leprosy patients. IL-1 production in response to lipopolysaccharide was significantly lower in LL, BL, BB, and BT patients than in normal controls. However, there were no differences in IL-1 levels between TT patients and normal controls. The percentages of nonspecific-esterase positive cells adhering to the plastic surfaces were not different in LL, BB and TT patients when compared to normal controls. However, they were significantly higher in BT and BL patients than in normal controls.

When PBML from leprosy patients were stimulated with concanavalin-A (ConA) for IL-2 production, there were no differences in the IL-2 levels in treated BULL, untreated BULL, treated BUTT, and untreated BT/TT patients compared to normal controls. Similar results were obtained when PBML were stimulated with phytohemagglutinin-P (PHA-P). However, when purified protein derivative (PPD) was used as the stimulating agent, there were significantly lower IL-2 levels in treated BULL, untreated BULL, treated BT/TT, and untreated BUTT patients when compared to normal controls. There were also

lower IL-2 levels in untreated BULL and BT/TT patients compared to treated BULL and BT/TT patients, respectively.

PBML, were stimulated with PHA-P or ConA for IFN production. There were no differences in the IFN levels in treated BULL, untreated BULL, treated BT/TT, and untreated BT/TT patients compared to normal controls. However, when PPD was used as the stimulating agent, there were lower IFN levels in treated BULL, untreated BULL, and treated BT/TT patients compared to normal controls.

MEEKER, H.C. et. al. Sequential Monitoring of Leprosy Patients with Serum Antibody Levels to Phenolic Glycolipid-I, and Mycobacterial Lipoarabinomannan. *Int. J. Lepr.*, 58(3), p. 503-511, 1990.

Sequential serum samples from leprosy patients at various stages of antibacterial treatment were tested by an ELISA for antibodies to phenolic glycolipid I (PGL-I), a synthetic PGL-I analog (ND-BSA), and lipoarabinomannan (LAM) Mycobacterium tuberculosis to determine if these antibodies could be useful in monitoring response to therapy. Among patients with positive initial anti-PGL-I IgM, a significant decrease in this antibody was seen over time ($p < 0.01$), whether assayed by PGL-I or ND-BSA. The two antigens showed good agreement in the detection of decrease in anti-PGL-I IgM. The greatest decrease was seen in patients with a high initial anti-PGL-I IgM and a high bacterial index (BI). Patients with a declining BI were seen to have generally declining antibody levels to PGL-I and to LAM; in those patients with a fluctuating BI, antibody levels were less predictable. We conclude that antibodies to PGL-I and LAM can be useful in following response to therapy in leprosy patients and that either native PGL-I or ND-BSA can serve as antigens for the ELISA.

MOUDGIL, K.D. et. al. Comparative Evaluation of Enzyme Immunoassays based on synthetic Glycoconjugates and phenolic glycolipid-I for immunodiagnosis of leprosy. *Ind. J. Lepr.*,

62(1), p. 60-65, 1990.

Enzyme immunoassays (EIAs) based on synthetic glycoconjugates containing the terminal monosaccharide (M-BGG) or disaccharide (ND-BSA) residue of the trisaccharide component of phenolic glycolipid-I (PGL-I), for immunodiagnosis of leprosy are described. The results of the assays were compared with that of the EIA using PGL-I. All the three assays were highly specific for leprosy. The per cent positivity of active lepromatous leprosy (LL) patients with M-BGG was 78.05 in comparison to 85.36 with ND-BSA and 82.11 with PGL-I. Similarly, the positivity of tuberculoid (TT) leprosy patients in M-BGG assay was lower than that in EIAs using ND-BSA or PGL-I. However, the difference in the positivity of individual category of leprosy patients in the three EIAs was not statistically significant. The correlation between absorbance values of leprosy sera in EIAs based on M-BGG and PGLI, as well as that in assays using ND-BSA and PGL-I was statistically significant.

NAIR, I. & MAHADEVAN, P.R. Antigenic Protein from *Mycobacterium leprae* Released in Macrophages in vitro as Indicator of Viability of Bacteria. *Int. J. Lepr.*, 58(3), p. 540-547, 1990.

Peritoneal macrophages from randombred, Swiss white mice, when cultured and infected with *Mycobacterium leprae* for 24 hours, are able to show the presence of antigen(s) with binding affinity to antibodies present in the sera of bacteriologically positive, lepromatous leprosy patients. Such antibodies are not seen in sera from normal and health persons, tuberculoid leprosy patients, or long-term-treated, bacteriologically negative, lepromatous leprosy patients. The production of the antigen(s) is blocked by the anti-*M. leprae* drug rifampin. Other mycobacteria when incubated with macrophages from mice show very little antigens in the lysate but the antigens have an equal affinity for antibodies in sera from both normal individuals and lepromatous patients. Only the lysates from macrophages exposed to live *M. lepraecould* discriminate and could exhibit

differential binding to sera from leprosy patients compared to sera from normal individuals. This antigen(s) does not have any binding ability to the monoclonal antibodies available to the antigens of *M. leprae* identified at present and shown to be specific to *M. leprae*. This indicates a separate identity of this product which has potential for further exploitation in exploring host-pathogen interactions related specifically to the leprosy infection and the tolerance of *M. leprae* inside cells.

NAIR, I. et. al. Viability of *Mycobacterium leprae* Inside Macrophages from Different Strains of Mice and Possible Genetic Control. *Mt. J. Lepr.*, 58(3), p. 548-553, 1990.

Peritoneal macrophages from Swiss white mice in vitro tolerated *Mycobacterium leprae* and allowed metabolism of the bacteria leading to release of bacteria-specific antigenic protein. This was associated with the maintenance of viability of the bacilli inside the cells. Macrophages from C57BL mice reduced viability of *M. leprae* after phagocytosis, and this was associated with the production of superoxide. Blockage of superoxide production resulted in maintaining viability of the cells of these mouse strains. Associated with loss of viability of the bacilli is the absence of the production of antigenic protein in the lysate. Interestingly, the maintenance of viability or loss of viability and the factors controlling such viability in the macrophages of Swiss white and C57BL mice, respectively, appeared to be genetically controlled.

QINXUE, Wu. et. al. Rapid Serodiagnosis for Leprosy-A Preliminary Study on Latex Agglutination Test. *Mt. J. Lepr.*, 58(2), p. 328-333, 1990.

In this study, we have developed two latex agglutination tests (LATs) with phenolic glycolipid (PGL-I) and natural disaccharide-octylbovine serum albumin (ND-O-BSA) as antigens in 110 leprosy patients (LL=30, BL=30, BT=30, and TT=20), 50 tuberculosis cases, and 30 nor-

mal controls. These two LATs were compared with corresponding ELISAs (ND-O-BSA ELISA and PGL-I ELISA) and analyzed by the chi-squared test. There were no significant differences between the two LATs (PGL-I LAT and ND-O-BSA LAT) and their corresponding ELISAs. There was an increase in the proportion of positive cases detectable which coincided with the clinical classification of leprosy, i.e., lepromatous cases were more likely to be positive than tuberculoid cases. LATs are more simple and rapid than ELISAs and have high sensitivity (77% in ND-O-BSA LAT, 80.5% in PGL-I LAT) and specificity (99% in both LATs). LATs may become useful tools for the immunodiagnosis of leprosy in the field. The stability and repeatability of LATs are discussed in detail.

RAPOPORT, B.L. et. al. A study of Autoantibodies in Chronic *Mycobacterium* Infections. *Mt. J. Lepr.*, 58(3), p. 518-525, 1990.

Infections can cause autoantibody production. The purpose of this study was to determine the prevalence of autoantibodies in patients with chronic mycobacterial infections. Sera from 41 leprosy patients and from 49 untreated and 73 treated tuberculosis (TB) patients were tested for the presence of rheumatoid factor, antinuclear factor, and several other autoantibodies. The rheumatoid factor, measured by the RheumaTec RF latex test, was positive in 2.4% of the leprosy patients and 2.7% of the treated TB patients but absent in the untreated TB group. The titers ranged from 40 to 180 international units. Positivity was dependent upon the technique utilized, and existed in 21% of untreated TB group and 4% of the treated TB patients when using the Rheuma-Wellcotest technique. The antinuclear antibody was positive in 7.3% of the leprosy group, 6.1% of the untreated TB group, and 15% of the treated TB patients ($p=0.0125$). Antinuclear antibody positivity correlated with the duration of treatment of the TB patients ($p=0.025$). The antinuclear antibody titers were low and gave no specific pattern on staining. No patient had antibodies against native deoxyribonucleic acid, ribonucleic protein, Ro (SS-A) or La (SS-B) antigens.

Due to their low prevalence and frequency in these chronic infections, these autoantibodies should not lead to confusion in distinguishing these conditions from the connective tissue diseases.

ROCHE, P.W. et. al. Heterogeneity of Serological Responses in Paucibacillary Leprosy-Differential Responses to Protein and Carbohydrate Antigens and Correlation with Clinical Parameters. *Int. J. Lepr.*, 58(2), p. 319-327, 1990.

We have examined the serological responses of 154 untreated paucibacillary (PB) leprosy patients to two carbohydrate and one protein antigens of *Mycobacterium leprae*. There was a heterogeneous response with 20% of PB patients having IgM anti-PGL-1 antibodies and a similar proportion with IgG anti-LAM antibodies, while 33% had antibodies to the *M. leprae*-specific epitope on the 35-kDa protein. There was overlap in the responses such that 43% of the patients were seropositive in one of the two *M. leprae*-specific assays, while 49% were positive in any assay. There was a gradation in seropositivity with increasing extent of disease for each of the clinical parameters measured. Those with established disability at the time of presentation were more likely to be seropositive in each assay.

ROCHE, P.W. et. al. Operational Value of Serological Measurements in Multibacillary Leprosy Patients: Clinical and Bacteriological Correlates of Antibody Responses. *Int. J. Lepr.*, 58(3), p. 480-490, 1990.

The antibody responses of 100 previously untreated multibacillary (MB) leprosy patients to one protein and two carbohydrate antigens were examined: 94% of the patients had *Mycobacterium leprae*-specific antibodies; 89% directed to the species-specific epitope on phenolic glycolipid (PGL-I), 89% against the specific epitope on the 35-KDa protein, and 94% against one or both of the two. By contrast, 67% of the patients had anti-lipoarabinomannan (LAM) anti-

bodies. There were trends for the seropositivity rate and the antibody level to rise with the increasing extent of the disease and as patients moved to the polar lepromatous end of the spectrum. The bacillary load, as measured by the bacterial index, was moderately correlated with the IgM anti-PGL-I and the anti-35-kDa antibody levels and, to a lesser extent, with the IgG antibodies directed at the common mycobacterial carbohydrate LAM. The sensitivity of the IgM anti-PGL-I antibodies for detecting smear-positive MB disease was 91%; that for the anti-35-kDa antibodies was 92%.

ROY, A. et. al. Anti-arabinogalactan IgM/IgG Ratio: A screening index for leprosy patients. *Ind. J. Lepr.*, 62(4), p. 435-442, 1990.

The serological activities of arabinogalactan from *M. smegmatis* and phenolic glycolipid-1 from *M. leprae* were examined by Enzyme Linked immunosorbent Assay using sera from 88 patients with leprosy (44 treated and 44 untreated) and 45 normal healthy individuals. Both IgM and IgG type of antibodies were measured against these antigens. The results confirmed the previous observation that anti phenolic-glycolipid-1 IgM antibodies are higher in lepromatous leprosy cases than in normal individuals. However, with arabinogalactan, the ratio of IgM/IgG was more than one in normal individuals and less than one in untreated LL patients. Treated patients fell in both categories. Moreover, a reverse relationship was found between anti PGL1 IgM titers and anti arabinogalactan IgM/IgG ratio.

SCOLLARD, D.M. et. al. Studies of Human Leprosy Lesions in situ Using Suction-Induced Blisters. 2. Cell Changes and Soluble Interleukin 2 Receptor. *Int. J. Lepr.*, 58(3), p. 469-479, 1990.

To examine the pathogenesis of type 1 (reversal) reactions in leprosy, we studied cellular and soluble immunologic components of skin lesions in 10 patients with reactions, 24 active patients without reactions, and 33 control patients

whose leprosy had been treated and cured. Cells and Taceptide levels were obtained from fluid aspirated from blisters induced by suction directly over representative skin lesions. During reversal reactions: a) the lesions contained an increased number and percentage of CD4+ (T-helper) cells; b) Taceptide levels were elevated in half of the lesions; c) the increases in Tac peptide and (CD4 + cells) were directly correlated; and d) systemic administration of corticosteroids appeared to cause a reduction in the intralesional CD4+cell population. These findings were localized to the skin, and do not represent simple filtration of these components from the peripheral blood. We conclude that spontaneous lymphocyte activation in situ, primarily of CD4+cells, is an important feature of reversal reactions, and may be an intermittent or cyclic phenomenon during the reaction. Findings in active patients without reactions are consistent with the hypothesis that differing states of immunologic equilibrium have been established in different portions of the leprosy spectrum. In reversal reactions we may, therefore, be examining immunologic processes set in motion when a pre-existing equilibrium has been upset by spontaneous, natural events. The mechanism of such spontaneous changes in immunity in leprosy is of considerable interest, not only to understand the reaction, but also to examine the underlying determinants of delayed-type hypersensitivity and cell-mediated immunity in leprosy and the potential for artificially manipulating these responses, as proposed with vaccines or immunotherapy.

SHROFF, K.E. et. al. Pathogenesis of Route-related Variation in T-suppressor Response on Immunization with Mycobacteria. *Int.J. Lepr.*, 58(1), p. 50-57, 1990.

The route of immunization was observed to play a significant role in deciding the outcome of immunization with killed mycobacterial vaccines. Earlier we reported that the slow growers were immunogenic by both the intraperitoneal (i.p.) and intradermal (i.d.) routes. In contrast, the rapid growers were immunogenic by the i.d. route only. Both rapid and slow growers generated the clas-

sical, antigen-specific Lyt-2 positive, T-cell-mediated suppression after i.p. immunization but not after i.d. immunization. Thus, in the case of the slow growers, T-cell-mediated suppression was only a component of the immune response generated after i.p. immunization. In contrast, in the case of *Mycobacterium vacate* and the other rapid growers, the T-cell-mediated suppression was the predominant response with i.p. immunization. The T-cell-mediated suppression generated by i.p. immunization exhibited crossreactivity, the spectrum of which was dependent upon the dose of the immunization.

SHROFF, K.E. et. al. Route-related in Immunogenicity of Mycobacteria. *Int. J. Lepr.*, 58(1), p. 44-49, 1990.

The route of immunization was observed to play a significant role in deciding the T-cell response to immunization with killed mycobacterial vaccines. Slow-growing mycobacteria were found to be immunogenic by both the intraperitoneal (i.p.) and intradermal (i.d.) routes; rapid-growing mycobacteria were immunogenic by the i.d. route only.

The nonresponder state following i.p. immunization with *Mycobacterium vacate* could be corrected by treatment of the mice with poly I: poly C or indomethacin prior to immunization. Both poly I: poly C, an interferon inducer, and indomethacin, a prostaglandin inhibitor, are known to enhance the expression of major histocompatibility complex glycoproteins. Since they are so important in antigen preparation, it was concluded that the inability of mice to respond to *M. vacate* by the i.p. route is likely due to defective presentation of the bacterial antigens by the antigen-presenting cells at the site, namely, the peritoneal macrophages. These findings are significant because *M. leprae* has been reported to be antigenically similar to *M. vaccae*, and the response of mice to i.p. Immunization with both of these mycobacteria is very similar.

SHROFF, K.E. et. al. Variation in Immunogenicity of Mycobacteria: Role of Antigen-presenting Cells. *Int. J. Lepr.*, 58(1), p. 58-64, 1990.

The antigen-presenting efficiency of peritoneal cells and irradiated spleen cells was compared using *Mycobacterium tuberculosis* - and *M. vaccae*-primed T cells and corresponding sonicates as antigens in an in vitro lymphocyte transformation test. The presentation efficiency of irradiated spleen cells was reasonably good for both antigens. However, with peritoneal cells as the antigen-presenting cells, the proliferative response against only *M. tuberculosis* sonicate was good. Proliferation of *M. vaccae*-primed T cells was very poor when the antigen was presented by peritoneal cells. Poly I: poly C treatment of mice prior to harvesting the peritoneal cells resulted in distinct improvement in their efficiency to present *M. vaccae* sonicate, maximal proliferative response was obtained with peritoneal cells from mice receiving two and three doses of poly I: poly C 24 hr apart. Even paraformaldehyde-fixed peritoneal cells from poly I: poly C-treated mice gave an efficient *M. vaccae*-specific stimulation to primed T cells. Based on these data, it was concluded that failure of mice to respond to *M. vaccae* by intraperitoneal immunization is the result of the poor efficiency of presentation of *M. vaccae* antigen.

SULCEBE, G. & NAKUÇI, M. Anti-phenolic glycolipid 1 IgM antibodies in leprosy patients and in their household contacts. *Leprosy Review*, 61(4), p. 341-346, 1990.

Through they have no apparent protective action, the specific antibodies are important markers of the infection with *Mycobacterium leprae*. For their detection we employed an ELISA method using as substrate a synthetic immunodominant disaccharide of phenolic glycolipid I antigen of *M. leprae*, conjugated with bovine serum albumin (D-BSA). Increased levels of anti D-BSA antibodies of the IgM class were detected in 61.5% of the 13 leprosy patients and in 13.3% of their 53 household contacts, where as they were not found in any of the 37 normal blood donors. A strong correla-

tion ($r=-0.846$) was found between the antibody levels and the duration of the disease among the 12 patients with lepromatous leprosy.

These preliminary data demonstrate the usefulness of this method for epidemiological studies and for the detection of cases with of cases with subclinical infection.

TRUMAN, R.W. et. al. Antibodies to the phenolic glycolipid-1 antigen for epidemiologic investigations of enzootic leprosy in armadillos (*Dasypus novemcinctus*). *Leprosy Review*, 61(2), p. 19-24, 1990.

Other than man, nine-banded armadillos (*Dasypus novemcinctus*) are the only known natural hosts of leprosy with high rates of disease. The origin, range and risk of their infection is not yet clear and a better description of the rate of leprosy over the armadillo's range is needed. Both histopathological examination of armadillo ear tissues and serologic screening for IgM antibodies to the phenolic glycolipid-I (PGL-I) antigen of *Mycobacterium leprae* are good relative indices of enzootic prevalence. A survey of 216 armadillos from Louisiana and Florida detected infection only among Louisiana animals. Average antibody prevalence (12.5%) was five times higher than the fully disseminated disease rate described histopathologically (2.7%). The differences in antibody and histopathological prevalence are due to the sensitivity of the methods for detecting early infection. Histopathological examinations describe an advanced disease. The higher antibody prevalence of wild armadillos is not likely to be result of false positive serologies from self-healing infections or other casual encounters with *M. leprae* as might be mimicked by lepromin injection. The environmental reservoir of *M. leprae* represented by infected armadillos is greater than could be previously estimated.

TYAGI, P. et. al. Activation of Complement by Circulating Immune Complexes Isolated from Leprosy Patients. *Int.J. Lepr.*, 58(1), p. 31-38, 1990.

Circulating immune complexes isolated from different types of leprosy sera as polyethylene glycol (PEG) precipitates were found to be efficient activators of the alternative pathway of complement. PEG precipitates from BULL leprosy patients and those with erythema nodosum leprosum were found to activate both classical pathway and the alternative pathway of complement efficiently, while PEG precipitates from TT/ BT leprosy patients and borderline tuberculoid patients in reaction were found to activate the alternative pathway of complement but not the classical pathway. No significant differences were observed between the PEG precipitates from reactional and nonreactional TT/BT and BULL patients in their complement activating ability.

VACHULA, M. et. al. A Comparison of Monocyte Oxidative Responses in Leprosy Patients and Healthy Subjects as Influenced by Mycobacterial Lipid Pretreatment. *Int J. Lepr.* 58(3), p. 534-539, 1990.

Superoxide anion (O_2^-) release by monocytes from leprosy patients in a paired study was lower than that released by monocytes from healthy controls. Pretreatment of healthy control monocytes with phenolic glycolipid-I (PGL-I) of *Mycobacterium leprae* resulted in the release of less O_2^- than released by buffer-treated cells or cells pretreated with structurally similar lipids. However, pretreatment of patient monocytes with PGL-I did not affect the O_2^- generation, perhaps because the cells already had a lower capacity to produce O_2^- . Upon further examination of the data from the patient population, monocytes from lepromatous patients released significantly less O_2^- than cells from normal controls, while tuberculoid patient cells released O_2^- in amounts similar to that generated by cells from normal controls. In addition, monocytes from patients with a high bacterial index had a lower capacity to generate O_2^- when compared to cells from healthy

individuals.

VACHULA, M. et. al. Effect of Mycobacterium leprae's Phenolic Glycolipid-I on Interferon-gamma Augmentation of Monocyte Oxidative Responses *Int J. Lepr.*, 58(2), p. 342-346, 1990.

Peripheral blood monocytes were pretreated with phenolic glycolipid-I (PGL-I) dimycocerosyl phthiocerol (DIM), or mycoside A, then cultured in the presence or absence of interferon-gamma ($IFN-\gamma$). Their oxidative responses to *Mycobacterium leprae*, phorbol myristate acetate (PMA), and opsonized zymosan were evaluated. In response to *M. leprae*, monocytes pretreated with PGL-I released less O_2^- than nonlipid-treated control cells. The $IFN-\gamma$ augmentation of oxidative responses was suppressed only in PGL-I-pretreated monocytes and only when the stimulus was *M. leprae*. This suggests that PGL-I, by affecting the $IFN-\gamma$ enhancement of phagocytic cell oxidative responses, aids further the intracellular survival of *M. leprae*.

ANDERSEN, P. et. al. Proliferative Response to Seven Affinity Purified Mycobacterial Antigens in Eight Strains of Inbred Mice. *Int.J. Lepr.*, 59(1), p. 58-67, 1991.

This study compares the T-cell-stimulating ability of different mycobacterial antigens. The responses to crude culture filtrates and seven affinity-purified antigens were investigated in eight strains of inbred mice. Large differences in the stimulating abilities of the antigens were observed, and four antigens were found to give a powerful T-cell stimulation. Some antigens divided the strains into high and low responders, while a 17-kDa antigen was found to be exceedingly T-cell stimulatory in mice of all tested haplotypes. The responses of the eight strains were analyzed by comparing the response patterns of the strains. Using a statistical model based on antigen ranking, five strains were found to have a similar response pattern: three strains were found to differ. These results demonstrate the significance

of the choice of mouse strain in studies of mycobacterial immunology and, furthermore, indicate that when research is conducted to develop new mycobacterial vaccines, it is important to include panels of antigens.

CHANTEAU, S. et. al. Evaluation of gelatin particle agglutination assay for the detection of anti-PGLI antibodies. Comparison with ELISA method and applicability on a large scale study using blood collected on filter paper. *Leprosy Review*, 62(3), p. 255-261, 1991.

Given the technical difficulties of the ELISA method, a gelatin particle agglutination test (MLPA) has been developed recently for the detection of anti-PGLI antibodies. The purpose of this study was to compare these 2 tests. MLPA was found to be less specific than ELISA (91% versus 98%, $\chi^2=66.8$, $p<0.001$). The sensitivity of both tests was of 95% for the diagnosis of multibacillary patients. In the case of paucibacillary patients. MLPA was found to be less sensitive than ELISA (21% versus 35%, $\chi^2=6.98$, $p<0.01$). The agreement between the 2 tests for a positive or a negative result was satisfying (85% to 100%), except for the weakly seropositive individuals (71%). The correlation between OD obtained with ELISA and antibody titre obtained with MLPA was statistically significant ($r=0.70$, $p<0.001$). Conversely to ELISA, MLPA was not applicable on blood samples absorbed on filter paper without a serious loss of sensitivity. In conclusion, this study demonstrated that the MLPA test can only reliably detect anti-PGLI antibodies in a multibacillary cases.

CHATURVEDI, Vinita. et. al. Association of mycobacterial-specific and Mycobacterium leprae specific antibody levels with clinical activity in tuberculoid leprosy: a comparative study of three serological enzyme-immunoassays. *Leprosy Review*, 62(2), p. 122-133, 1991.

The ELISA for polyclonal antibodies

against Mycobacterium leprae (ML-ELISA) and specific antibodies against epitopes on 35 kDa protein (SACT-ELISA) and phenolic glycolipid I (PG-ELISA) of M. leprae were evaluated comparatively in a group of 88 tuberculoid leprosy patients. The overall seropositivity rate with a battery of 3 tests (68%) was not significantly higher than that obtained with ML-ELISA alone (55%) for IgG class of antibodies. Seropositivities for SACT ELISA and PG ELISA were, respectively, 38% and 26%, ML-ELISA for IgM class of antibodies was least sensitive, showing only 8% positivity.

A significant correlation was noted between individual values of the three assays, but the positive proportions overlapped maximally in the case of ML ELISA (IgG) and SACT ELISA. Further, positivity for the latter two assays, particularly SACT-ELISA, showed significant associations with the extent of 'active' (largely untreated) infection.

Immunoblotting revealed that the main antibody response was directed towards M. leprae antigens in the molecular weight range 20-40 kDa and the densitometry results of this zone correlated significantly with corresponding SACT-ELISA and ML-ELISA (IgG) values.

CHO, S.N. et. al. Detection of Phenolic Glycolipid I Antigen and Antibody in Sera from New and Relapsed Lepromatous Patients Treated with Various Drug Regimen. *Int. J. Lepr.*, 59(1), p. 25-31, 1991.

Since phenolic glycolipid-I (PGL-I) is an unequivocal marker of Mycobacterium leprae, the antigen has been a good candidate for the serodiagnosis and monitoring the effectiveness of leprosy chemotherapy. As an effort to define the kinetics of the PGL-I antigen and its antibodies in leprosy patients, this study was initiated to examine the serum specimens obtained serially from lepromatous patients under chemotherapy trials. PGL-I was detectable in 64 (94.1%) of 68 new lepromatous (bacterial index, BI=3.2 to 5.8) and in 26 (78.8%) of 33 relapsed lepromatous patients (BI=3.0 to 5.3). Meanwhile, virtually all of the new and relapsed patients were strongly

seropositive to PGL-I. PGL-I was not detectable in any of the patients about 18 months after chemotherapy was initiated; however, anti-PGL-I reactivity declined by 50% at 2 years and by about 70% at 5 years after chemotherapy regardless of the drug regimens under study. Considering the rapid disappearance of the PGL-I antigen and steady decrease in anti-PGL-I IgM antibodies following chemotherapy, the PGL-I based serology may be useful for monitoring the effectiveness of treatment, at both the early and late stages, in leprosy patients whose initial sera contain a significant level of PGL-I antigen or antibodies.

CHUJOR, C.S.N. et. al. Serum Antibodies Against Peripheral Nervous System Antigens in Leprosy. *Int.J.Lepr.* 59(4), p.590-597, 1991.

Since antibodies against peripheral nervous system (PNS) antigens may play a pathogenetic role in the mechanism of nerve damage in leprosy, sera from leprosy patients and contacts were investigated for anti-PNS antibodies by ELISA and immunoblot. In ELISA, elevated anti-PNS antibody levels were detected in 4 of 98 (4.1%) leprosy patients (4 of 52, 7.7%), lepromatous leprosy patients, in 1 of 28 (3.6%) contacts, and in 1 of 18 (5.6%) normal controls. There was no correlation between anti-PNS antibody levels and the bacterial index or neuropathy in leprosy. Immunoblot with a sample of six leprosy and five control sera showed that the antigenic binding pattern (mainly within the 100-200-kDa region) was very similar in patients and controls. Staining intensity, however, appeared to be higher with the leprosy sera than with the control sera. IgM and IgG were found to contribute to the staining pattern: IgM in the 150-200-kDa range, IgG with multiple bands between 25 kDa and 200 kDa. Thus, the presence and levels of serum anti-PNS antibodies in leprosy appear to be unrelated to parameters of disease activity, neuropathy in particular, and do not seem to be critically involved in the pathogenesis of nerve damage.

CHUJOR, C.S.N. et. al. Serum IgA and IgM Antibodies Against Mycobacterium leprae-

derived Phenolic Glycolipid-I: A Comparative Study in Leprosy Patients and Their Contacts. *Int.J.Lepr.*, 59(3), p.441-449, 1991.

In order to evaluate the potentials of IgA, versus IgM as well as of native phenolic glycolipid I (PGL-I) versus PGL-I-disaccharide coupled to bovine serum albumin (D-BSA) as antigens in the serodiagnosis of leprosy, anti-D-BSA IgA, and anti-PGL-I IgM were investigated and compared to anti-PGL-I IgA, in sera from patients and contacts.

Anti-D-BSA and anti-PGL-I IgA, significantly correlate in patients and contacts. The higher IgA, positivity rates obtained with D-BSA as compared to PGL-I may suggest D-BSA as the favorable antigenic material. In patients but not in contacts anti-PGL-I IgM and IgA, correlate, IgM predominating over IgA. In all three antibody systems, the mean values as well as the positivity rates increased from the tuberculoid toward the lepromatous disease pole. Also, the levels of all three antibodies significantly increased with the bacterial index (BI).

However, anti-D-BSA (PGL-I) IgA appears to be preferable to IgM with respect to sensitivity, i.e., detection of disease activity, in paucibacillary or BI-negative patients. A number of contacts were detected as seropositive with anti-D-BSA and/or anti-PGL-I IgA, but not with anti-PGL-I IgM. This suggests that IgA is a better tool than IgM for the detection of leprosy in its subclinical stage.

KAUR, J. et. al. Enzyme Immunoassay of Phagocytosis Stimulating Tetrapeptide "Tuftsin" in Normal and Leprosy Sera. *Int.J.Lepr.*, 59(4), p. 576-589, 1991.

The serum concentrations of the phagocytosis stimulating tetrapeptide, tuftsin, were determined by competitive enzyme immunoassay in borderline tuberculoid/tuberculoid (BT/TT, 16 cases), borderline lepromatous/lepromatous (BL/LL, 16 cases), and in healthy controls (20 cases). Using checkerboard titration, 10 ng/well of diphtheria toxoid-p-

amino phenylacetyl tuftsin (DTPT) conjugate when incubated with tuftsin antisera at 1:15,000 dilution with a preincubation time of 60 min with the competitor (tuftsin) followed by a further 60 min incubation onto the DTPT-coated wells gave consistent results with a sensitivity of 5 ng/well tuftsin. The mean serum tuftsin concentration was significantly lower in BULL patients (134.42 ± 48.7 ng/ml, $p < 0.01$) than in healthy controls (262.86 ± 59.8 ng/ml), while BT/TT sera (210.94 ± 75.5 ng/ml) showed slightly decreased levels than did normals, which was not statistically significant. The mean serum IgG levels in BULL and BT/TT patients (37.26 ± 10.99 mg/ml; 28.08 ± 6.57 mg/ml, respectively) showed significantly ($p < 0.001$) higher concentrations than did healthy controls (12.3 ± 3.6 mg/ml). These observations on the serum concentrations of tuftsin and IgG in leprosy individuals suggest that there is splenic dysfunction in BULL patients in terms of the processing of leukokinin to release the free, active molecule tuftsin.

LAUNOIS, P. et. al. *M. leprae* and BCG - induced Chemiluminescence Response of Monocytes from Leprosy Patients and Healthy Subjects: Effects of Gamma-Interferon and GM-CSF. *Int.J.Lep.*,59(4), p. 582-589, 1991.

Mycobacterium leprae, in contrast to BCG, failed to trigger any chemiluminescence (CL) response in mononuclear cells from either leprosy patients or healthy subjects a deficit not reversed by either interferon-gamma or GM-CSF. Chemiluminescence responses induced without mycobacteria or with BCG were found to be lower in leprosy patients than in controls. *M. leprae* were also less well phagocytosed than BCG. However, there was a significant difference in phagocytosis between healthy and tuberculoid leprosy subjects. Phagocytosis was not altered by the addition of either lymphokine, and no major differences between healthy subjects and patients were observed. Preincubating mononuclear cells with anti-mycobacteria antibodies (lepromatous patients' sera) did not increase the CL response nor the phagocytosis of *M. leprae* or BCG.

LEFFORD, M.J. et. al. The Value of IgM Antibodies to PGL-I in the Diagnosis of Leprosy. *Int.J.Lep.*,59(3), p. 432-440, 1991.

An ELISA has been used to measure IgM antibodies to phenolic glycolipid-I (PGL-I) in previously undiagnosed patients who were suspected of leprosy on purely clinical grounds. The certainty of clinical diagnosis was classified as either "firm" or "indefinite." Leprosy was confirmed in 133 of 161 patients on the basis of positive slit-skin smears and/or skin and/or nerve histopathology. All 58 patients with multibacillary leprosy (BB, BL, or LL) were correctly diagnosed clinically, as were 50 of 54 patients (93%) with a firm diagnosis of BT or TT leprosy. The firm clinical diagnoses were more accurate than either the slit-skin smear or ELISA data. However, there were 44 patients (27% of total), designated "rule out leprosy" (RO), for whom the clinical diagnosis was indefinite. The clinical suspicion of leprosy (RO) was correct in only 24 (55%) of these patients who had BT leprosy. The slit-skin smears were positive in only 20% of these patients compared to 50% for the ELISA. It was concluded that the PGL-I IgM ELISA may have its greatest diagnostic confirmatory value in paucibacillary disease because paucibacillary leprosy comprises the major source of clinical diagnostic difficulty.

RAMESH, V. et. al. Multibacillary Leprosy Presenting as a Solitary Skin Lesion; Report of Three Cases and its Significance in control Programs. *Int. J. Lep.*,59(1), p.1-11, 1991.

It is held that immune complexes (IC) play a vital role in the pathogenesis of some of the reactions in leprosy. The complement system is known to solubilize and render IC innocuous. We have previously shown that patients undergoing lepra reactions had lowered complement-mediated IC solubilization (CMS). We, therefore, undertook a prospective study of untreated multibacillary leprosy patients and monitored their CMS levels sequentially while on therapy. In addition, the concentrations of the complement component C3d, immunoglobulins G, A and M, and circulating immune complexes (CIC) were also

estimated. A total of 26 patients were included in the study and were investigated at 3-month intervals for 3 years. Thirteen of the 14 patients who did not develop reactions at all had normal CMS values, although all of them showed elevated CIC. From the inception of treatment, 10 of the 12 patients who developed lepra reactions had low CMS values which remained below normal levels even after evidence of complement activation disappeared and long after the subsidence of reaction. It is suggested that this defective CMS acts as a predisposing cause of lepra reactions.

RASHEED, F.N. et. al. Specificity of lymphocytotoxic autoantibodies (LCAbs) found in the serum of leprosy patients: Class I MHC antigens. *Leprosy Review*, 62(1), p. 13-20, 1991.

Lymphocytotoxic autoantibodies (LCAbs) of the IgM class have been identified in patients with borderline tuberculoid (BT) and borderline lepromatous (BL) leprosy with Type I reactions (I) as well as lepromatous leprosy (LL) patients with *erythema nodosum leprosum* reactions (ENL). The observation that lymphocytotoxic activity (LCA) was reduced in the presence of platelets led us to determine whether LCABs had specificities for Class I Major Histocompatibility Complex (MHC) determinants. Absorption of LCA positive sera with platelets, classically used to deplete Class I specific lymphocytotoxic antibodies, reduced LCA towards autologous as well as allogeneic target cells. This was true for LCA positive sera from all patient classifications (group BT in the autologous system, $p < 0.01$; in all other patient groups, $p < 0.001$). Introducing B-2m to cytotoxicity assays only marginally reduced LCA when added at high concentrations (5 mg/ml). An anti-Class I MHC; antiserum which blocked the lytic activity of Class I tissue typing sera did not inhibit lymphocytotoxic activity. The data indicate that LCABs while absorbed by platelets, are not specific for the Class I MHC antigens. The autoantigen recognized by these autoantibodies therefore remains to be identified.

SEHGAL, V.N. Soluble Interleukin-2 receptors: levels in leprosy, and during and after Type 1(lepra) and Type 2 (ENL) reactions. *Leprosy Review*, 62(3), p.262-268, 1991.

Twenty-five patients with Type I (lepra) and Type 2 (ENL) reactions, were assayed for SIL-2R in serum-before and after treatment for their acute condition-and the results were compared with 10 normal healthy adults and 20 patients of leprosy per se. Classification of each subject into different leprosy groups, and into various types and subtypes and of reactions, was done according to standard criteria, prior to inclusion into the study. Detailed statistical evaluation of the data revealed significantly higher levels of SIL-2R in all leprosy patients, as compared to normal controls, with higher levels in the multibacillary groups as compared to the paucibacillary group. SIL-2Rs appeared higher in Type I upgrading reaction than in other forms of reaction, though this was not statistically significant.

There was no significant change in levels following treatment and clinical remission.

SHAW, M.A. et. al. Setting up HIV serology for the Karonga leprosy vaccine trial in Malawi. *Leprosy Review*, 62(1), p. 87-104, 1991.

As part of the leprosy vaccine trial taking place in Karonga District, Northern Malawi, it is essential to establish whether the presence of HIV infection in the population is affecting the incidence rate or clinical presentation of leprosy or the effectiveness of the trial vaccines. To obtain the appropriate information, a rapid and economical HIV testing protocol, which could be performed in a rural laboratory and would be robust under variable environmental conditions, had to be developed. This paper reports on the development/evaluation phase of a multitest protocol based on commercially available particle agglutination and ELISA anti-HIV antibody detection kits. The protocol was devised by first evaluating a range of kits in London using a battery of African and non-African sera and then field testing 1455 sera in Malawi, which included 184 sera from leprosy patients and 60 sera from syphilis patients to

check for cross-reactivity. According to the protocol developed, all sera are screened initially both by indirect ELISA (Organon) and using a rapid and economical modification of the Serodia particle agglutination test. Positives are retested using both a competitive ELISA (Wellcome or Behring) and the standard Serodia particle agglutination test. The validity of this multitest protocol was confirmed by Western blotting a large sample of the positive and negative Malawian sera in London. Factors affecting kit selection, and problems associated with individual kits, are discussed. While the specific multitest protocol developed for Malawi might not be suitable for every project, the principle of developing economical alternatives to Western blotting is an important consideration for any field investigation of HIV.

SINGH, N.B. et. al. Detection of *M. leprae*-specific Antigens with Dot-ELISA in Urine and Nasal Samples from Leprosy Patients. *Int.J.Lepr.*,59(3), p.396-404, 1991.

One-hundred-two urine and nasal samples collected from leprosy patients of different classifications of disease were studied for the presence of *Mycobacterium leprae* antigens, including phenolic glycolipid-I (PGL-I). Lipids were extracted from the urine samples, and nasal washings were concentrated and used as such in the dot-ELISA. Two types of primary antibodies, a polyclonal antibody obtained from lepromatous (LL) leprosy patients' pooled and absorbed sera and an anti-PGL-I monoclonal antibody, were used for the detection of *M. leprae* antigens from these samples. The polyclonal sera detected 23% to 36% of the paucibacillary (PB) and 100% of the multibacillary (MB) leprosy cases from the urine samples. Corresponding values for nasal detection were 0% to 18% for PB and 100% for MB cases. The monoclonal antibody against PGL-I could not detect tuberculoid (TT) leprosy cases. From the urine samples, however, 16% of the borderline tuberculoid (BT), 25% of the borderline (BB), 80% of the borderline lepromatous (BL), and 100% of the LL leprosy cases were detectable. It was interesting to note that PB, skin-smear negative cases were detectable from urine exam

[nation. The specificity and sensitivity of the test is discussed in relation to the crossreacting antigens.

SHROFF, K.E. et. al. Major Histocompatibility Complex Restriction of T-cell Suppression of Immune Response to Mycobacteria. *Int.J.Lepr.*,59(1), p.49-57, 1991.

In earlier work, intraperitoneal (i.p.) immunization with *Mycobacterium vaccae* was shown to generate a T-suppressor (Ts) response but intradermal (i.d.) immunization did not. We have now-studied the major histocompatibility complex (MHC) restriction of this Ts response. The ability of C57BU6 (H-2^b), BALB/c (H-2^d), and the (C57BU6 x BALB/c) F₁ mice to generate suppression after i.p. immunization with 10⁸ killed *M. vaccae* was investigated. The BALB/c and the F₁ mice generated suppression, but the C57BU6 mice failed to do so. The suppression could be ascribed to Lyt-2+, L3T4- antigen-specific T cells. The F₁ suppressors generated after i.p. immunization could suppress the generation of T-cell responses to i.d. immunization with *M. vaccae* in the parental BALB/c but not in the C57BU6 mice. Monoclonal anti-I-A antibody could suppress the antigen-induced proliferative response of mice primed i.d. with *M. vaccae*. In contrast, monoclonal anti-I-E antibody enhanced antigen-specific proliferation of spleen cells primed i.p. with *M. vaccae*. The suppressors generated by i.p. priming of mice with *M. vaccae* could also suppress the *in vitro* antigen-induced proliferative response of i.d.-primed spleen cells; the suppression could be blocked by anti-I-E antibody. Thus, the T-cell-mediated suppression in the above experimental model was I-E restricted. The inability of the C57BU6 mice to generate suppression after i.p. immunization with *M. vaccae* was ascribed to the lack of I-E expression by mice of H-2^b strain.

ULRICH, M. et. al. IgM Antibodies to Native Phenolic Glycolipid-I in Contacts of Leprosy Patients in Venezuela: Epidemiological Observations and a Prospective Study of the Risk of Leprosy. *Int.J.Leprosy*, 59(3), p. 405-415, 1991.

In a randomized, double-blind vaccine trial in Venezuela, about 29,000 contacts of leprosy patients have been vaccinated with either a mixture of heat-killed *Mycobacterium leprae* and BCG or BCG alone, and are being resurveyed annually to detect new cases of leprosy. All contacts had a serum sample collected at the time of entry into the trial, and 13,020 of these sera have been analyzed for antibodies to phenolic glycolipid-I (PGL-I). Antibody levels have been related to various characteristics of the contacts and to their risk of developing leprosy in the following 4 years. A strong association was found between PGL-I antibody level and the risk of developing leprosy, in spite of possible modification of the incidence rate induced by vaccination. Antibody levels were higher in females than in males, and declined progressively with age. Household contacts had higher levels than did nonhousehold contacts, and levels were higher in individuals from the state in Venezuela which has the highest incidence of the disease. No substantial differences were found in antibody levels between contacts of multibacillary and paucibacillary patients, which may in part reflect the influence of treatment, and there was no clear association with the presence of BCG or lepromin scars or with skin-test responses to PPD and leprosy soluble antigen.

The assay of antibodies to PGL-I seems unlikely to provide a sensitive or specific test for infection with *M. leprae* and measuring PGL-I antibody levels as a screening procedure to identify those at high risk of developing leprosy is unlikely to be particularly useful in most leprosy control programs. Such assays may be useful for the epidemiological monitoring of changes in the intensity of infection with *M. leprae* in a community and for the study of carefully defined groups of contacts during some phases of control programs.

CARTEL, J.L. et. al. Chemoprophylaxis of Leprosy with a Single Dose of 25 mg per kg Rifampin in the Southern Marquesas. Results after Four Years. *Int.J.Leprosy*, 60(3), p.416-420, 1992.

In January-February 1988, a program of chemoprophylaxis for leprosy, using a single 25 mg/kg dose of rifampin, was conducted among 2786 (98.7%) inhabitants of the Southern Marquesas and 3144 South Marquesan "emigrants" and their families. Among the treated population, during the 4 years which followed the implementation of the program, two leprosy patients were detected, one of whom can be considered as a failure of chemoprophylaxis because she was not known by the leprosy control unit. During the same period (1988-1991), a decrease in detection rates for leprosy in the entire French Polynesian population has been observed, an event which makes the interpretation of these findings very difficult. Nevertheless, according to presently available data, the effectiveness of chemoprophylaxis with a single dose of 25 mg/kg rifampin is estimated to be about 40% to 50%. When considering not only the results of the present study but also the financial and logistic constraints raised by such a program, one is led to the conclusion that chemoprophylaxis, even with a single dose of rifampin, is not likely to become an effective component of leprosy control programs.

CHANTEAU, S. et. al. Assessment of the Diagnostic Value of the Native PGLTB1 its Synthetic Neoglycoconjugate PGLTBO and the Sulfolipid IV Antigens for the Serodiagnosis of Tuberculosis. *Int.J.Leprosy*, 60(1), p.1-7, 1992.

A major phenolic glycolipid (PGLTB1) from *Mycobacterium tuberculosis*, that resembles the phenolic glycolipid-I (PGL-I) from *M. leprae*, and its synthetic terminal diglycosyl conjugate (PGLTBO) were reported and raised the prospects of a specific serodiagnostic test for tuberculosis (TB). The diagnostic use of a sulfolipid, namely the SLIV, was also reported. The objective of this investigation was to assess the relative sensitivity,

specificity, and predictive values of three ELISAs using the PGLTB1, the PGLTBO, and the SLIV as antigens for the serodiagnosis of TB. Similarly to leprosy patients for the PGL-I antigen, the TB patients responded preferentially in IgM against the phenolic glycolipid. We screened the sera from 191 active tuberculous patients, 29 healthy subjects living in France, 102 healthy Polynesian blood donors, 82 contacts of new TB patients, and 20 leprosy patients before treatment for IgG anti-SLIV, and for IgM anti-PGLTB1 and IgM anti-PGLTBO. TB patients showed significantly higher activity than did healthy Polynesians when tested against SLIV and PGLTBO, and the smear-positive group gave higher activity than did the smear-negative but culture-positive group, especially for IgG anti-SLIV. The leprosy patients did not show higher activity than the Polynesian controls. Respectively, for SLIV, PGLTB1 and PGLTBO antigens, the specificities were of 95%, 85%, and 89%; the sensitivities of 36%, 16% and 15%; the efficiencies of 58%, 40% and 39%; the predictive values for a positive result, assuming a prevalence of 15% among patients with respiratory symptoms, were of 30%, 16% and 19%.

CHATTER JEE, B.R. Leprosy immunopathogenesis and vaccine development. *Ind.J.Lepr.*,64(3), p.359-374, 1992.

The truly effective immunity against intracellular parasites, including mycobacteria, is mediated by monocyte/macrophages, and in the immunologically responding (resistant) host these phagocytes need minimal antigenic stimulus, specific or non-specific, to become activated and be microbicidal. T-cell mediated delayed hypersensitivity (DTH) causes tissue damage and destruction, which is particularly unwelcome in leprosy because of its nerve-damaging potential. Gamma interferon (INF- γ), the terminal lymphokine of a DTH response, promotes mycobacterial survival and growth. There are T-cells (TH1 subtypes) that produce DH response either Independent of, or, only partly dependent on INF- γ , this type of DH peaking at 24 hours appears similar to the Jones-Mote type rather than to the Tuberculin type of DTH peaking at 48-72 hours and is devoid of the

necrotic component of tuberculin type of DTH. *M. leprae* antigens normally elicit this Jones-Mote type of DH. Suppressor T-cells are associated with a protective immune response, while helper T- cells mediating DTH are harmful. In view of this immunobiology, it would appear that pathogenic mycobacteria that generate atuberculin type DTH response should not be used as immunogens in leprosy.

CHO, S.N. et. al. Prevalence of IgM antibodies to phenolic glycolipid I among household contacts and controls in Korea and the Philippines. *Lepr.Rev.*,63(1), p. 12-20, 1992.

Phenolic glycolipid I (PGL-I) is a *Mycobacterium leprae*-specific antigen and the antibodies to the antigen may suggest an *M. leprae* infection. To compare the *M. leprae* transmission among the populations, we compared the prevalence of anti-PGL-I IgM antibodies among household contacts and controls between Korea and the Philippines. In Korea (prevalence of leprosy 0.04:1000), the prevalence of anti-PGL-I antibodies were 4.8% among controls and 8% among contacts, respectively. On the other hand, the seroprevalence rate was 10.8% among controls and 13.4% among contacts in the Philippines (prevalence of leprosy - 0.70:1000). Interestingly, a marked difference was noted in the prevalence of anti-PGL-I antibodies among children between the countries; 10-14% among children under 10 years old and 15.18% among those aged between 10 and 19 in the Philippines compared to 0% and 2.9-6.4% in Korea, respectively. This study, therefore suggests that a high prevalence of anti-PGL-I IgM antibodies among children may indicate an active transmission of *M. leprae*, resulting in a higher incidence of leprosy in the population.

DAVID, H.L. et. al. Relationships Between Titers of Antibodies Immunoreacting Against Glycolipid Antigens from *Mycobacterium leprae* and *M.tuberculosis*, the Mitsuda and Mantoux Reactions, and Bacteriological Loads: Implications in the Pathogenesis, Epidemiology and Serodiagnosis of Leprosy and Tuberculosis. *Int J. Lepr.*,60(2), p.208-224, 1992.

Analysis of cell-mediated immunity [(CMI) as judged from the Mantoux, Fernandez, and Mitsuda reactions and the presence of granulomas in biopsy material] against humoral immunity (measurements of anti-PGL-I, PGL-Tb1, and SL-IV IgG and IgM antibody titers by ELISA) were performed in selected human populations. The investigations yielded data indicating that humoral (B-cell) responses preceded protective CMI in both tuberculosis and leprosy. The B-cell responses were unrelated to (unfavorable) cell-mediated delayed type hypersensitivity (DTH). Notwithstanding the difficulty inferring sequential events from studies in humans, it was shown that in humoral responses there was an initial rise of specific IgM immunoglobulins that switched afterward to IgG production during subclinical tuberculosis and leprosy infections. In patent tuberculosis disease the IgM-to-IgG switch was observed in the majority of patients; in patent leprosy disease the switch was impaired in the majority of patients. The clinical, immunological, and laboratory data indicated that the B-cell responses were suppressed as protective CMI was re-established in the patients during the protracted subclinical infection. According to the data, the diagnosis of subclinical tuberculosis and leprosy may be accomplished using ELISA. The yearly risk of tuberculosis in apparently healthy persons but with significant antibody titers was estimated at 44%; the yearly risk for leprosy has not yet been established. The clinical, epidemiologic, and diagnostic implications of these findings are discussed.

DOUGLAS, J.T. et. al. Evaluation of four semisynthetic *Mycobacterium leprae* antigens with sera from healthy populations in en-

demic and non-endemic areas. *Leprosy Review* 63(3), p. 199-210, 1992.

In order to determine the frequency of occurrence of antibodies to semisynthetic antigens of *Mycobacterium leprae* in clinically healthy nonpatient populations and to establish a 'baseline' for comparison with antibody frequencies in both patients with a history of leprosy and their contacts, ELISAs were conducted using representative sera from two areas: a leprosy endemic area, Cebu City, Philippines and a nonendemic area for leprosy Chicago, Illinois, USA. These sera were tested, by an indirect IgM ELISA, for the presence of antibodies reacting with four semisynthetic antigens based on the phenolic glycolipid I antigen of *M. leprae*: ND-O-BSA (natural disaccharide with octyl linkage to bovine serum albumin), NT-O-BSA (natural trisaccharide with octyl linkage to BSA), ND-P-BSA (natural disaccharide with phenolic ring linkage to BSA) and NT-P-BSA (natural trisaccharide with phenolic ring linkage to BSA). Using an OD reading ≥ 0.16 as positive, the antigen with the lowest background seroreactivity was ND-O-BSA, which reacted with 5/398 (1.3%) sera from Cebu, and 3/426 (0.7%) sera from Chicago. A total of 10 (2.5%) of 398 sera from the endemic area reacted with at least one antigen and 5 (1.3%) sera reacted with all four semisynthetic antigens. Of the 426 sera from Chicago, 12 (2.8%) were reactive with at least one antigen and 3 (0.7%) were reactive with all four semisynthetic antigens. Mean ELISA values for the 22 positive sera for each antigen ranged from 0.17 to 0.3 OD units, while the mean values for all sera in each area ranged from 0.01 to 0.04 OD units for all four antigens. Reactivity of 14 of the positive sera to some antigens, but not all four semisynthetic antigens, indicated that the carrier and linker arms might be associated with this background reactivity. Investigation of alternative linker arms and carriers is warranted. We conclude that nonspecific background reactivity to the semisynthetic antigens representing the PG-I molecule of *M. leprae* is 0.7-1.3%, based on a > 0.16 OD cutoff value. From these data it was concluded that reactivity in individuals free of leprosy was low enough to warrant use of these antigens in a diagnostic setting, such as screening

household contacts and highly endemic populations. When incidence and prevalence of leprosy are low, testing with these antigens would not be cost effective, unless applied to high risk individuals. Serological screening with these antigens might be useful in detecting and differentiating bacteriological relapse, type 1 or 2 reactions, early detection of leprosy, and monitoring treatment in endemic areas.

GULLE, H. et. al. T-Cell Responses of Leprosy Patients and Healthy Contacts Toward Separated Protein Antigens of *Mycobacterium leprae*. *Int.J.Lepr.*, 60(1), p.44-53, 1992.

Sonicated extracts of *Mycobacterium leprae* were separated by two-dimensional gel electrophoresis and electroeluted into 400 distinct soluble fractions. These fractions were probed with T lymphocytes from leprosy patients of different disease types, healthy contacts, and unexposed healthy individuals: Proliferative responses were visualized using three-dimensional stimulation profiles. T cells from many patients and contacts responded to a multitude of antigen fractions of different molecular masses and isoelectric points. T cells from unexposed individuals gave significant responses to lysates or whole organisms of *M. leprae*, but no or only marginal responses to separated antigen fractions. T cells of polar tuberculoid (TT) and the majority of polar lepromatous (LL) leprosy patients responded only to separated antigen fractions but not to lysates or whole organisms of *M. leprae*. The remaining LL patients were totally unresponsive and even failed to respond to separated *M. leprae* fractions. Thus, in some leprosy patients unresponsiveness to *M. leprae* seems to be caused by distinct components and can be broken by using separated antigen fractions; whereas in others, anergy remains. T cells of borderline tuberculoid (BT) patients, who were under chemotherapy, responded to separated antigen fractions as well as to lysates of *M. leprae* organisms. In contrast, BT patients who were untreated failed to react with any of the *M. leprae* preparations. Similarly, T cells of the majority of

LL patients responding to separated fractions were under chemotherapy; whereas T cells from untreated LL patients gave no or only marginal responses to any of the *M. leprae* antigen preparations. These findings suggest some linkage between the degree of T-cell responsiveness and antileprosy drug treatment.

GUPTE, M.D. et. al. Effect of Skin Test with *M. leprae* Soluble Antigen on Reaction to a Subsequent Test with the Same Antigen. *Int J.Lepr.*, 60(1), p.54-60, 1992.

Soluble skin-test antigens (STA), produced from armadillo-derived *Mycobacterium leprae* by Drs. Rees and Convit, were expected to meet the long-felt need of a test for leprosy infection and also to serve as tests for measuring postvaccination sensitization induced by vaccine preparations against leprosy. The present paper reports results from two studies examining the influence, if any, of skin testing with Rees' STA on reaction to a subsequent test with the same antigen.

In the first study, 2168 persons from households of leprosy patients and from neighboring households were skin tested with Rees' STA twice at an interval of 6 months. In the second study, 1700 persons, free from leprosy, received either Rees' STA or normal saline by random allocation. A random subset of 850 persons was tested with Rees' STA after 3 months. The remaining 850 persons were tested with Rees' STA after 6 months. In addition, 242 leprosy patients were given Rees' STA or normal saline by random allocation, and all of these patients were tested with Rees' STA after 6 months.

The results of the two studies showed that among persons reacting with a small size of reaction to Rees' STA, the size of the reaction to the repeat test was significantly larger. However, from the results of the second study, which included a control group, it was clearly seen that the quantum of boosting or sensitizing effect of the first test as well as that of new sensitization was small over a period of 3-6 months. Thus, the significant increase in reaction size to the second test among those with a small-size reaction to the

first test was mostly due to the design effect and was not attributable to the STA.

In view of the finding that even without any intervention, reactions to a repeat test would be much larger among those with a small-size reaction to the first test, it becomes important while designing studies for measuring postvaccination sensitivity that provision be made for a control group to ensure a direct measure of the effect of a vaccine.

GUPTA, M.D. et. al. Sensitization Potential and Reactogenicity of BCG with and without Various Doses of Killed *Mycobacterium leprae*. *Int.J.Lepr.*, 60(3), p.340-352,1992.

A study was conducted in 997 individuals in two villages in south India to find the acceptability and sensitizing effect of the antileprosy combination vaccine of BCG plus killed *Mycobacterium leprae* (KML). Three preparations of the combination, BCG 0.1 mg + 6 x 10⁸ KML (I), BCG 0.1 mg + 5 x 10⁷ KML (II), and BCG 0.1 mg + 5 x 10⁶ KML (III), along with BCG 0.1 mg (IV), and normal saline (V), were used in the study. Each individual received one of the above five preparations by random allocation. They were also tested with Rees' M. leprae soluble skin-test antigen (MLSA) and lepromin-A, both at intake and 12 weeks after vaccination. Reactions to Rees' MLSA were measured after 48 hr, those to lepromin-A after 48 hr and 3 weeks. The character and size of the local response at the vaccination site were recorded at 3, 8, 12, 15, and 27 weeks after vaccination.

The mean sizes of postvaccination sensitization to both Rees' MLSA and lepromin A in the vaccine groups were significantly larger than those in the normal saline group, clearly demonstrating the ability of the vaccines to induce sensitization as measured by responses to the two skin tests. The sensitizing effect was the highest following vaccination with vaccine I. It was not significantly different for vaccines II, III, and IV, although, generally, a dose-response effect was observed. The sensitizing effect attributable to the vaccine was more clearly seen in children than in adults. The above conclusions

were the same irrespective of which results were considered, reactions to Rees' MLSA or Fernandez or Mitsuda reactions to lepromin-A. A significant finding of the study was that at intake the Mitsuda reactions provided a measure of sensitizing effect due to vaccine

The healing of vaccination lesions was uneventful. In more than 90% of vaccinated individuals, the lesions had healed by the 12th week in vaccine groups II, III, and IV, and by the 15th week in vaccine group I. The results showed that vaccination with BCG or combination vaccines was equally safe in individuals with or without previous BCG scars: Thirteen persons, aged 10 years or older, developed suppurative lymphadenitis around the 8th week (7 in vaccine group I, 3 each in vaccine groups II and III). However, healing was prompt after drainage in these individuals.

HUSSAIN, R. et. al. Recognition of *Mycobacterium leprae*. Recombinant 18-kDa Proteins in Leprosy. *Int. J.Lepr.*, 60(3), p. 368-375, 1992.

Three different, purified, *Escherichia coli* derived, recombinant preparations of the *Mycobacterium leprae* 18K protein were compared for their immunological recognition in leprosy. The preparations tested were 18K fusion proteins containing 70% (amino acids 38-148) of the full 18K protein fused to either a short leader sequence containing six asparagine residues or to B galactosidase, and the full length 18K protein. All three recombinant antigens were recognized by IgG antibodies which were restricted mostly to lepomatous leprosy patients. The 18K antigen with the asparagine leader sequence showed better reactivity with IgG antibodies compared with the other two 18K preparations. In lymphocyte proliferation assays, the truncated 18K and the full-length 18K showed equivalent responses in the same donors with strongest recognition in donors who were also strongly responsive to the M. leprae soluble sonicate. These results indicate that the major human B- and T-cell epitopes are located within the segment 38-148, although some individuals may recognize additional epitopes at the NH₂-terminal end.

KHAN, M.B. et. al. Sero-Immunoreactivity of Cloned Protein Antigens of *Mycobacterium leprae*. *Int.J.Lepr.*, 60(2), p.195-200, 1992.

Sera from 173 leprosy patients with various types of disease (tuberculoid=TT, borderline tuberculoid=BT, borderline lepromatous=BL, and lepromatous=LL), 12 intrafamilial contacts, and 40 normal healthy individuals were assayed in an indirect enzyme-linked immunosorbent assay (ELISA) using *Mycobacterium leprae* antigens. Recombinant clones carrying *M. leprae* antigens, namely, Y3184 (12 kDa), Y3179 (18 kDa), Y3164 (28 kDa), Y3180 (36 kDa), and Y3178 (65 kDa) and a cell sonicate from armadillo-derived *M. leprae* were used for the study. A high degree of reactivity with the 65-kDa, 36-kDa, and 28-kDa protein lysates was observed in most of the sera from multibacillary patients, with a low degree of positivity with 18 kDa and 12kDa. Only a few sera from paucibacillary patients showed positive reactions. The majority of the contact's sera tested showed no reactivity with these antigens.

KANCHANA, M.V. et. al. An appraisal of enzyme linked immunosorbent assay (ELISA) and serum antibody competition test (SACI) in leprosy. *Ind.J.Lepr.*, 64(1), p. 42-50, 1992.

Seventy-eight untreated leprosy patients, 104 treated patients and 105 healthy contacts were tested using two serological tests, SACT (serum antibody competition test based on competitive inhibition of monoclonal antibody binding to the MY2a determinant of *M.leprae*) and ELISA (measurement of IgM antibodies to the neoglycoproteins D-BSA and ND-BSA representing the phenolic-glycolipid antigen of *M. leprae*). The controls included normal healthy individuals, patients with sputum positive pulmonary tuberculosis, and active cases of rheumatoid arthritis from the department of rheumatology. The specificity of SACT was found to be very high. ELISA was found to be positive in two patients with rheumatoid arthritis, one each for D-BSA and ND-BSA ELISA.

Both tests had a high sensitivity in BL and lepromatous patients. The sensitivity to both

tests was considerably lower in tuberculoid and BT patients i.e., below 40%. Therefore the diagnostic value of a negative test in suspected cases of leprosy was very low employing either of the two tests. A proportion of patients with paucibacillary tuberculoid and BT leprosy were positive after six months or longer after therapy. Similarly a large number of BL and lepromatous patients were positive after considerable longer periods of treatment. The use of either tests for determining the duration of therapy is therefore limited. SACI appears to be more sensitive than ELISA with ND- BSA in detecting subclinical infection. The cumulative positivity of the two tests may be used as a measure of the infectivity of the disease in the community and for evaluating disease control methods.

KAR, H.K. et. al. Induction of lepromin positivity by a candidate anti-leprosy vaccine mycobacterium w in lepromin negative healthy contacts of multibacillary leprosy patients. *Ind.J.Lepr.*, 64(4), p. 495-500, 1992.

In a hospital based study, 362 household contacts of multibacillary leprosy patients were screened for evidence of leprosy and 54 (14.9%) were found to be having leprosy. The remaining 308 apparently healthy contacts were lepromin tested and 109 (35.4%) were observed to be negative to Mitsuda lepromin. M.w vaccine was administered intradermally to 95 of these 109 lepromin negative contacts. Sixty eight of them could be retested for lepromin A reactivity. Fifty six (82.35%) manifested lepromin conversion. The twelve subjects who did not show lepromin conversion, received a second dose of the vaccine, and eleven subsequently became lepromin positive. The overall lepromin conversion rate was thus 98.5% (67 out of 68). Follow-up of these contacts upto a period of 30 months did not demonstrate reversion of lepromin positivity back to negativity status. No untoward effects of vaccination were observed except for local ulceration at the site of vaccine administration.

KASHYAP, A. et. al. Delayed Clearance of Circulating Immune Complexes in Mice Following Administration of Antileprosy Drugs. *Int.J.Lepr.*, 60(3), p.404-409, 1992.

In this report we describe an animal experiment which showed delayed clearance of preformed α -I-HSA-anti-HSA immune complexes (with five times excess HSA) from the circulation of mice treated with antileprosy drugs (dapson, ciprofloxacin, and rifampin - multidrug therapy for 7 days) in comparison with normal (untreated) mice. The results also showed delayed retention of the preformed immune complexes in the spleen and kidneys of the antileprosy-drug-treated animals. The exact mechanism of the delayed handling of preformed immune complexes in mice fed antileprosy drugs could not be ascertained. However, in light of the anticomplementary effects of ciprofloxacin and dapson, as reported earlier, and in light of the large accumulation of ciprofloxacin and rifampin in macrophages, it has been postulated that in the drug-fed animals either the immune complexes could not be phagocytosed by macrophages, through the avenue of their C3b receptors, or the immune complexes could not be downgraded easily within the macrophages overloaded with ciprofloxacin and rifampin. These results might have clinical significance and might throw some light on the prolonged persistence of circulating immune complexes in the vascular bed of lepromatous patients even after clinical remission of *erythema nodosum leprosum*.

LASZLO, A. et. al. Comparison of Bisdi-*octadecylamide* of Trehalose Dicarboxylic Acid (BDA-TDA) with Glycolipid SL-IV as ELISA Antigens for the Serodiagnosis of Leprosy. *Int.J.Lepr.*, 60(3), p. 376-381, 1992.

Two glycolipids-one synthetic and nonnatural (BDA.TDA), the other natural and *Mycobacterium tuberculosis species-specific* (SL-IV) - were tested to determine their serological activity in sera obtained from leprosy patients, and to determine their discriminating ability in the

detection of disease. The ELISA results obtained in the IgG antibody class show that both were useful substances capable of detecting multibacillary and paucibacillary disease in about 2 out of 3 leprosy patients. When these antigens were tested in parallel, the sensitivity of the ELISA test was increased by 10% without a decrease in specificity.

LAUNOIS, P. et. al. Human Phagocyte Respiratory Burst by *Mycobacterium bovis* BCG and *M. leprae*: Functional Activation by BCG is mediated by Complement and its Receptors on monocytes. *Int.J.Lepr.*, 60(2), p. 225-233, 1992.

We have measured the role of serum components on two parameters of the phagocytosis reaction: a) the chemiluminescence (CL) response associated with the oxidative respiratory burst in response to *Mycobacterium bovis* BCG and *M. leprae*, and b) the uptake of these two mycobacteria by healthy human monocytes. Pre-incubations of fresh or heat-inactivated serum or serum containing EGTA or EDTA indicate that these two mycobacteria activate the alternative complement pathway. Monoclonal antibodies against CR 1 and CR3 inhibit the responses of *M. bovis* BCG and *M. leprae*, demonstrating that complement receptors mediate the phagocytosis of these two mycobacteria. Thus, complement and its receptors on the surface of the monocytes (CR 1 and CR3) are important in the functional activation of phagocytosis of *M. bovis* BCG and *M. leprae*.

MAHAJAN, P. et. al. Gelatin particle agglutination assay to detect anti-PGL-I antibodies in leprosy patients and in household contacts: A preliminary study. *Ind.J.Lepr.*, 64(4), p. 461-467, 1992.

A preliminary study of anti-phenolic glycolipid-I (PGL-I) IgM antibody detection using *M. leprae* gelatin particle agglutination (MLPA) test kit is described. Antibodies were demonstrated in 70% of our leprosy patients taking antileprosy treatment. The percentage of positivity of

multibacillary cases was 86.0, whereas that of paucibacillary cases was 30.0. Good correlation was found between bacteriological index and the presence of antibodies. Antibodies were detected in 28% of our patients released from treatment. Fourteen out of 27 household contacts were found to have antibodies but none of the normal controls were seropositive. These preliminary data demonstrate that MLPA test is not applicable as sero-diagnostic test or as a test of cure, but may be useful for epidemiological studies and as a research tool.

MULLINS, R.J. et. al. Serological Response to Purified Mycobacterial Phosphatidylinositol Mannoside in Healthy Controls and In Patients with Tuberculosis and Leprosy. *Int.J.Leprosy.* 60(3), p. 353-367, 1992.

The serological response to a monoclonal antibody-defined phosphatidylinositol mannoside (L4-PIM) present in all mycobacteria was examined in patients with various mycobacterial diseases and healthy subjects from different populations. IgG but not IgM antibodies were detected in most patients with untreated lepromatous (84%) or borderline lepromatous (65%) leprosy, but in only a minority of those with disease at the tuberculoid end of the leprosy spectrum (<17% positive). The response to L4PIM was correlated with the IgM response to disaccharide octyl-bovine serum albumin (dBSA), and decreased with successful treatment. On the other hand, the test proved to be of little value in the diagnosis of untreated tuberculosis (4/15 positive) or atypical mycobacterial infection in patients with AIDS (0/11 positive). IgG antibodies to L4PIM were also found in a significant proportion of healthy individuals, irrespective of their Mantoux status. These antibodies were shown to be specific for L4-PIM on immunoblotting, and their incidence increased with age in random donors from both urban Australia and rural Papua New Guinea. Despite the limited value of the assay in diagnosis of any particular mycobacterial disease, the presence of antibodies to L4-PIM appears to be a sensitive indicator of subclinical infection with environmental mycobacteria. In subjects with an

Intact immune system.

NAVALKAR, R.G. et. al. Enzyme Linked immunosorbent Assay of 12-kDa Protein of *Mycobacterium leprae* with Sera from Leprosy Patients. *Int.J.Leprosy.*, 60(3), p. 382-389, 1992.

A low molecular weight protein was obtained from a sonicate of armadillo-derived *Mycobacterium leprae* cells and from a λ gt11 phage lysate of *Escherichia coli* (specifying the *M. leprae* 12-kDa protein) by a single step of ultrafiltration. Both proteins had an approximate molecularweight of about 12,000 (by SDS-PAGE) and were recognized by the *M. leprae* 12-kDa-specific monoclonal antibody ML06 by immunoblotting. Sera from 79 leprosy patients across the clinical spectrum, 17 contacts, and 12 normal healthy individuals were screened in an enzyme-linked immunosorbent assay (ELISA) using the 12-kDa proteins as the antigens. Antibodies to the 12-kDa protein (from lysate as well as sonicate) were detected in patients' sera across the clinical spectrum (44% - 100% positivity), while no detectable reactivity was observed with control or contact sera. Sera from patients who had undergone a year or more of chemotherapy exhibited no reactivity compared to those from patients with only 3-6 months of chemotherapy. The 12-kDa proteins were also recognized by rabbit hyperimmune *M. leprae* antiserum.

REDDY, B.S.N. et. ai. Utility of gelatin particle agglutination test (MLPA) for rapid serodiagnosis of leprosy in a hyperendemic area. *Ind.J.Leprosy.*, 64(4), p. 469-474, 1992.

The anti-PGL *M. leprae* specific antibodies were estimated by MLPA test. In 79 patients of leprosy, 8 contacts of lepromatous cases and 10 healthy controls in a hyperendemic area. The results indicated an overall seropositivity of 50.6% in leprosy patients. Three of the eight contacts and five of the controls also gave positive results. Higher seropositivity rates were noted in multibacillary patients (73% in lepromatous, 53.6%

in borderline, 40% each in tuberculoid and Indeterminate and 10% in pure neuritic types). The practical application of MLPA test in its present form as a serodiagnostic procedure for screening subclinical or clinical infections in leprosy patients appear to be of limited value in hyperendemic areas. Further studies involving large series of subjects are necessary for reaching definite conclusions.

ROCHE, P.W. et. al. Antibody Responses to the 18-kDa Protein of *Mycobacterium leprae* in Leprosy and Tuberculosis Patients. *Int.J.Lepr.*, 60(2), p. 201-207, 1992.

The 18-kDa protein of *Mycobacterium leprae*, as recognized by the monoclonal antibody L5, has a restricted species distribution, being confined to *M. leprae* and *M. habana*. We have developed a solid-phase ELISA using purified, recombinant *M. leprae* 18-kDa protein and compared the serological responses of Nepali leprosy and tuberculosis patients and endemic control subjects to the protein and the *M. leprae* phenolic glycolipid-I (PGL-I). Few control subjects had anti-18-kDa antibodies. A small proportion of paucibacillary (PB) leprosy and 42% of multibacillary (MB) leprosy patients had IgG anti-*M. leprae* antibodies. A similar proportion (47%) of Nepali tuberculosis (TB) patients were seropositive, and IgG anti-18-kDa antibody levels were significantly higher in MB and TB patients than in control subjects. By comparison, IgM anti-PGL-I antibodies were detected in 88% of MB leprosy patients and only 7% of TB patients. The possible reasons for the 18-kDa protein seroreactivity in TB patients are discussed, and the anti-18-kDa assay is compared with other antibody assays for protein and nonprotein antigens of *M. leprae*. It is concluded that the sensitivity and specificity of the anti-*M. leprae* 18-kDa ELISA are insufficient for the assay to be of clinical utility in leprosy patients.

ROCHE, P.W. et. al. Cellular Immune Responses to Mycobacterial Heat Shock Proteins in Nepali Leprosy Patients and Controls.

Int.J.Lepr. 60(1), p. 36-43, 1992.

Sixty-three leprosy patients, representing the entire leprosy spectrum from tuberculoid to lepromatous disease, and 17 healthy Nepali subjects were tested for their T-cell responses to the purified p65 and p70 protein antigens of *Mycobacterium bovis* BCG using a lymphocyte proliferative assay. There was strong correlation between the responses to BCG and *M. leprae* and the responses to the two antigens. Patients and controls lacking a response to either of the whole cell preparations failed to respond to the purified antigens, while BCG responders at the lepromatous pole of the disease did mount a response to both antigens. Significant differences in the magnitude of the responses to these antigens were obtained between controls and the disease groups. In individual subjects, responses to the two antigens were significantly correlated to each other.

RODRIGUES, M.L.O. et. al. Protective Effect of Intradermal BCG Against Leprosy; a Case-control Study in Central Brazil. *Int.J.Lepr.*, 60(3), p. 335-339, 1992.

A case-control study was undertaken to evaluate the protective efficacy of intradermal BCG against leprosy in a high-endemic area of leprosy in central Brazil. Sixty-two cases and 186 controls were included in the study. Cases were all newly diagnosed leprosy patients under 16 years of age attending an outpatient health service, and all of them were schoolchildren. Three controls under 16 years old, frequency matched by sex and age group, were selected from schools geographically located in the area from which the cases came. The presence of BCG was negatively associated with leprosy, indicating a 5.3 risk of leprosy for those nonvaccinated and protective efficacy of 81%. Paucibacillary patients were more likely to have a BCG scar than multibacillary patients.

SEKAR, B. & ANANDAN, D. Evaluation of *Mycobacterium leprae* particle agglutination test, using eluates of filter paper blood spots. *Leprosy Review* 63(2), p. 117-124, 1992.

A comparison of the ELISA test with newly-developed MLPA test was carried out, using eluates of blood spots from filter paper for the detection of the anti-PGL-I antibody. A very good positive correlation was observed between these two tests. The concordance rate was found to be 92.6%, ranging from 71.4% to 100%. This nonconcordance was not found when freshly-collected samples were used. The MLPA test is simple and reliable. The use of eluates from bloods spots collected on filter paper further simplifies the test in the collection and transportation of blood samples. This accurate and rapid method makes the MLPA test logistically feasible for large-scale screening. With our modification of MLPA with eluates more samples can be screened with the kit than with sera.

SHARMA, V.K. et. al. Detection of a *Mycobacterium leprae* cell wall antigen in the urine of untreated and treated patients. *Lepr. Rev.*, 63(1), p. 28-35, 1992.

A total of 90 leprosy patients, 12 household contacts and 10 normal subjects were studied for the detection of *Mycobacterium leprae* cell wall antigen in urine using monoclonal antibody (ML30A₂IgG). In untreated multibacillary leprosy (BL-LL) the *M. leprae* cell wall antigen could be demonstrated in the urine of 14 (64%) patients by immunofluorescence (IF) and 22 (100%) by ELISA. In untreated paucibacillary leprosy (TT-BT), it could be demonstrated in 3 (11.5%) and in 13 (50%) patients by IF and ELISA methods respectively. All but 1 household contact (later confirmed to have BL leprosy) and all 10 normal subjects'urine was negative for *M. leprae* cell wall antigen by both methods. The same antigen was, however, demonstrated in urine of 50% paucibacillary patients who had received 6 months of treatment and in 68% multibacillary patients who had received 24 months of WHO

recommended multidrug therapy. *M. leprae* cell wall antigen assays in urine will not be useful in the follow-up of leprosy patients on multidrug therapy.

SINHA, S. et. al. Analysis of Circulating Immune Complexes from Leprosy Patients for *Mycobacterium leprae* Antigens. *Int.J.Lep.*, 60(3), p. 396-403, 1992.

Circulating immune complexes (CICs) from 31 leprosy patients (16 tuberculoid, 15 lepromatous) and 12 healthy volunteers precipitated by 3.5% polyethylene glycol, were individually subjected to SDS-PAGE and immunoblotting using a variety of monoclonal and polyclonal antibodies against *Mycobacterium leprae*. A common mycobacterial antigen of an apparent molecular size of 65 kDa was identified in CICs from about 40% of the patients. No correlation was observed between the positivity for this antigen and any of the following parameters: bacterial index, *M. leprae*-specific antibody titers, motor nerve involvement, duration of disease or treatment. Nevertheless, patients with a relatively recent and massive infection were more frequently positive for antigen than the others.

S. RADA, E.M. et. al. Preliminary Study of Cellular Immunity to *Mycobacterium leprae* Protein in Contacts and Leprosy Patients. *Int.J.Lep.*, 60(2), p. 189-194, 1992.

Because of the good results obtained in the mononuclear cell (T lymphocyte) proliferative response in tuberculoid leprosy patients and family contacts and healthy Mitsuda-positive volunteers using *Mycobacterium leprae* soluble extract, we prepared different protein fractions from the soluble extract. We used the T-cell Western blot technique with separation by electrophoresis in SDS-polyacrylamide gels and transfer onto nitrocellulose membranes. Each unstained blot was converted into 18 fractions of antigen-bearing particles and tested with peripheral blood mononuclear cells from 21 individuals including Mitsuda - positive contacts, vaccinated

lepomatous leprosy (LL) patients, borderline tuberculoid (BT) patients, and unvaccinated lepomatous patients. The simulation index (SI) of the contacts was higher to the different fractions in comparison with the leprosy patients. They showed four peaks of stimulation to fractions 66-55, 45-29, 22-18, and 14 kDa. The second highest responders were BT patients, followed by vaccinated LL patients. The unvaccinated patients did not respond significantly to any of the fractions (SI<1).

MICROBIOLOGIA

BASKIN, G.B. et. al. Pathology of Dual *Mycobacterium leprae* and Simian Immunodeficiency Virus Infection in Rhesus Monkeys. *Int.J.Lepr.*, 58(2), p. 358-364, 1990.

Three rhesus monkeys were experimentally inoculated with sooty-mangabey-derived *Mycobacterium leprae* and were inadvertently infected with the simian immunodeficiency virus (SIV) as well. They died of an immunodeficiency syndrome, and at autopsy all had lesions caused by *M. leprae*. One monkey was inoculated twice with *M. leprae*, initially with an inoculum from a sooty mangabey that was not infected with SIV and, subsequently, with an inoculum from a mangabey that was SIV infected. The monkey did not develop clinical lesions and became strongly lepromin skin test (LST) positive after the first inoculation, but became infected with both agents and LST negative following the second inoculation. These observations suggest that SIV-infected rhesus monkeys have an increased susceptibility to *M. leprae* infection and, by analogy, imply that HIV-infected human beings may have an increased susceptibility as well.

BHATIA, V.N. et. al. Some observations on skin smear examination. *Int.J.Lepr.*, 62(3), p. 338-345, 1990.

40 slit nad scrape smears in a planned study and 35 routine smears picked up from the laboratory were examined. An end-to-end examination of the smears detected additional positives and gave a higher bacterial index than what was reported in the routine. Acid-fast bacilli were found to be distributed in only 1 to 3 per cent of the fields in the smears. The bacilli were found mostly in the centre and in narrow bands between centre and periphery of the smears. Some of the high BI smears were found to contain areas completely free from bacilli.

CHAKRABARTY, A.N. et. al. Cultivation in vitro of acid-fast nocardioform chemo-autotrophic bacteria from mouse foot-pads infected with human strain of leprosy bacillus. *Ind.J.Lepr.*, 62(2), p. 169-179, 1990.

Four acid-fast nocardioform bacteria could be isolated and cultivated as pure cultures in vitro from mouse foot-pads (MFP), which were infected with serially passaged strains of human leprosy bacillus; the liquid mineral medium, such as paraffin urea minimal (PUM), paraffin gelatin minimal (PGM), gelatin minimal (GM), and GM agar (GMA) slants containing only simple sources of C and N were used, just like the human and the armadillo isolates of these organisms reported earlier. Morphologically, metabolically and enzymologically, these were closely related to the previous ones and were also chemoautotrophic in nature. Serologically there appears to be a heterogeneity in these isolates, i.e., some of them showing higher affinity to nocardio forms while others showing significant binding to several mycobacteria. Normal (uninfected) mouse foot-pad harvests were not found to harbour such organisms.

IBRAHIM, M.A. et. al. Analysis of Variation in Batches of Armadillo-derived *Mycobacterium leprae* by Immunoblotting. *Int.J.Lepr.*, 58(1), p. 73-77, 1990.

Several batches of cell-free extracts of armadillo-derived *Mycobacterium leprae* were

analyzed by SDS-PAGE and by immunoblotting with monoclonal antibodies. The presence or absence of protease inhibitors had a profound effect on the protein antigens, particularly the 65-kDa antigen. In the absence of protease inhibitors, there were both quantitative and qualitative differences between the different batches of *M. leprae* extracts.

KAZDA, J. et. al. Acid-Fast Bacilli Found in Sphagnum Vegetation of Coastal Norway Containing *Mycobacterium leprae*-specific Phenolic Glycolipid-I. *Int.J.Lepr.*, 58(2), p. 353-357, 1990.

In the grey layer of sphagnum vegetation originating from the former leprosy-endemic regions of coastal Norway, acid-fast bacilli (AFB) containing *Mycobacterium leprae*-specific phenolic glycolipid (PGL-I) on the surface have been found. These AFB survived in foot pads of nude mice with multiplication but without swelling. This contrasts to experimental leprosy with clinically derived *M. leprae* where swelling and unlimited multiplication takes place. The naturally occurring AFB may be of a lower pathogenicity than *M. leprae* obtained from clinical cases. The possibility of *M. leprae* surviving in sphagnum vegetation was assessed by inoculation of clinically derived *M. leprae* into the grey layer of the sphagnum. It multiplied more than tenfold and retained its pathogenicity in nude mice for 16 weeks, the duration of the experiment. The lack of pathogenicity of sphagnum-derived, *M. leprae*-like mycobacteria may be relevant to the decline of leprosy in Norway.

PAL, D. et. al. Is leprosy bacillus a chemoautotrophic nocardioform organism? *Ind.J.Lepr.*, 62(3), p. 351-357, 1990.

Numerous attempts at in vitro cultivation of the leprosy bacillus have all proved to be unsuccessful. Recently, we have repeatedly isolated chemo-autotrophic nocardioform (CAN) organisms in pure culture from multibacillary cases of leprosy. We find that these resemble the lep-

rosy bacillus in many respects and suggest that the leprosy bacillus may be closer to the genus *Nocardia* than to *Mycobacterium*, and that it may be a chemoautotroph, requiring only simple sources of carbon and nitrogen for its growth. This is in contrast to most other human pathogens, which are heterotrophs requiring complex sources of carbon and nitrogen for their growth. This could offer a possible explanation for the repeated failure at in vitro cultivation of the leprosy bacillus.

SILBAQ, F. et. al. The Disease of CBA and BALB/c Mice that Follows Inoculation of a small Number of *Mycobacterium lepraemurium* into the Hind Foot Pad. *Int.J.Lepr.*, 58(4), p. 681-689, 1990.

To learn if the lack of an immune response in mice infected with *Mycobacterium lepraemurium* (MLM) was a consequence of the organisms, we studied the disease that followed inoculation of 5 5000 organisms into the hind foot pads of CBA and BALB/c mice. The mice of both strains demonstrated a rapid increase of bacterial numbers soon after inoculation, with a slowing of the rate of multiplication once the number of organisms per foot pad passed 3×10^7 . By 1 year after inoculation, the numbers of organisms had reached levels $>10^{11}$ in the spleen and liver, and $>10^8$ in the femoral bone marrow. In mice that had been inoculated with as few as 5 MLM or 50 MLM, the organisms had multiplied to numbers $>10^8$ in the foot pads and to $>10^9$ in the spleens, suggesting that the ID^{50} of viable MLM may be <5 organisms per foot pad. No protection against superinfection could be demonstrated. On the other hand, initial multiplication of MLM in the foot pads was followed virtually immediately by the death of at least 97% of the organisms.

ABRAHAM, B. & CARIAPPA, A. Inter and Intra-Laboratory Variation in the Reporting of Skin Smears in Leprosy. *Int.J.Lepr.*, 59(1), p. 76-81, 1991.

This paper defines the variations in the reporting of skin smears between a base and field

laboratory in a leprosy control program. Ten percent of all slides read by the field laboratory in a control area were re-read by the base laboratory. There was almost no variations in the reporting of negative slides, but a variation of 1 + was present in approximately 92% of positive slides. Thus, there was agreement in approximately 8% of positive slides. This paper also defines the variations in the reporting of positive slides under "ideal" conditions by describing the results of a study on intraand inter-observer variations among technicians at the base laboratory. There was between 45% and 55% agreement within observers and about 36% agreement between observers. The results of both studies are compared. Simple guidelines are derived to monitor the reporting of skin smears in leprosy control programs.

BANERJEE, Rita et. al. Transmission of viable *Mycobacterium leprae* by *Aedes aegypti* from lepromatous leprosy patients to the skin of mice through interrupted feeding. *Leprosy Review*, 62(1), p. 21-26, 1991.

Female *Aedes aegypti* which took partial blood meals from the skin lesions of untreated lepromatous leprosy (LL) patients were then allowed to continue feeding on 72-96-hr-old Swiss albino suckling mice (Rockefeller strain). The bitten portion of skin was removed, divided into two parts and processed for the extraction of bacilli by two different methods using chloroform and petroleum ether. The proboscis of some of the fed mosquitoes was dissected out and examined for viable bacilli (stained by fluorescein diacetate and ethidium bromide) and acid-fast bacilli (AFB). Out of 50 proboscis dissected 45 were found positive for AFB, with bacillary counts ranging up to 246 (average $40.20 \pm SD 41.80$) per proboscis. The average percentage of viable bacilli (green solid) in the proboscis immediately after feeding on LL patients was 43.90 and thereafter it decreased gradually to 3 on the seventh day. In the petroleum ether extract of mouse skin viable bacilli were observed in numbers up to 37 (average $15.25 \pm SD 10.25$) per smear. The number of fluorescing bacilli (green and red) corre-

lated with the total number of AFB.

HEYING, W. et. al. The susceptibility testing of 13 strains of *Mycobacterium leprae* to rifampicin and the determination of minimal effective dosage. *Leprosy Review*, 62(3), p.276-279, 1991.

By use of the mouse footpad technique, the susceptibility testing of 13 strains of *Mycobacterium leprae* to rifampicin (RFP) and the determination of minimal effective dosage (MED) were carried out. Among these strains of *M. leprae*, 8 were obtained from previously untreated multibacillary leprosy patients and 5 from relapsed leprosy patients and 5 from relapsed leprosy patients without using RFP previously. The results showed that the MED of all strains to RFP were 5 0.001% FRP in the diet, 5 strains being equal to 0.001%, 5 < 0.0001%, 2 > 0.0003% and 1 < 0.0003%. The results indicated that the MED value of RFP could be lower than that of other reports. Because the critical concentration of RFP for assessment of RFP resistant strains is not well established a further study would be worthwhile. The results of the determination of sera RFP concentration in mice administered the RFP diet were identical with that of Holmes' report. Five of the 13 strains also showed that the growth of bacilli were suppressed by 10 mg/kg RFP using the gavage method.

JAYAPAL, V. et. al. Fluorescein diacetate and ethidium bromide staining to determine the viability of *Mycobacterium smegmatis* and *Escherichia coli*. *Leprosy Review*, 62(3), p. 310-314, 1991.

The ability of the fluorescein diacetate and ethidium bromide fluorescent staining method to assess the percentage of viable bacterial cells in suspension was compared with the plate counting method *Mycobacterium smegmatis* and *Escherichia coli* bacterial cell suspensions were incubated at 60°C. At different time intervals samples were taken and the percentage of viable cells in each sample was assessed by the fluorescent staining method and compared with the plate

counting method. The fluorescent staining method showed a positive correlation with the plate counting method. However, the viable counts by the plate counting method were lower than the staining method when incubated at 60°C, indicating a lag period in the decay of enzymes after bacterial death. Hence, the fluorescent staining technique can be used to assess the trend of bacterial death rather than to assess the exact number of viable bacilli.

PALOMINO, J.C. et. al. Assessing the viability of *Mycobacterium leprae* by the fluorescein diacetate/ethidium bromide staining technique. *Ind.J.Lepr.*, 63(2), p. 203-208, 1991.

In the present study we have evaluated the Fluorescein Diacetate/Ethidium Bromide (FDA/EB) staining technique to assess the viability of *Mycobacterium leprae* obtained from biopsies of leprosy patients under different periods of treatment. Bacillary suspensions were obtained from skin punch biopsies and stained with the FDA/EB solution. The average percentage of green cells seen which were deemed to be viable were: 67.2% of green cells in patients without previous treatment; 45.6% in patients with 1 to 6 months of treatment; 25.9% for patients with 7 to 12 months of treatment and 10.5% in patients with 13 to 24 months of treatment. All the patients studied were on multidrug therapy. The differences obtained in the percentages of green cells in the different groups of patients were statistically significant as determined by the Wilcoxon's test. The decrease in the percentage of green cells observed with increasing periods of treatment suggests that the FDA/EB technique correlates with the actual viability of *M. leprae*. The application of this technique in the routine procedures performed with Hansen's disease patients could be very useful for monitoring the effectiveness of treatment in leprosy patients.

RASTOGI, N. et. al. Differential Handling of Bacterial Antigens in Macrophages Infected with *Mycobacterium leprae* as Studied by Immunogold Labeling of Ultrathin Sections.

Int J.Lepr., 59(2), p. 278-291, 1991.

Mycobacterium leprae were purified from the livers of experimentally infected armadillos, and the purity of the bacterial preparation was established by electron microscopy, immunoelectrophoresis of purified bacilli with rabbit serum raised against liver tissues from a noninfected armadillo, and gas chromatography. Such purified and intact bacilli were fixed and embedded by a gelatin-Lowicryl method for electron microscopy which preserved in the mycobacterial antigens. Ultrathin sections were labeled with antisera raised in rabbits against the total antigens of the following species of mycobacteria: *M. leprae*, *M. bovis* BCG, *M. avium*, and a rapid-growing, nonpathogenic species, *M. fallax*. Bacteria were also labeled using serum raised against 2,3-diacyl-trehalose-2'-sulfate (sulfolipid-IV or SL_{IV}) isolated and purified from *M. tuberculosis*. The immunolabeling was visualized under the electron microscope (EM) by using a secondary probe (goat-antirabbit IgG, H+L, coupled to 5 nm gold particles; GAR-%). EM results showed that *M. leprae* bacilli were highly labeled with all of the antisera used except SL_{IV}, which was present only in discrete amounts. All of the antisera used labeled the bacterial "capsule", showing that this structure was not an artifact since it contained mycobacterial antigens. In parallel experiments, the murine J-774 macrophage cell line was infected with purified *M. leprae* and fixed for EM at various time intervals for 1 week. Although the phagocytized bacteria did not multiply during the 1-week experiment, macrophages were unable to lyse them. Immunogold labeling of bacterial antigens in ultrathin sections of infected macrophages helped us to conclude: a) bacterial death and/or lysis is not a prerequisite for processing of antigens by infected macrophages; b) there was conclusive evidence for a differential antigen handling, i.e., some antigens were rapidly released (within 2 days, mostly capsular antigens) inside infected macrophages and transported to the macrophage surface, whereas others (the majority of them located in the cell-skeleton and in deeper bacterial structures) remained unreleased even after 4 to 7 days of infection; c) although relatively fewer epitopes reacting with rapidly

released (within 2 days) inside macrophages, and exocytized to the macrophages surface. These novel findings are discussed in relation to leprosy and the current knowledge about the processing of bacterial antigens.

BHATIA, V.N. & RATHINAVEL, L. Isolation of a dopa positive rapid growing mycobacterium from blood of a leprosy patient. *Ind.J. Lepr.*, 64(1), p. 88-90, 1992.

A rapid growing acid-fast organism was isolated from the blood of a borderline leprosy patient. The isolate appeared to be close to *Mycobacterium chelonii* group of organisms but showed globi, cigar shaped bundles and was positive for DOPA-oxidase. Catalase, iron uptake, sodium chloride tolerance, tellurite reduction, Tween 80 hydrolysis and pyridine extraction tests were also positive. The 3-days arylsulphatase test and nitrate reduction test were negative.

HERBERT, D. & PRABHAKAR, R. Observations on the cultivation of *M. leprae* and *M. tuberculosis* in medium "V" and "V1". *Ind.J.Lepr.*, 64(3), p. 341-348, 1992.

Skin scrapings from five different active sites were collected from 14 leprosy patients and inoculated into medium V. Skin scrapings from three leprosy patients were inoculated into medium V 1. All the cultures were incubated at 37°C. *M. tuberculosis* H₃₇Rv, pretreatment isolates and streptomycin resistant strains were inoculated into medium V, with and without antibiotics, and incubated at 8-10°C as well as 37°C. Smears were made from the *M. leprae* and *M. tuberculosis* cultures at 0 hours and at different time points. The number of bacilli in the smears were counted. There was no increase in the number of *M. leprae* or *M. tuberculosis* in any of the cultures.

ISHAQUE, M. Energy Generation Mechanisms in the in Vitro - grown *Mycobacterium*

lepraemurium. *Int J.Lepr.*, 60(1), p. 61-70, 1992.

Mycobacterium lepraemurium was cultivated on Ogawa egg-yolk medium and its energy coupling mechanisms were investigated. Cell-free extracts prepared from in vitro-grown cells catalyzed phosphorylation coupled to the oxidation of generated NADH, added NADH, and succinate yielding ratios of phosphorus moles incorporated into high-energy bonds to oxygen atoms utilized (P/O ratios) of 0.75, 0.52, and 0.36, respectively. Ascorbate oxidation alone or in the presence of tetramethyl-p-phenylene-diamine (TMPD) did not yield any adenosine triphosphate (ATP). However, ascorbate in the presence of added cytochrome c was coupled to ATP synthesis and yielded a P/O ratio of 0.12. The oxidative phosphorylation was uncoupled by all of the uncouplers used without any inhibition of oxygen consumption. ATP generation coupled to NADH oxidation was completely inhibited by the flavoprotein inhibitors, such as rotenone and antimycin; these inhibitors had no effect, however, on ATP synthesis associated with succinate oxidation. Antimycin A or 2-n-heptyl-4-hydroxy-quinoline-N-oxide (HQNO) and cyanide inhibited markedly the oxidations of NADH and succinate as well as the coupled ATP generation. The phosphorylation coupled to ascorbate plus cytochrome c was not affected by either of the flavoprotein inhibitors or by antimycin A or HQNO, but was completely inhibited by cyanide. The thiolbearing agents p-chloromercuribenzoate (PCBM) and N-ethylmaleimide were the potent inhibitors of the phosphorylation associated with the oxidation of NADH and succinate. The results indicate that the three energy-coupling sites are functional in the respiratory chain of in vitro-grown *M. lepraemurium*.

PAIN, S. et. al. On structural aspects of peptidoglycan of bacterial cell wall with special attention on mycobacteria by computer modelling. *Ind.J.Lepr.*, 64(1), p. 28-41, 1992.

The cell wall components of mycobacteria are said to be vitally linked with their pathogenicity. Peptidoglycan, one of the major cell wall

component in most of the bacteria are multilayered in gram positive bacteria and it is diverse in nature for the Gram positive strain rather gram negative. The cell wall of bacteria are primary targets for many drugs and antibiotics and conformation of the major cell wall components provide invaluable information and understanding at molecular level to medicinal chemists and drug designers. mycobacterial peptidoglycan has been studied critically by computer modelling on various aspects. A plausible structure and conformation has been identified and glycan chain is found to have a pseudo two fold symmetry taking disaccharide unit as monomer with Knox & Murthy H-bond scheme. This paper attempts to clarify the understanding of organisation and possible interaction mode of peptidoglycan of organisation in complex mycobacterial cell wall structure.

PORICHHA, D. et. al. BI of patients vs BI of individual sites. *Ind. J. Lepr.*, 64(2), p. 179-182, 1992.

An analysis of 200 skin smear results from multibacillary patients showed that the average bacteriological index (BI) of a patient varied considerably from his site-wise highest B I. The average BI was equal to site wise highest BI only in 17.5% of cases and in the rest, it ranged from 99% to as low as 36% of the highest site-wise BI. In follow-up smears, site-wise consistency of the highest BI was found in 96% of cases. It is suggested that for follow-up purposes, repeating smear from only one such site would be adequate.

SHANNON, E.J. et. al. Competency of human-derived *Mycobacterium leprae* to use palmitic acid in the synthesis of phenolic glycolipid-I and phthiocerol dimycocerosate and to release CO₂ in axenic culture. *Leprosy Review*, 63(2), p. 101-107, 1992.

Insufficient numbers of viable *Mycobacterium leprae* have hampered metabolic studies using human-derived *M. leprae*. In this study, sufficient numbers of *M. leprae* were obtained

from an untreated lepromatous patient to titrate the effects of pH on the metabolism of ¹⁴C-palmitic acid by *M. leprae*.

Catabolic metabolism (oxidation of ¹⁴C-palmitic acid and release of ¹⁴CO₂) was maximal when *M. leprae* were incubated at 33°C and suspended in Middlebrook 7H9, ADC supplemented medium that had been buffered to maintain a pH of 4.8. Anabolic metabolism (synthesis of ¹⁴C-phenolic glycolipid-I and its precursor, ¹⁴C-phthiocerol dimycocerosate) was maximal when the pH was maintained at 6.8.

OUTROS EXAMES LABORATORIAIS

BABU, S.S.S. et. al. Adenoside deaminase activity in leprosy. *Ind. J. Lepr.*, 62(4), p. 473-477, 1990.

Adenoside deaminase (ADA) activity was studied in serum and peripheral blood lymphocytes of leprosy patients and healthy controls. Serum ADA levels were found to be elevated in tuberculoid as well lepromatous cases compared to control subjects. Serum ADA activity was significantly higher in tuberculoid cases than in the lepromatous group. lymphocyte adenosine deaminase activity showed a similar trend. These results suggest that, since the overall activity of the enzyme is not deficient in leprosy, the cellular immune aberration seen in the different types of leprosy may be due to abnormal proliferation of different subsets of lymphocytes in response to *M. leprae*.

CHANTEAU, S. et. al. Relationships between PGL-1 antigen in serum, tissue and viability of *Mycobacterium leprae* as determined by mouse footpad assay in multibacillary patients during short-term clinical trial. *Leprosy Review*, 61(4), p. 330-440, 1990.

In connection with a 56-day controlled clinical trial for comparing the therapeutic effects

between pefloxacin and ofloxacin in 21 lepromatous patients, we have studied the relationships between PGL-1 antigen level in serum and in skin and serum PGL-1 antibody titre on the one hand, and the viability of *Mycobacterium leprae*, as measured by serial mouse footpad inoculations, and other bactericidal parameters on the other. Before and during treatment significant correlation was found between serum PGL-1 level and the morphological index (MI), and with the number of viable organisms per mg skin tissue. However, neither serum PGL-1 antibody titre nor skin PGL-1 antigen level showed significant change during the 56-day trial. Because the reduction of serum PGL-1 level was well correlated but less pronounced as compared with the evolution of viable organisms during treatment, the serum PGL-1 antigen assay may be useful as an early indicator of response to chemotherapy in short-term clinical trial, but it is unlikely to replace mouse footpad inoculation for the evaluation of viability of *M. leprae*.

DHAWAN, V. et. al. Prostaglandin $F_2\alpha$ in Leprosy - A Preliminary Study. *Ind.J.Leprosy*, 62(1), p. 45-49, 1990.

Prostaglandin $F_2\alpha$ was estimated in the sera of fifty patients in the leprosy spectrum to find out the status of prostaglandins in response to *Mycobacterium leprae*. Contrary to expectation, $PGF_2\alpha$ could be detected in only twenty-eight percent of leprosy patients. This preliminary findings is discussed in detail in the paper.

GARG, R. et. al. Glucose Tolerance Test in Leprosy. *Ind.J.Leprosy*, 62(1), 1990.

Glucose tolerance test was carried out in 43 cases of leprosy. They included cases of tuberculoid, borderline, lepromatous leprosy and those with lepra reaction. Flat glucose tolerance curve was observed in borderline and lepromatous leprosy. However, the diabetic curve was common in Lepra reaction.

Fasting blood was low in lepromatous leprosy and it tended to be marginally high in

lepra reaction. Normal GTT response was observed in those with duration of disease between 0-6 months, flat curves in those with duration of disease between 7-12 months while diabetic curve was more common in those with disease duration of more than 2 years.

GARG, R. et. al. Thyroid function in leprosy. *Ind. J. Lepr.*, 62(2), p. 215-218. 1990.

Thyroid function tests were carried out in 43 cases of leprosy. The study subjects included of tuberculoid, borderline and lepromatous leprosy and those with lepra reaction. The parameters studied included serum cholesterol, protein bound iodine, serum T_3 level and serum T_4 levels. The levels of serum cholesterol and protein bound iodine were normal in all the four groups of leprosy patients. However, the mean serum T_3 and T_4 were low in all the four groups. The difference in the levels of serum T_3 was statistically significant only in the lepra reaction group. The levels of T_4 were statistically significantly decreased in borderline leprosy, lepromatous leprosy and in lepra reaction.

JADHAV, V.H. et. al. Fibrinolytic phenomenon in leprosy. *Ind. J. Lepr.*, 62(2), p. 208-214, 1990.

Fibrinolytic activity in patients eighty-one with different types of leprosy and thirty-two normal healthy controls was studied by Euglobulin Lysis Time Method. Fibrinolytic activity was markedly decreased in patients with lepromatous leprosy and those with ENL reaction. Decline in fibrinolytic activity during ENL was independent of frequency of attacks. Fibrinolytic activity was partly restored after subsidence of ENL reaction, though it failed to attain normal levels. Cutaneous vasculitis seems to be most probable cause of fall in fibrinolytic activity in lepromatous leprosy and ENL reaction.

RAV, S.D. et. al. Mast cell in leprosy. *Ind. J. Lepr.*, 62(4), p. 467-472, 1990.

Mast cell distribution in the affected skin and in the apparently normal skin at least 10 cm away from the lesion was studied in 250 leprosy patients. These cells were found and were more numerous in the apparently normal skin of established cases of leprosy as well amongst indeterminate group. Absence of mast cells was conspicuous in 16.7% BB, 40.9% BT, and 68.0% TT lesions. It is suggested that mast cells might play a role in the early stages of the disease and in postreational connective tissue proliferation.

SAXENA, N. et. al. Serum iron and total iron binding capacity in leprosy patients. *Ind.J.Lepr.*, 62(2), p. 219-222, 1990.

Serum Iron and total Iron binding capacity was estimated by Ramsay's Method in 40 leprosy patients having different types of leprosy and 20 normal subjects serving as controls. Significantly low serum Iron and total Iron binding capacity were observed in lepromatous leprosy patients.

SEN, R. et. al. Bone marrow cyto-morphological changes in multibacillary leprosy. *Ind.J.Lepr.*, 62(3), p. 321-327, 1990.

Seventy-two cases of multibacillary leprosy were investigated for cytomorphological changes and presence of lepra bacilli in bone marrow. These patients were divided in two groups. Group A (28) comprised of new cases and group B (44) of those receiving treatment. Myeloid hyperplasia was mostly seen in patients of group B who had erythema nodosum leprosum. Mega-Ioblastic change in erythroblasts was seen frequently in both the groups. While average number of plasma cells and macrophages was on the higher side normal range, detection of large number of plasma cells underline enhanced humoral response and created diagnostic problem with multiple myeloma. Morphological changes in the macrophages, their collections and epithelioid

cell granulomas were observed in bone marrow. Their nature and significance is discussed.

TANEJA, K. et. al. Hepatic ultrasonography in patients with lepromatous leprosy. *Ind.J.Lepr.* 62(4), p. 443-447, 1990.

Hepatic Sonography was done in 36 patients with lepromatous Leprosy and 3 patients with borderline lepromatous leprosy with view to assess abnormalities of size, changes in the echotexture and to observe the presence of any nodules and calcification in the liver. Routine liver function tests were also done in these patients. No definite abnormal sonography findings were seen in the liver in a large majority of these patients. One patient, however, showed nodular changes in the liver.

VIJAYALAKSHMI, K. et. al. Effect of Presensitization with BCG and *Mycobacterium leprae* on Granuloma Formation to *M. leprae*. *Int.J.Lepr.*, 58(4), p. 674-680, 1990.

Granulomas which develop in draining lymph nodes, following the intradermal injection of cobalt-irradiated *Mycobacterium leprae* into the ear of the guinea pig 2 and 5 weeks earlier, were studied in animals which had been presensitized with BCG vaccine or *M. leprae* and compared with granulomas that developed in previously unsensitized guinea pigs. Presensitization with mycobacteria accelerated the development of the granulomas. Granulomas in previously unsensitized guinea pigs were found ultrastructurally to contain phagocytosing macrophages similar to those in lepromatous leprosy, and *M. leprae* presensitization did not alter the type of granuloma found. Those in BCG-presensitized guinea pigs contained secretory epithelioid cells with rough endoplasmic reticulum similar to those found in borderline tuberculoïd leprosy or reversal reactions. The significance of these findings in relation to the current use of vaccines in leprosy is discussed.

FOSTER, R. et. al. Profile of blood elements in leprosy patients. *Ind.J.Lepr.*, 63(1), p. 12-33, 1991.

Blood levels of 40 elements in 14 leprosy patients and 5 control subjects living near Mukinge Hospital in the North Western Province of Zambia were determined by spectrophotometry. In patients, compared to controls, serum levels of titanium, silicon, potassium and platinum were significantly higher; red cell levels of phosphorus were lower but those of antimony, bismuth, nickel, titanium, yttrium, silicon and platinum were higher, and whole blood levels of phosphorus, selenium, antimony and silver were lower. There were also significant differences in levels of certain elements when histologically active and inactive patients were compared and between the polar forms of leprosy. The data are consistent with a hypothesis of metabolic and nutritional involvement in the etiology of leprosy.

GEORGE, J. et. al. Serum Zinc/Copper Ratio in Subtypes of Leprosy and Effect of Oral Zinc Therapy on Reactional States. *Int.J.Lepr.*, 59(1), p. 20-24, 1991.

Serum zinc and copper levels and zinc/copper ratios were studied in 86 healthy controls, 45 cases of borderline tuberculoid (BT), 31 cases of borderline lepromatous (BL), 117 cases of lepromatous (LL) leprosy patients, 16 cases with severe erythema nodosum leprosum (ENL) reaction, and 16 cases with ENL reaction receiving oral zinc therapy. A significant reduction in serum zinc levels was noticed in all types of leprosy, the maximum decrease being seen in cases with ENL reaction. Conversely, the copper levels were significantly increased from BT to LL cases with ENL reaction in a progressive manner. A very good negative correlation ($r = -0.998$) was noticed between mean serum zinc and copper levels from healthy controls to active LL cases with ENL reaction. After oral zinc therapy, the serum zinc levels were significantly increased in all of the 16 LL patients with ENL reaction. In contrast, the copper levels were not decreased, indicating that oral zinc therapy can restore normal zinc levels in leprosy patients but is unable to reduce

the increased copper levels.

HAAS, M. et. al. Determination of in vivo and in Vitro Drug Effects of Mycobacteria from the Mass Spectrometric Analysis of Single Organisms. *Int.J.Lepr.*, 59(2), p.262-270,1991.

Laser microprobe mass analysis of single bacterial organisms allows the determination of their intrabacterial ratio of sodium-to-potassium ions and the registration of fragment ions originating from their organic bacterial cell matrices as mass fingerprint spectra. It has been established previously that the intrabacterial cation ratio provides information on the physiological state of an individual bacterial cell. In the present experiments it is also shown, with different cultivable mycobacterial species and strains (drug sensitive and resistant) exposed to various drugs, that data derived from the evaluation of the mass fingerprint spectra reflect changes in the degree of impairment. The analysis of Mycobacterium leprae derived from a limited number of skin biopsies of lepromatous/borderline lepromatous leprosy patients under World Health Organization-recommended multiple-drug therapy (WHO/MDT) showed impairment of the organisms with both of the methods of measurement in proportion to the duration of treatment except in one case. In one M. leprae population from a patient who had been treated for 19 months, the fingerprint evaluation gave the first evidence for an insufficient response to treatment. This was further confirmed by the unusual frequency distribution of the Na^+, K^+ ratios which revealed the existence of two subpopulations, one impaired and one unimpaired.

JAIN, V.K. et. al. Gamma-glutamyl transpeptidase in leprosy. *Ind.J.Lepr.*, 63(1), p. 93-96,1991.

Activity of the enzyme gamma-glutamyl transpeptidase (GGTP) was measured in sera of 20 patients each of paucibacillary and multibacillary leprosy and 20 healthy controls. None of the subjects had any systemic or hepatic disease and none had taken any hepatotoxic or antileprotic drugs in the past 3 months. Mean values in the paucibacillary group (38.62 ± 1.99 U/L) and in the

multibacillary group (59.04 ± 3.13 U/L) were significantly higher compared to that in controls (32.04 ± 0.66 U/L). Mean value in the multibacillary group was also significantly higher compared to that in the paucibacillary group.

JOB, C.K. et. al. Comparison of polymerase chain reaction technique with other methods for detection of *Mycobacterium leprae* in tissues of wild nine-banded armadillos. *Lepr.Rev.*, 62(4), p. 362-373, 1991.

Thirty, nine-banded armadillos weighing between 3 and 5 kilograms trapped from an area endemic for armadillo leprosy were collected at random; killed, autopsied and examined histopathologically. Also, one of the right inguinal lymph nodes was removed under sterile precautions and examined using PCR, direct smear examination, mouse footpad study, culture in laboratory media and histopathology with a view to detecting *Mycobacterium leprae*. Blood was collected at death and tested for IgM antibodies to PGL-1.

According to the PCR study of the inguinal lymph nodes 16 of 30 armadillos (53.3%) had evidence of *M. leprae*. Significant levels of IgM antibodies to PGL-1 and identifiable lepromatous granuloma in inguinal lymph nodes were found in 2 animals (6.7%) with advanced disseminated disease. The prevalence of generalized leprosy according to autopsy study was 13.3% and according to histopathological examination of ear tissue 3.3%. The presence of *M. leprae* in the tissues evoked no special tissue reaction in the early stages. The pattern of spread of the disease in 2 animals closely resembled that found in experimental animals infected intracutaneously. Initiation of infection by inoculation of *M. leprae* through thorn pricks remains a distinct possibility.

MAHADEVAN, P.R. et. al. Delipidified cell components of *Mycobacterium leprae* and its applications. *Ind.J.Lepr.*, 63(3,4), p. 371-387, 1991.

Delipidified cell components (DCC) of *Mycobacterium leprae* obtained as an Insoluble material consist of several proteins. This preparation, DCC, has ability to differentially bind to sera from lepromatous leprosy patients and antibodies to this complex get reduced as patients improve under chemotherapy. The antigenic complex has no ability to bind to proteins of sera from normal healthy individuals or tuberculoid leprosy patients. The DCC is antigenic and is recognised by immune deficient cells of lepromatous leprosy patients, leading to lymphocyte proliferation, production of Interleukin II and interferon γ , and resulting in activation of the phagocytes to initiate killing of endocytosed *M. leprae* through reactive oxygen intermediates, primarily superoxide. The DCC has also immunomodulatory properties to protect mice against *M. leprae* infection. Experiments with mice and isolated peripheral blood cells from patients have indicated the probable molecular mechanism of immunomodulation by DCC.

SEN, R. et. al. Lipid-laden macrophages in bone marrow of leprosy patients. *Lepr. Rev.*, p. 374-380, 1991.

While conducting a study to observe bone marrow cytomorphological changes in multibacillary leprosy, lipid laden macrophages as seen in sphingolipidoses were noted. The present study was planned to observe the occurrence and morphological characterization of these macrophages in various types of leprosy. Bone marrow records from 48 cases of paucibacillary and 72 cases of multibacillary leprosy were analysed. The macrophages accounting at the most for 3.5% of marrow cells were observed in 5 cases of paucibacillary and 43 cases of multibacillary leprosy with a maximum incidence being observed in patients with ENL (16/17). The lipid present in the cytoplasm of these cells could be derived from the lipid of the cell wall of *Mycobacterium leprae*. To the best of our knowledge, these cells have not been reported in leprosy so far.

WRIGHT, S. et. al. Essential Fatty Acids in Plasma of Patients with Leprosy. *Int.J.Lepr.*, 59(2), p. 271-277, 1991.

We have investigated the fatty-acid composition of plasma phospholipids in 61 patients with leprosy of various clinical types with either a short or long duration of treatment. All patients had significantly decreased levels of linoleic acid and alphinoleic acid, the parent fatty acids of the n-6 and n-3 families, respectively. Patients with a treatment duration of more than 6 months had significantly low levels of arachidonic acid and eicosapentaenoic acid compared to controls or to patients with a treatment duration of less than 6 months. There were no differences in the fatty-acid composition between multibacillary patients and paucibacillary patients. We conclude that dietary supplementation with essential fatty acids may be indicated in patients with leprosy, particularly in those with a long treatment duration.

YODER, L.J. et. al. Comparison of a urine spot test and blood tests as indicators of patient compliance. *Ind.J. Lepr.*, 63(2), p. 195-202, 1991.

Irregular drug intake has been a concern of leprosy control programmes for many years and various methods have been used to monitor and encourage patient compliance. This study compare the results of a urine spot test for dapsone as proposed by Huikeshoven, with blood levels measured in the same patients by the modified Bratton Marshall method and by high performance liquid chromatography. Two hundred-sixty urine and blood specimens were obtained from subjects who were taking supervised and unsupervised medications as well as from controls who were taking no medications.

The results indicate that the urine spot is simple and easily performed, and for monitoring patient compliance under routine clinical conditions (hospital or field work) it compare favourably with blood levels of dapsone estimated by the Bretton Marshall method or by high performance liquid chromatography. The study also shows

that dapsone level is not a good indicator of compliance in patients who are also taking daily rifampicin but the urine spot test remains useful in such patients.

AHALEY, S.K. et. al. Correlation of serum lipids and lipoproteins in leprosy. *Ind.J.Lepr.*, 64(1), p. 91-98, 1992.

Serum lipids and lipoproteins were assessed in sixty and forty age and sex matched healthy controls. The study subjects included cases of LL with reactions, LL without reactions, BL with reactions, BL without reactions, BT and TT types of leprosy.

The levels of serum phospholipids, triglycerides, total cholesterol, LDL and VLDL fractions were significantly decreased in leprosy patients compared to control subjects. The levels of serum HDL cholesterol and HDL fraction were significantly elevated in leprosy patients.

Maximum elevation in serum HDL cholesterol level and HDL fraction and maximum reduction in the levels of serum phospholipids, triglycerids, total cholesterol and LDL and VLDL fractions were observed in lepromatous leprosy (LL) patients with reactions.

HARSHAN, K.V. et. al. Uptake of Purine and Pyrimidine Nucleosides by Macrophage-resident *Mycobacterium leprae*: H-Adenosine as an Indicator of Viability and Antimicrobial Activity. *Int.J.Lepr.*, 58(3), p. 526-533, 1990.

Freshly extracted human- and armadillo-derived *Mycobacterium leprae* maintained within murine macrophages incorporated significant levels ($p < 0.05$ to $p < 0.001$) of ^3H -adenoside and ^3H -hypoxanthine by 6 and 9 days of the culture period. The incorporation of ^3H -adenoside was twofold or more higher than ^3H -thymidine in 10 out of 15 human-derived *M. leprae* isolates. Macrophage-adapted bacilli incorporated 10-14-fold higher levels of ^3H -adenosine compared to the same bacilli maintained in axenic cultures. The incorporation of these two labels was Inhibited by dapsone and

rifampin, indicating the utility of in vitro radiometric assays for screening antileprosy drugs and drug sensitivity/resistance in patients.

PROGRAMAS E TRABALHOS DE CAMPO E ASPECTOS SOCIAIS EPIDEMIOLOGIA

KRISHNAMURTHY, K.V. & RAO, S.P. A study of leprosy affected beggars in Aska. *Ind. J.Lepr.*, 62(1), p. 113-119, 1990.

A study conducted among beggars in and around Aska, Orissa revealed 41 of them to be leprosy patients. Almost all had taken treatment and had been released from control. Only 2 of them were mildly positive in their skin smears for AFB. All of them had disabilities and deformities. It is evident that at least in this area beggar leprosy patients cannot be contributing to the transmission of the disease. Their treatment regularity record was also very good.

MOITA, C.P. & ZUNIGA, G.M. Time Trends of Hansen's Disease in Brazil. *Int.J.Lepr.*, 58(3), p. 453-461, 1990.

In an analysis of the trend of Hansen's disease in Brazil, the "incidence register" or "detection rate" per 100,000 was used. The operational data analyzed were presumed to be related to true incidence because of the time elapsed (38 and 19 years) and because of the large number of cases. The statistical method used was the exponential curve fit. From 1950 to 1968, there was an average annual decrease in the rate of 3% as indicated by the regression coefficient (slope), but from 1969 to 1987 an increase of 6% per year was observed. If this last trend is sustained, the detection rate in the year 2000 will be 35.03 per 100,000 or, in a population estimated as 190,000,000 inhabitants, 66,600 new cases. For comparison, in 1983 there were 18,759 new cases registered. The

trend analysis for each of Brazilian political-administrative areas (states and territories) is more accentuated in the Center-West and Northeast Macroregions, with a slope of 8% and 10%, respectively. In some states, such as Paraíba, Rio Grande do Norte, and Alagoas, there were astonishingly positive slopes of 20, 18% and 17%, respectively. The distribution of the new cases by clinical forms during most of the period studied (1969-1987) confirms the overall trends observed. There was an increase in the detection rate of the tuberculoid form of 5% annually - compared to the lepromatous (combined with borderline) rate of 3% per year - and, also the increase in the tuberculoid form was greatest in the Center-West and Northeast Macroregions. In conclusion, there is strong probability of an increase in the transmission of Hansen's disease in Brazil a situation of great concern for public health authorities.

NAIK, S.S. et. al. Leprosy Survey in Night High Schools in Greater Bombay. *Int.J.Lepr.*, 62(1), p. 116-119, 1990.

A survey of 6096 students attending night high schools in Bombay the prevalence rate of leprosy 9.3 per 1000 in this group. 10.5% of the cases identified were having more serious forms of leprosy characterised by nerve involvement or skin smear positivity. Night school screening has limited value as it can only be conducted in big industrial cities and such surveys cover only a very small proportion of the population. However, in view of the current tendency of population shift from rural to urban areas and since such survey can identify a number of established cases it can be included among the other routine leprosy case detection activities in big cities, where night schools exist.

RAO, P.S. & SIRUMBAN, P. Screening of registered leprosy cases and its effects on prevalence rate. *Ind.J.Lepr.*, 62(2), p. 180-192, 1990.

Prevalence rates of leprosy in 6 endemic

districts in Andhra Pradesh, India with a population of 168.71 lakhs (1981 census) were studied before and after screening of registered cases. The screening was carried out as part of multidrug treatment project implementation. After such a sharp fall in the registered prevalence rate, by 26.2% on the average, was observed in all the districts. About 34.8% of the total cases were declared as Released from control. The implication of these findings regarding registered cases fit for such release and the overall registered prevalence rates in the country must be kept in mind.

WELE, D.S. Health education for the successful implementation of MDT. *Ind.J.Lepr.*, 62(3), p. 346-359, 1990.

The importance and goals of health education in leprosy are pointed out. The responsibilities of the health education are outlined. The role of health education in the context of the MDT programme is discussed.

CAMPOS-OUTCALT, D. An evaluation of a microcomputer information system for leprosy control two years post-implementation. *Leprosy Review*, 62(1), p.65-71,1991.

As part of a national programme to improve the management of health services in Papua New Guinea, a microcomputerized information system was designed and implemented in seven provinces. Four other provinces later adopted this system. One component of this information system was a program to assist disease control officers to monitor the treatment received by leprosy and tuberculosis patients.

In contrast to other components of the information system, the leprosy and TB computer program was not maintained nor used after two years. This article describes the computer program developed and discusses possible reasons for its nonuse.

CROOK, N. et. Al. An educational approach to leprosy control: an evaluation of knowledge, attitudes and practice in two poor localities in Bombay, India. *Lepr. Rev.*, 62(4), p. 395401, 1991.

Based on the hypothesis that a systematic, carefully planned educational approach to leprosy would yield results in terms of knowledge, attitudes and case presentation superior to those of the established and traditional mass survey method, ALERT-India launched a programme in S ward of Bombay in February 1985, to compare the two. An intensive programme of healthy education, using trained teams, was carried out in one zone of this ward over a period of 12 months. Eight months later, mass survey work (as used routinely in previous years and on a country-wide basis) was carried out in an adjacent zone. In 1987, the Centre for Social and Technological Change in Bombay, in association with the School of Oriental and African Studies, University of London, was requested to evaluate the effect of the above educational approach in terms of knowledge, attitudes and practice in both the trial and control zones. Other aspects of this experimental approach, including its cost and effectiveness in identifying cases of leprosy, will be published separately. The design of the 'KAP' evaluation and the social and environmental controls introduced in the statistical analysis are described. The results pointed to a considerable degree of ignorance about leprosy as a disease (and its treatment) in both the study and the control zones. Knowledge about early symptoms was particularly weak and on all aspects scores for women were invariably lower than men. General education enhanced the absorption of specific knowledge, and the education of children compensated adequately for lack of parental education in this respect. Overall the evaluation indicated that the intensive educational approach was superior to the survey approach in terms of improving knowledge, attitudes and practice.

KRISHNAMURTHY, P. et. al. Seroepidemiological Study of Leprosy in a Highly Endemic Population of South India Based on an ELISA Using Synthetic PGL-I. *Int.J.Leprosy*, 59(3), p. 426-431, 1991.

As part of a continuing longitudinal immunoepidemiological study, blood samples were collected by finger prick from 4243 individuals living in a highly endemic area for leprosy in South India. The samples were tested for IgM antibodies against phenolic glycolipid-I using an ELISA. Seropositivity defined as optical density ≥ 0.2000 was marginally higher in the age group 10-30 years and in females. There was no evidence for a higher level in contacts than in noncontacts. The future prospect for the large scale use of this ELISA in high-endemic populations in special epidemiological investigations or routine control programs as a serological tool to detect leprosy infection appears questionable.

KUMAR, A. et. al. The factors influencing the operational efficiency of leprosy case detection programme. *Ind.J.Leprosy*, 63(2), p. 180-194, 1991.

Under our National Leprosy Eradication Programme, Leprosy cases are being detected by para-medical workers by conducting population surveys. In order to detect the leprosy cases early, for their timely anti-leprosy treatment, it is necessary that the leprosy surveys are implemented and supervised efficiently. However, present experience indicates that the existing survey efficiency needs to be improved, for which it is necessary to analyse the factors which may interfere with the optimal survey efficiency of para-medical workers. An attempt has been made through present piece of work to identify such factors in relation to (i) the para-medical workers and survey facilities, (ii) the implementation and supervision of leprosy survey and (iii) the community involved in survey. These factors are discussed in detail to assist the NLEP Administrators in devising a suitable action plan to improve leprosy case detection efficiency.

KUMAR, R.P. et. al. Transmission of health information on leprosy from children to their families: another approach to health education. *Leprosy Review*, 62(1), p. 58-64, 1991.

A controlled study was carried out in the North Arcot District of Tamil Nadu, South India to determine whether health information given to schoolchildren would influence the knowledge and attitudes of their families concerning leprosy. A total of 41 children and almost all of their household members participated in the study.

The study, conducted by questionnaire, involved a pre-test of knowledge and attitude about leprosy of seventh standard and their families. After one group of children received health education about leprosy and the other received information about tuberculosis, an identical post-test questionnaire was administered to all participants.

Although significant improvement in knowledge about leprosy was detected in the leprosy educated group of children compared with controls, no transmission of information on leprosy was detected in the family members of either group. The attitudes of the children who had been educated about leprosy may have been adversely affected by the health education session.

The reasons for our failure to detect significant transfer of information about leprosy in this setting are discussed, as well as the need for additional research in this area.

MURTHY, P.K. et. al. A computerized information system for evaluation of NLEP through monthly progress reports. *Ind.J.Leprosy*, 63(1), p. 70-77, 1991.

A computerized system for monitoring district-wise operational performance and epidemiological progress using existing regular and special monthly reports of the National Leprosy Eradication Programme (NLEP) is presented. The same system, with which some minor modifications could be used for programme assessment at the Leprosy Control Unit level also. The

advantage of the system is the speed with it can generate output in the form of comparative tables and graphs for different regions for use by programme managers for making overall assessments in time and for sending feedback reports to workers at various levels, for self-assessment and for taking timely corrective action. The system presented provides immediate and easy access to the stored and/or processed information (indicators etc.) at any time. The system has been pilot-tested using monthly reports from eighteen districts of Tamil Nadu.

NAIK, S.S. et. al. Problems and needs of women leprosy patients in Bombay and Goa - preliminary report. *Ind.J.Lep., 63(2)*, p. 213-217, 1991.

By studying the status of 151 women leprosy patients (24 from a leprosy asylum and 127 attending urban leprosy centres at Goa and Bombay), it was noticed that a sizeable proportion experienced problems in society ascribable to the disease especially at the initial stages of the disease. However, most of them seemed to have managed to settle well in their families as housewives subsequently. Younger women leprosy patients expressed the need for financial assistance for completing their own education and for starting small scale business. The older women were more interested in educating their children.

RAVEENDRANATHAN, O. et. al. Epidemiological significance of indeterminate leprosy - A hospital based study. *Ind.J.Lep., 63(1)*, p. 5-11, 1991.

An epidemiological analysis of 100 cases of indeterminate leprosy attending the Department of Dermatology and Venereology of Medical College Hospital, Trivandrum, is presented. It was found that indeterminate leprosy formed 13.23% of all cases of leprosy and 1.3% of all out-patients attending this department. Only 27% of patients with indeterminate leprosy were below 15 years of age. There was a predominance of males especially over 20 years of age. There was

no history of contact with leprosy in any of the patients with indeterminate leprosy. All patients with indeterminate leprosy came for hypopigmented patches, suspecting leprosy. Majority had the disease for more than 6 months. single lesion on the outer aspect of extremity was the most common presentation. The lepromin test was positive in only 2% of patients with indeterminate leprosy, while it was positive in 80% of control subjects. Three cases of dapsone resistance were suspected in this series. The epidemiological significance of the findings is discussed.

REE, G.H. Pattern of leprosy in Queensland, Australia, 1855-1990. *Lep.Rev., 62(4)*, p. 420-430, 1991.

Leprosy was first diagnosed in Queensland in 1855. From then until 1990, 929 patients with the disease were notified. The pattern of notification has varied with the passage of time, and with the changing pattern of migration into Queensland. In the early days, Chinese, Melanesians and Caucasians featured prominently. The first Aboriginal notification was in 1892. In the latter part of this century, significant numbers of Torres Strait Islanders and migrants from South East Asia have been recorded. Among Caucasians, the incidence peaked in the decade 1931-1940, although the prevalence rate in this population remains much higher than in Caucasians. The control of leprosy is at a high level in Queensland today, but there is a continuing low level of new case reporting, many of them imported.

SAMY, A.A. et. al. ALERT-India 1981-89: nine years' experience of leprosy controle in the slums of Bombay. *Leprosy Review, 62(3)*, p. 315-328, 1991.

Bombay has a population of about 8 million people, one-half of whom live in slums. In 1981, ALERT-India started its first leprosy control project in N, S and T Wards of Greater Bombay Municipal Corporation covering an area of 122 sq km in the north-eastern suburbs of Vidhayavihar, Ghatkopar, Vikhroli, Kanjurmarg, Bhandup and

Mulund, with a total population of 1,100,000 according to the 1981 census. In the 9 years of operation, over 12,000 patients have been registered and treated and of these 7425 have been released from treatment, having satisfactorily completed courses of chemotherapy. However, over 1000 cases are still identified every year by house-to-house or school surveys, or by self-reporting, including a considerable percentage in children. The origin, development, staff structure, operational procedure, administration and recording system of ALERT-India are described in detail, with emphasis on what has been accomplished with purely outpatient facilities, using paramedical workers, all of whom have received inservice training from Government recognized training centres for their specific tasks. The account includes a brief description of an expansion of the organization's work into townships in New Bombay, where preliminary surveys in 1988 confirmed the presence of leprosy cases and the need for treatment facilities. The discussion addresses: 1, the better use of the large volume of statistical information which has been collected by ALERT-India during the past 9 years, with emphasis on its value in assessing the impact on the control programme and modifying future policy; 2, the need to radically examine the present policy of survey, versus an education campaign approach with regard to increasing early case-detection and self-reporting; 3, the establishment of a central coordinating body for leprosy control in Bombay to exchange information, coordinate efforts and formulate a future plan of action, the latter in association with the National Leprosy Eradication Programme; and 4, the development of a healthy education resource centre in association with the Bombay Municipal Corporation.

AWOFESO, N. Appraisal of the Knowledge and attitude of Nigerian nurses towards leprosy. *Leprosy Review*, 63(2), p. 169-172, 1992.

The attitudes of nurses toward leprosy are studied and in this paper. The findings show that their knowledge of leprosy is lacking and that they also fear leprosy. This study recommends

that leprosy should be included in the basic nursing curriculum in order to increase awareness and to the decrease stigma of leprosy.

BHORE, P.D. et. al. Child-to-parent education: A pilot study. *Ind.J.Lepr.*, 64(1), p. 51-57, 1992.

A controlled study carried out in hilly Konkan region on the West coast of India showed that school children have the potential for transmitting their newly acquired knowledge to their parents. Though the results indicate that acquisition of knowledge does not mean a change in attitudes concerning leprosy, child-to-parent education may show promising results in leprosy education in developing countries where most parents of school children are illiterate and are not easily reached by conventional methods of health education.

CARTEL, J.L. et. al. Leprosy in French Polynesia. Epidemiological trends between 1946 and 1987. *Leprosy Review*, 63(3), p. 211-222, 1992.

Summary The analysis of computerized data (OMSLEP system) on patients from French Polynesia followed since 1940 has shown a decrease in the mean annual detection rates for leprosy, all forms combined, from 24.73 per 100,000 inhabitants in 1946 to 8.1 per 100,000 in 1987 ($y = -0,49x+45.83$; $p<0.05$). In fact, the decrease was significant ($y = -1.18x+83.54$; $p<0.05$) during the first half of the study period (1946-66), but not during the second half (1967-87). Similarly, a significant decrease in all of the specific mean annual detection rates (according to the form of leprosy and to the sex and age patients), in the proportion of multibacillary patients among the total of newly detected cases, and in the proportion of all patients with disabilities at the onset of leprosy was observed only during the first half of the study period (1946-66). Nevertheless, when comparing age-specific cumulative detection rates, calculated by 10-year age groups over the period 1946-66, to those of the period 1967-87, an ageing of the leprosy population was

noted. Finally, the decrease of mean annual detection rates was greater in the smaller populations of remote islands than in the population of Tahiti, the main island, where 70% of the total population were living during the study period. This decline was shown to correspond to an effective improvement of the leprosy situation which could be attributed, among other factors (such as economic development and systematic BCG vaccination), to the implementation of a control programme for leprosy in 1950. The introduction in 1982 of multidrug therapy for all patients suffering active leprosy has raised the hope of a subsequent decline of leprosy in French Polynesia in the near future.

DAY, R.; LEVER, P. & ASRI, M. Leprosy control in 7 districts of South Sulawesi, Indonesia, 1986-91. *Leprosy Review*, 63(3), p. 247-254, 1992.

This paper describes the leprosy control programme in 7 districts of the South Sulawesi Province in Indonesia. This province is reported to have the highest prevalence of leprosy in the country. The programme started in 1986 with re-registration of all patients on the cumulative registers. Strict criteria for admission of patients to MDT were initially applied. In 1990 it appeared that these criteria had been too strict, thus necessitating a second re-registration of patients still on DDS monotherapy. More flexible criteria for admission to MDT led to an increase in MDT coverage from 45% to 78% within 6 months.

By April 1991, 5 years after the start of the programme, the registered prevalence had decreased from 4.4 per 1000 in 1986 to 1.6 per 100; the coverage with MDT had increased from 6% in 1986 to 78%, and the case detection rate remained stable around 4 per 10,000 after an initial increase at the start of the programme.

KANNAN, N. & SILVARAM, M. Variables influencing regularity of leprosy patients in attending treatment clinics. *Ind.J.Leprosy*, 64(4), p. 505-512, 1992.

Regularity in attending clinics as well as drugs assume a very significant place in leprosy control programme since irregularity of leprosy patients can lead to poor disease control, drug resistant disease, and development of physical deformities and disabilities thus leading to programme failure. Further, these complications also create socio-economic and psychological problems to the victims as well as their families in myriad ways. This paper reports a study aimed at identifying the variables, among a list of 29 selected demographic, socio-economic and disease-related variables, having significant association with regularity of leprosy patients in attending treatment clinics. It was found that age of the patients, type of family, duration of the disease, time lag between diagnosis of the disease and starting treatment and knowledge of patients and their families about the disease were significantly associated with treatment regularity.

LENNON, J.L. & COOMBS, D.W. An application of the LePSA methodology for health education in leprosy. *Leprosy Review*, 63(2), p. 145-149, 1992.

This paper describes how the innovative LePSA technique can be used by community health workers to appropriately educate and increase compliance among leprosy patients. A lesson plan illustrating the interactive nature of the technique in a hypothetical Third World community is presented. The lesson plan, using MDT default, shows how the technique can elicit individual participation in a group setting and serve as both an educational and a behaviour change tool.

MURTHY, P.K. et. al. Time lag between case registration and commencement of treatment in a leprosy control unit. *Ind.J.Leprosy*, 64(1), p. 8-13, 1992

Analysis of client-based data as a part of computerised management information system in a Government leprosy control unit in Tamil Nadu reveals that there was delay in initiating treatment of leprosy patients. The mean and standard deviation

tion of the period of delay for cases registered before, within 6 months and after 6 months of start of MDT in the Unit were 6.80 ± 6.40 , 1.97 ± 3.60 and 0.90 ± 2.21 months respectively. Further, the delay was longer in PB, female and child cases. Giving priority to therapy for backing cases and an effective monitoring system with specific indicator for time lag in starting treatment is indicated.

MYINT, T. et. al. A comparative KAP study of leprosy patients and members of the community in Hlaing and Laung-lon townships. *Ind.J.Lepr.*, 64(3), p. 313-324, 1992.

A KAP study was conducted in the peri-urban Hlaing and rural Laung-Lon Townships in Myanmar. It was found that both the leprosy patients as well as community members were still not sure about the cause of leprosy. Social stigma of leprosy encountered by patients needs to be addressed especially in peri-urban areas. It was also found that the patient's understanding of treatment regularity was still very unsatisfactory for which health education measures needs to be introduced.

MYINT, T. et. al. Risk factors among defaulters in the urban leprosy control centre of Thaketa Township in the City of Yangon, Myanmar, 1986. *Lepr. Rev.*, 63(4), p. 345-349, 1992.

A total of 884 registered cases from the city of Yangon were retrospectively analysed. The defaulter proportion among cases registered for treatment at the Thaketa Health Centre was 34.16%. It was established that patient sex and occupation are not a factor in defaulting. Paucibacillary cases and cases with no disability are more likely to default.

NOORDEN, S.K. et. al. Estimated number of leprosy cases in the world. *Ind.J.Lepr.*, 64(4), p. 521-528, 1992.

Planning for disease control requires estimates of number of leprosy patients from local

to global levels. From the mid-sixties to the mid-eighties, global estimates appeared to be constant at between 10 and 12 million. The introduction of multidrug therapy (MDT) in many countries and the consequent reduction of prevalence of the disease has necessitated a reassessment of the global estimate. Based on available information and its interpretation, the number of leprosy cases in the world in 1991 has been estimated at 5.5 million. The number of individuals with deformities due to leprosy, including persons now cured of the disease, has been estimated at between two and three million.

PATTYN, S.R. et. al. Polymerase Chain Reaction Amplifying DNA Coding for Species-specific rRNA for *Mycobacterium leprae*. *Int. J.Lepr.*, 60(2), p. 234-243, 1992.

The sensitivity of the polymerase chain reaction (PCR) on the DNA coding for the species-specific fragment of 16S rRNA of *Mycobacterium leprae* studied on mouse foot pad harvests and human skin biopsies varies widely between 1 and 3×10^6 organisms. This is probably the result of variations in the proportions of organisms with sufficiently intact DNA suitable for PCR. Preserving human skin biopsies for 3 weeks at an ambient temperature even after boiling for 6 minutes gives rise to a 10-fold decrease in sensitivity. Fixation of tissues in formol 10% or Lowy fixative or preserving in Dubos OAA broth is very harmful to the PCR, mainly due to the enhancement of an inhibitory effect on the PCR reaction. For preservation, the best choice at the moment seems to be alcohol 70%. Sample preparation of five cycles of freeze-boiling is simple and generally more efficient than proteinase K treatment and DNA extraction.

PREMKUMAR, R. & DAVE, S. Relationship problems between doctors and paramedical professionals working in leprosy with reference to a possible solution. *Leprosy Review*, 63(2), p. 173-182, 1992.

An empirical investigation was conducted

on the in-group dynamics of health personnel working in leprosy. The sample populations were taken from the National Leprosy Eradication Programme (NLEP) employees of two state governments in India. They consisted of 21 doctors and 335 paramedicals, the former constituting a formal group and the latter a semi-formal group. Two separate scales were developed for each of these groups to elicit information on five potential areas of intergroup relationships.

The results indicated that there was very poor acceptance of the out-group and its roles, i.e. poor acceptance of the paramedicals by the doctors and vice versa. Three reasons were elicited from this study. First, doctors held their professional standing to be on a higher level than the paramedicals, leading to excessive social distancing between doctors and paramedicals. Second, multiprofessional involvement in NLEP work has increased the trend of professional overlapping, leading to a significant apprehension of the encroachment of skills. Third, there was a mutual lack of trust of each others professional skills. Despite these problems the otherwise more severe human relationship problems, such as domineering behaviour and prejudiced perception against the out-group were found to be significantly less in this study.

In order to improve working relationships between these groups a method that has been used at Karigiri is recommended. The method has two parts. This first is aimed at intrapersonal understanding and the second at the development of interpersonal skills. Role play that mimics their original work situation and an analysis of case histories were the methods of teaching were found to be more advantages in internalizing these skills.

SAHA, S.P. & DAS, K.K. Study of the characteristics and causes of relapse amongst leprosy cases in an urban area (Calcutta). *Ind.J.Leprosy*, 64(2), p. 169-178, 1992.

In this retrospective study of the 3737 cases of leprosy released from treatment and followed-up during 1975 to 1990, 63 had relapsed giving an overall relapse rate of 1.69%.

The relapse rate was significantly higher in the immunologically unstable N?L (Borderline) cases (2.9%). It was also higher in those who had dapsone monotherapy (1.92%) compared to those had multidrug therapy (1.01%). The relapse rate was higher in the 10 a 29 years age group and among those who became pregnant suggesting puberty and pregnancy could be risk factors. Males had a significantly higher relapse rate (2.1%) than females (1.1%) 45.2% of relapses in N (Non-lepromatous) cases occurred within 24 months and 71.4% within 36 months of stopping treatment. In those having monotherapy, 57.1% of relapses occurred within 24 months and 76.8% within 36 months. Regularity in treatment did not seem to have much influence on relapses rates.

SUITE, M & GITTENS, C. Attitudes towards leprosy in the outpatient population of dermatology clinics in Trinidad. *Leprosy Review*, 63(2), p. 151-155, 1992.

We interviewed a total of 92 dermatology clinic patients using a brief questionnaire to determine their knowledge, attitudes and beliefs about leprosy. This small survey helped to confirm our suspicions that some knowledge of leprosy is lacking and that much stigma still remains.

SUNDARESAN, T.K. issued involved in the rapid assessment of the leprosy problem. *Leprosy Review*, 63(3), p. 11 s-20s, 1992.

Sample surveys for estimation can prove very expensive and time-consuming because of the enormous sample sizes usually required.

Where sample surveys have to be undertaken, diagnoses should be limited to detecting a case of leprosy, without attempting skin smears etc. in order to classify by types. Usually enough knowledge is available on the approximate proportion of multibacillary (MB) cases in most communities, and this knowledge could be utilized for estimating the caseload by types of leprosy. Again intensive tracing of nonrespondents could be limited to either males or females depending on convenience, and well-known sex ratios among

patients utilized for deriving estimates for the other sex.

The type of rapid methods of estimation depend on three types of situations: (1) before multidrugtherapy (MDT); (2) 5 years or more after MDT; and (3) less than 5 years after MDT.

In the first situation one or more of the following methods are suggested:

- (i) extrapolation from registered cases;
- (ii) extrapolation from child prevalence; and
- (iii) conducting rapid village surveys.

In situations where MDT has been introduced for 5 years or more the registered cases plus a small number, depending on local experience, would seem to be adequate.

When MDT was introduced less than 5 years before, it is suggested that the prevalence rates be obtained by statistical interpolation drawing on the experience from areas which have had more than 5 years of MDT.]

TEKLE-HAIMANOT, R. et. al. Attitudes of rural people in central Ethiopia towards leprosy and a brief comparison with observations on epilepsy. *Leprosy Review*, 63(2), p.157-168, 1992.

To find out public attitudes toward leprosy a door-to-door survey was carried out in 1546 sampled households in the rural farming community of Meskan and Mareko in central Ethiopia, where the prevalence of leprosy is estimated to be 1:1000. Attitudes toward leprosy were compared with attitudes to epilepsy, studied in a previously performed survey in the same community. Eighty-seven per cent of the respondents were above the age of 25, and 59.5% were females. There were slightly more Muslims (54%) than Christians. The majority of the interviewees (87%) were farmers, with an illiteracy rate of 84%. Ninety-five per cent and 83%, respectively, were not willing to employ or work with a person having the disease. Seventy-five per cent would not allow their children to associate with a playmate suffering from leprosy. Comparative analysis of attitudes in the same community showed that negative attitudes toward leprosy were stronger than those toward epilepsy, particularly with regard to

matrimonial associations, sharing of accommodation, and physical contact with an affected person. The reasons for these differences appear to be community's deeply entrenched belief that leprosy is both hereditary and contagious, expressed respectively by 48% and 53% of the respondents. In order to minimize the perpetuation of negative attitudes, there is a need to educate and impress on the population that leprosy is a treatable infectious disease which is not congenitally acquired, and that it is even curable if detected early. In the study reinforces previously proposed suggestions that, in developing countries such as Ethiopia, leprosy care should be integrated into the general health services.

REABILITAÇÃO

ANTIA, N.H. Plastic footwear for leprosy. *Leprosy Review*, 61(1), p. 73-78, 1990.

The anaesthetic foot in leprosy poses the most major problem in the rehabilitation of its patients. Various attempts have been made to produce protective footwear such as the microcellular rubber-car-tyre sandals. Unfortunately these attempts have had little success on a large scale because of the inability to produce them in large numbers and the stigma attached to such unusual footwear. While such footwear may be superior to the 'tennis' shoe in protecting the foot from injury by the penetration of sharp objects, it fails to distribute the weight-bearing forces which is the major cause of plantar damage and ulceration in the anaesthetic foot. This can be achieved by providing rigidity to the sole, as demonstrated by the healing of ulcers in plaster of paris casts or the rigid wooden clog.

A new type of moulded plastic footwear has been evolved in conjunction with the plastic footwear industry which provides footwear that can be mass produced at a low price and which overcomes the stigma of leprosy. Controlled rigidity is provided by the incorporation of a spring steel shank between the sponge insole and the

hard wearing plastic sole. Trials have demonstrated both the acceptability of the footwear and its protective effects as well as its hard wearing properties.

CHATURVEDI, R.M. & KARTIKEYAN, S. Employment status of leprosy patients with deformities in a suburban slum. *Ind.J.Lepr.*, 62(1), p. 109-112, 1990.

In a poor slum area in suburban Bombay, a study of 129 leprosy patients with deformities revealed that only 46% were employed before the appearance of deformities and most of them had lost their jobs after deformities had appeared. Health education on care of anesthetic extremities did not have the desired impact on the patients, many of them had worsening of their deformities during the phase of their employment because they had to take up any kind of work in order to make a living. They were mostly poorly educated and lacked special skills. The only feasible alternative in this kind of situation appears to be a selective community-based rehabilitation of leprosy patients with deformities.

DUERKSEN, F. & VIRMOND, M. Carvable silicone rubber prosthetic implant for atrophy of the first web in the hand., *Leprosy Review*, 61(3), p. 267-272, 1990.

Muscular atrophy of the first web space in the hand is a common finding following ulnar nerve palsy and this deformity is very stigmatizing among leprosy patients in some countries and cultures.

We present our experience with the carvable soft-silicone rubber block implant to correct this deformity. We discuss the procedure, results and advantages over other techniques.

Fifteen operations were performed at the 'Lauro de Souza Lima' Research Institute, Bauru, Brazil during a period of six years. One complication was encountered due to an implant that was too large. The results were considered good in twelve instances and fair in three.

IYERE, B.B. Leprosy deformities: experience in Molai Leprosy Hospital, Maiduguri, Nigeria. *Leprosy Review*, 61(2), p. 171-179, 1990.

A total of 410 patients (288 males, 122 females) aged between 9 and 60 years with an average age of 32.5 years were assessed for deformities of the eyes, hands and feet. The objectives were to find out the number and types of leprosy deformities in the leprosy population of the hospital, the proportion of those deformed among them and to establish the deformity baseline for the hospital. The study lasted 1 year, 38.78% (26.59% males, 12.20% females) of those investigated had one or more deformities. Apart from plantar and palmar insensitivity which accounted for 17.91% and 17.24% of all deformities, the most frequent deformities were mobile claw hand 12.94%, plantar ulcers 10.78% and palmar ulcers 5.97% respectively. With the exception of eye deformities, males accounted for a higher proportion of all deformities. Hand deformities were the most frequent of the three parts of the body studied. The patient's problems were highlighted and the need for adequate management and self-care were emphasized.

KULKARNI, V.N. et. al. Newer designs in footwear for leprosy patients. *Ind.J.Lepr.*, 62(4), p. 483-487, 1990.

Micro-cellular rubber (MCR) foot-wear has been used widely over the past several years for the anaesthetic feet of leprosy. Although MCR has got good shock absorbing and moulding qualities, many tend to reject the foot-wear because of the stigma of the disease which it carries. Two newer models of foot-wear which would meet the demands of anaesthetic sole and avoid the stigma because of their resemblance to foot-wear available in the market were tried. Model mark II fulfilled the needs and was acceptable to the patients. Such models must be tried and acceptable and effective foot-wear need to be made available.

PREMKUMAR, R. et. al. Foot soaks for callosities and fissures. *Ind.J.Lepr.*, 62(4), p. 478-482, 1990.

A study to assess the effect of soap soaks and plain water soaks on the dry anaesthetic sole of 15 leprosy patients bearing multiple fissures and callouses is reported. A callous scraper devised by us was found effective. It is recommended that a hypotonic keratolytic solution such as toilet soap or plain water be used for soaking which has the effect of softening the Keratin. It may be better to use soap solution for this purpose.

THAPPA, D.M. et. al. Disability index of hands and feet in patients attending an urban leprosy clinic. *Ind.J.Lepr.*, 62(3), p. 328-337, 1990.

189 leprosy patients including 20 from a leprosy colony having disabilities and deformities were graded by the WHO (1960) classification and their disability indices were calculated. Disabilities occurred more frequently in males and the disability index was significantly higher in those with longer duration of the disease and in multibacillary patients. Majority of the disabled patients (82.5%) were manual workers, but the highest disability index was observed in beggars. Irregularly treated and untreated patients had significantly higher disability indices (DI 2.40 and DI 1.40) than those taking regular treatment (DI 1.09). No correlation was found between severity of disability and occurrence of type I and type II reactions. Disabilities of hands and feet occurred with equal frequency.

KARAÇORLU, M.A. et. al. The protective effects of methyl cellulose and conoid shields for lagophthalmos and corneal hypaesthesia in leprosy. *Leprosy Review*, 62(2), p. 201-205, 1991.

Lagophthalmos and corneal hypaesthesia are amongst the most frequently encountered lesions in leprosy and they can give rise to blind-

ness. Many measures (such as eye drops, protective conoid shields, muscle exercises, surgical treatment, etc.) have been used to protect the eyes under such circumstances and this paper examines the protective role of methyl cellulose and conoid shields in 41 patients. All of them had lagophthalmos (5 mm or more) and corneal hypaesthesia. They were divided into three groups. Group one had 15 leprosy control patients (27 eyes) who did not use methyl cellulose or eye shields. Group two had 16 leprosy patients (28 eyes) and they used methyl cellulose and eye shields when they felt discomfort in their eyes. Group three had 10 leprosy patients (17 eyes) and they used methyl cellulose and eye shields regularly. Statistically significant improvement was seen in group three. Further studies on larger groups of patients including the effects of different concentrations of methyl cellulose, on Schirmer test and tear break up time, may be of value.

RAMANATHAN, U. et. al. Psychosocial aspects of deformed leprosy patients undergoing surgical correction. *Lepr. Rev.*, 62(4), p. 402-409, 1991.

A psychosocial study conducted on 25 randomly selected leprosy patients undergoing corrective surgical procedures for their deformities. High anxiety and depression levels found preoperatively, reduced significantly after operation. Psychiatric assistance is needed for these patients in order to clear their psychic aberrations, create awareness, boost morale and to give self-confidence.

Only 50-75% of preoperative expectations were satisfied but that was only in 40% of patients. This call for a preoperative counselling session with the patients to help them reach the realistic goals that they can achieve. They should be told what benefits surgery can offer them and be made aware of the problems which persist after operation, such as anaesthesia and analgesia.

BRANDSMA, J.W. et. al. The international classification of impairments, disabilities and handicaps in leprosy-control projects. *Lepr. Rev.*, 63(4), 1992.

The use of a uniform language, which includes definitions of terms, is very important in the field of health care. It is important to have a common language for educational, research and communication purposes. Classifications can play a major role in the development of uniform reporting and registration systems. The purpose of this article is to familiarize leprosy workers with two classifications that are in common use in health care, a classification of diseases and classification used to describe the overall health status of a person, and to relate the 3 terms that are used in the latter classification, impairments, disabilities and handicaps, to leprosy.

GERSHON, W. & SRINIVASAN, G.R. Community-based rehabilitation: an evaluation study. *Lepr. Rev.*, 63(1), p. 51-59, 1992.

Leprosy gives rise to two types of stigmatization, one from the disease and its neuropathetic manifestations, with their resultant disability and handicaps, and the other due to social ostracism.

The process of rehabilitation should begin from the moment the disease is diagnosed, and the earlier its detection the better the prognosis for patients.

The family unit to which the patient belongs plays a vital role in his social life, ensuring and enhancing his self-respect and dignity in society, and this fact must be recognized when evolving a strategy for rehabilitation. In no circumstances should a patient be removed from his natural home environment.

It is important that the community is made leprosy conscious and gets more involved in the social assimilation of patients. Communication plays an important role throughout the rehabilitation process. One of the major functions is the removal of the social stigma in the family and in the community and this involves communication skills to ensure interaction between the

staff and patients' families and the education of the community.

A highlight of community-based rehabilitation is the excellent rate of repayment of loans by the patients to whom they were made. Also of note is the extent to which former defaulters make repayments due to the continuous rapport and good interpersonal relationship between the staff and patients.

Most of the subjects of this study were drawn from the lower economic strata of society and for them the most essential consideration is to make a living, however meagre. This problem is augmented in the case of leprosy sufferers, not only because of the fear and hostility which their disease excites in others, but because of their deformity and handicap. No rehabilitation programme can afford to ignore these factors which so seriously disturb the normal life of patients.

KARTIKEYAN, S. & CHATUVERDI, R.M. Pattern of leprosy deformities among agricultural labourers in an endemic district: A pilot study. *Ind.J.Lepr.*, 64(3), p. 375-380, 1992.

A study of 1,338 leprosy affected agricultural labourers in an endemic district revealed that 12% had deformities. The patient's sex, type of disease, duration and educational status seemed to influence pattern of leprosy deformities. The patients continued working despite deformities in order to avoid financial dependence on their family members and loss of dignity.

RAO, S.P. & BHUSARI, P.S. Evaluation of disability knowledge and skills among leprosy workers. *Ind.J.Lepr.* 64(1), p. 99-104, 1992.

The leprosy workers' knowledge and skills regarding disability prevention and control were quantified by a specially designed Objective Structured Clinical Examination (OSCE). The scorings were similar and showed no significant difference between supervisors and peripheral workers. It is suggested that the training component of disability control be improved with emphasis on problem-oriented learning.

SHWE, T. Prevalence of colour blindness among patients with leprosy. *Ind.J.Lepr.*, 64(4), p. 483-486, 1992.

Using Ishihara test plates the prevalence of colour blindness was studied on six hundred and ninety-seven leprosy patients and two hundred and ninety-two normal healthy controls. 7.88% of male patients with tuberculoid leprosy, 12.18% of male patients with lepromatous leprosy, and 0.67% of male controls were detected to be colour blind (red-green deficiency or total colour weakness). The differences between the different groups are significant. Among female patients and controls, only one lepromatous leprosy patient was detected to have red-green deficiency. This suggests the possibility of a genetic predisposition to *Mycobacterium leprae* infection in patients with leprosy.

THAPPA, D.M. et. al. Radiological changes in hands and feet in disabled leprosy patients: A clinico-radiological correlation. *Ind.J.Lepr.*, 64(1), p. 58-66, 1992.

Seventy-six consecutive leprosy patients with disabilities were subjected to radiological examination of hands and feet, and bone changes were found in 63 of them (82.9%). Specific, non-specific and osteoporotic bone changes were observed in 22.4%, 78.9% and 28.9% of cases respectively. Bone cysts (10.5%), subarticular erosions (10.5%) and enlargement of nutrient foramina (5.3%) were the common specific bone changes whereas bone absorptive changes (59.2%), soft tissue changes (39.5%) and concentric absorption (39.5%) were the most frequent nonspecific bone changes. Specific bone changes were more common in older patients (age 40 years) and nonspecific bone changes correlated with, duration of disease, duration of deformity, and disability index. Osteoporotic bone changes were found to be affected by ageing and severity of disability of hands and feet.

WEBER, M.W. et. al. Results of surgical procedures for the correction of foot-drop and of

lagophthalmus due to leprosy. *Leprosy Review*, 63(3), p. 255-262, 1992.

Leprosy mutilations of the muscles and skeleton can be relieved by reconstructive surgery, but evaluation of the results of these operations is seldom undertaken. Between 1975 and 1984, 59 leprosy patients were operated on at the Marie Adelaide Leprosy Centre, Karachi, Pakistan, for Lagophthalmus with the transposition of the posterior tibial muscle.

We were able to re-examine 39 patients: tibialis posterior transposition was performed 25 times, and temporalis transposition was carried out 33 times; 18 of the 25 patients with the tibialis posterior transposition were pleased with the result, 7 were not: 21 patients could extend their feet above the neutral position, 24 of the patients with the temporalis transposition were satisfied, 9 were not: complete closure was demonstrated in 21 eyes; Persistent corneal damage was noted in 15 eyes; 12 of the 23 male patients cared for themselves, 16 lived with their families; 7 of the 8 females patients lived with their families.

The results of the rehabilitation, in relation to the degree of mutilation, are considered satisfactory for a developing country. These surgical procedures give a good result, provided they are followed by intensive physiotherapy.

YAWALKAR, S. et. al. Modulan Gripaids for Leprosy Patients. *Int.J.Lepr.*, 60(2), p. 250-254, 1992.

Made-to-measure Modulan grip-aids were fitted to 755 articles for 155 patients with hand deformities due to leprosy. The acceptance of the grip-aids was, in general, good. No instance of contact dermatitis or skin irritation was reported. These grip-aids facilitated a normal grip with crippled hands, and thus considerably improved the quality of the patient's personal and working life. They increased the patient's self-esteem and self-confidence because he/she could handle everyday objects or tools without the help of others and could do his/her job - an important step toward social and economic rehabilitation.

TERAPÊUTICA

BANERJEE, D.K. & McDERMOTT LANCASTER, R.D. Effect of Simultaneous Administration of Interferon- γ and Chemotherapy Against *Mycobacterium leprae* in Experimental Infection In Nude Mice. *Int.J.Lepr.*, 58(4), p.690-696, 1990.

The possibility of synergy between immunotherapy with recombinant interferon-gamma (IFN- γ) and chemotherapy with rifampin (RMP) and dapsone (DDS) against *Mycobacterium leprae* was examined in nude mice. IFN- γ alone failed to show any effect on the growth of *M. leprae* in the nude mouse foot pad. No synergy was demonstrable between DDS, either at 0.0001% or at 0.001%, and IFN- γ . A subinhibitory level of RMP with IFN- γ was also ineffective, but RMP at 0.006% with IFN- γ produced a statistically significant enhancement of killing (26-fold) when compared with RMP at 0.006% only. It should be emphasized, however, that results obtained in the immunodeficient nude mouse model may not be comparable to those which might have been given by lepromatous leprosy patients.

CELLONA, R.V. et. al. Joint Chemotherapy Trials in Lepromatous Leprosy Conducted in Thailand, The Philippines, and Korea. *Int J.Lepr.*, 58(1), p.1-11, 1990.

Chemotherapy trials in lepromatous leprosy using various combinations of existing antileprosy drugs were conducted jointly by Korea, The Philippines, and Thailand. The general objective of these trials was to determine the most effective and practicable regimen or regimens for field application.

Lepromatous patients were divided into two groups: Group I was comprised of new, untreated patients infected with dapsone-sensitive *Mycobacterium leprae* and Group II consisted of relapsed patients with dapsone-resistant disease. Four different regimens were ad-

ministered to each group for 5 years. Comparison among the regimens was based on antileprotic efficacy, drug safety, acceptability, field practicability, and economic feasibility.

No significant differences were noted among the various regimens as judged by the reduction in the bacterial index (BI), clinical response, and change in biopsy index. Toxicity was seen only in the regimens containing prothionamide and rifampin. The regimens were acceptable to the patients and all were found practical for field use. Clofazimine, even in low doses, was found to suppress the frequency and severity of erythema nodosum leprosum. A multidrug regimen effective against both new and relapsed cases of lepromatous leprosy, whether dapsone sensitive or dapsone resistant, is recommended for field use. Given priority, the cost of the regimens is affordable in the three countries.

CHIPLUNKAR, S.V. et. al. Natural Killer-cell-mediated and Antibody-dependent Cellular Cytotoxicity in Leprosy. *Int J.Lepr.*, 58(2), p.334-341, 1990.

We have assessed the natural killer (NK cell-mediated) cytotoxicity and antibody-dependent cellular cytotoxicity (ADCC) in the peripheral blood lymphocytes (PBL) from untreated lepromatous leprosy (LL) patients, LL patients on multidrug therapy (MDT) with favorable responses (MDT-R), LL patients clinically classified as nonresponders to MDT (MDT-NR), treated tuberculoid leprosy (TT) patients, and healthy donors. NK cytotoxicity was modulated by treating the PBL with recombinant interferon-alpha (IFN- α) and recombinant interleukin-2 (IL-2).

The mean percent NK cytotoxicity of untreated LL patients (15 ± 3), treated MDT-R patients (20 ± 4), and treated MDT-NR patients (12 ± 4) was significantly lower than that of TT patients (39 ± 6) and healthy donors (37 ± 5). Treatment of effectors with IL-2 or IFN- α enhanced NK cytotoxicity in 5 of 6 untreated LL patients, 6 of 6 treated MDT-R LL patients, 4 of 5 and 3 of 5 treated MDT-NR LL patients, respectively, and 5 of 8 and 3 of 8 treated TT patients, respectively.

Although PBL from TT patients showed

initial NK activity comparable to that of healthy donors, fewer TT patients showed modulation of NK activity by IL-2, and IFN- α to a lesser extent. The ADCC activity was lower in untreated LL patients compared to treated patients, while TT patients had normal ADCC activity. The results indicate that although LL patients show lowered spontaneous cytotoxicity, it can be modulated favorably by lymphokines.

CHOPRA, N.K. et. al. A study of relapse in paucibacillary leprosy in a multidrug therapy project, Baroda District, India. *Lepr. Rev.*, 61(2), p.157-162, 1990.

In order to judge the value of therapeutic regimens in paucibacillary leprosy, knowledge of incubation time of relapses is essential, as this will define the length of time patients have to be followed up after treatment has been stopped. The prospective study of relapse includes paucibacillary cases of leprosy belonging to a nonlepomatous group consisting of tuberculoid, neuritic and indeterminate. Data are presented on the incubation time of 21 relapses after multidrug therapy in Baroda district; 76.19% of relapses occur during the first 2 years. This figure is most important in the analysis of results of drug trials in paucibacillary leprosy. This figure should also be relevant to regimens including drugs that are more bacteriocidal than dapsone, since the bacteriocidal activity has a bearing on the minimal necessary duration of treatment, but not on the incubation time of relapses.

With the introduction of bacteriocidal drugs e.g. rifampicin in multidrug therapy, the incidence of relapse are very low, hence relapse rates fall down to a very low level after multidrug therapy. Our study shows a mean relapse rate of 0.19% after multidrug therapy. Factors associated with the occurrence of relapse are discussed.

DHOPLE, A.M. & ORTEGA, I. An In vitro culture method for screening new drugs against *Mycobacterium leprae*. *Ind.J.Lepr.*, 62(1), p.66-75, 1990.

An in vitro culture system has been devised for the maintenance and growth of *M. leprae* in a cell-free medium. Cells from four-week old cultures could be transferred to fresh medium and growth was observed in subcultures. Using this system, the M.I.Cs of dapsone and rifampicin were determined. Dapsone at 25 ng/ml and rifampicin at 300 ng/ml completely inhibited the growth of host-grown as well as in vitro-adapted *M. leprae*. It was further shown that the effects of both the drugs were bacteriocidal; this observation was subsequently confirmed using mouse foot pad technique.

DHOPLE, A.M. et. al. Effect of Brodimoprim on *Mycobacterium leprae* in vitro and in mouse foot-pads. *Ind.J.Lepr.*, 62(1), p.76-86, 1990.

The new in vitro screening system reported earlier was adopted to determine anti-*M.leprae* activity of a dihydrofolate reductase inhibitor, brodimoprim, and the results were compared with those obtained using mouse footpad technique. Even though the MIC of brodimoprim against *M. leprae* was very high compared to other commonly used anti-leprosy drugs, in combination with dapsone it showed a remarkable synergistic activity in inhibiting the growth of *M. leprae* at concentrations much lower than the MICs of each of the drugs used singly. Similar effects were also demonstrated in mouse footpad experiments.

GROSSET, J.H. et. al. Clinical Trial of Pefloxacin and Ofloxacin in the Treatment of Lepromatous Leprosy. *Int.J.Lepr.*, 58(2), p. 281-295, 1990.

Twenty-one previously untreated lepomatous patients were randomized into two groups and treated with either 800 mg pefloxacin (PEFLO) or 400 mg ofloxacin (OFLO) once daily. The trial consisted of two parts: monotherapy from day 0 to day 56; and combined with the World Health Organization multidrug therapy (WHO/MDT) regimen for multibacillary (MB) leprosy from day 57 to day 180. Four patients were removed

from the trial because the organisms recovered from their pretreatment biopsies failed to infect mice. Among the remaining 17 cases, four (23.5%) had primary resistance to dapsone but all of them were susceptible to rifampin. The initial (day 0) proportion of viable organisms, as measured by mouse foot pad inoculation, varied tremendously from patient to patient despite randomization during admission. Definite clinical improvement was noticed in virtually all patients after 22 doses of treatment with either PEFLO or OFLO. A significant fall in the morphological index (MI) occurred as early as after 8 doses of PEFLO or after 22 doses of OFLO; the bacterial load also showed a moderate degree of reduction during the period of monotherapy. Although single-dose PEFLO or OFLO displayed only a modest degree of bactericidal effect against *Mycobacterium leprae*, about 99.9%, or 4 logs, of organisms viable on day 0 were killed by 22 doses either PEFLO or OFLO. No significant difference in the therapeutic effect was detected between the two regimens. During PEFLO or OFLO monotherapy, except in one patient (case monotherapy, except in one patient (case n° 10), the side effects were few and mild. Case n° 10 developed a psychic disorder after 27 days of PEFLO monotherapy, presumably due to the treatment with PEFLO. All of the patients tolerated the period of combined therapy extremely well, although some asymptomatic and transient laboratory abnormalities were observed. Because both PEFLO and OFLO displayed rapid bactericidal activities in human leprosy and were well tolerated by the patients, further clinical trials and field trials in evaluating the therapeutic effects of combined regimens containing both rifampin and PEFLO or OFLO are being organized. Since this is the first clinical trial in leprosy employing nude mice in combination with normal mice, for monitoring the therapeutic effects of antimicrobials, the advantages, limitations and appropriate timing in using nude mice are discussed.

GRUGNI, A. et. al. Relapses in Paucibacillary Leprosy After MDT-A Clinical Study. *Int. J. Lepr.*, 58(1), p.19-24, 1990.

A study was undertaken in a field-based project to assess the incidence and clinical profile of relapses occurring in paucibacillary leprosy patients after adequate doses of multidrug therapy (MDT). Of the 1509 paucibacillary patients who had received not less than 6 doses of MDT (WHO regimen), 85 relapsed; a relapse rate of 5.63% (17.5/1000 person years at risk). These relapses included 12 cases with features of reversal reaction. Seventy-nine percent of the patients relapsed with skin lesions. The relapse rate was higher in borderline cases and in those with more lesions, and it was lower in those who had received dapsone for at least 6 months after cessation of MDT. Seventy-four percent of the relapses were detected between 7 and 24 months of follow up. We feel that uniform clinical criteria should be formulated for the diagnosis of relapse. Individualization of therapy, rather than adhering to a fixed duration of MDT, would be likely to achieve satisfactory cure rates and fewer relapses.

JADHAV, V.H. et. al. Thalidomide in type-2 lepra reaction - a clinical experience. *Ind. J. Lepr.*, 62(3), p. 316-320, 1990.

A clinical experience of using thalidomide in type-2 lepra reaction (ENL) in 90 male patients - 57 with lepromatous leprosy (LL) and 33 with borderline lepromatous leprosy (BL) - is described. All the patients responded well although some took a longer time to improve. No major side effects were observed except for giddiness in 10 and gastrointestinal upsets in 7 patients. Thalidomide thus appears to be a very effective drug in the treatment of severe type-2 lepra reaction and apart from its historically well documented embryopathic effects, does not seem to have any other serious side effects in the patients under study.

KAR, P.K. et. al. Clinico-histopathological study of multidrug therapy in indeterminate leprosy. *Ind. J. Lepr.*, 62(1), p.98-103, 1990.

A Study was undertaken in 42 patients with indeterminate leprosy, to evaluate the efficacy of multidrug therapy (MDT) in Indeterminate

leprosy for 12 months. The main clinical finding was a single hypopigmented macule in 31 (73.8%) of the 42 cases. Histopathologically all cases showed lymphohistiocytic infiltration around skin appendages and dermal nerves. At the end of six months of MDT all the cases were evaluated clinically and 33 (85.5%) showed marked improvement or total inactivation while the lesions were still active clinically in 21.4% cases. Histopathological examination of lesions in 30 patients showed complete histological resolution in 9 cases only. At the end of one year of treatment it was found that 28 cases (66.3%) had become inactive and only 2 (4.7%) were found to be still active.

KAUR, I. et. al. Effect of Clofazimine on eye in multibacillary leprosy. *Ind.J.Lepr.*, 62(1), p.87-90, 1990.

Seventy-six patients of multibacillary leprosy received clofazimine as part of multidrug therapy (MDT) for periods ranging between 6 and 24 months. Complete ocular examination including slit lamp microscopy and examination of tears was carried out in all these patients. Reddish brown conjunctival and corneal pigmentation was seen in 46% and 53% of the patients respectively. Clofazimine crystals in tears were found in 32% of the patients. Apart from this no other eye changes or symptoms attributable to clofazimine were observed.

LECHAT, M.F. et. al. Selection of MDT Strategies Through Epidemiometric Modeling. *Int.J.Lepr.*, 58(2), p.296-301, 1990.

The epidemiometric model of leprosy, built on Polambakkam, India, data, is used to compare the impact on incidence of dapsone and different multidrug therapy (MDT) strategies. The simulations show that generalization of MDT could have a dramatic impact on transmission of the disease. Relapses after MDT, although important from an individual point of view, have a negligible influence on the incidence. Introduction of MDT requires investments that, during the first few

years of the program, are much greater than for dapsone monotherapy. These are, however, rapidly absorbed due to the rapidly declining number of new cases, particularly when MDT is not limited to multibacillary cases but is administered to all patients.

NAIK, S.S. et. al. Pattern of drug compliance in leprosy patients attending urban centres - a longitudinal study. *Ind.J.Lepr.*, 62(3) p.305-309, 1990.

The pattern of drug compliance in 485 leprosy patients attending urban leprosy centres in Bombay was studied for 2 years. The study subjects included 113 patients with paucibacillary leprosy under dapsone monotherapy, 241 patients with paucibacillary leprosy under multidrug therapy and 131 patients with multibacillary leprosy under multidrug therapy. Their urine samples had been checked at least 6 times during the 2 years by DDS tile test at the time of their clinic attendance. The urine test results were not disclosed to the patients, but patients showing negative results were counselled about the need for regular drug intake.

35% of the patients were "Regular through out", 13% were "Irregular through out" and the other 52% who "Tended to be irregular" in their drug intake become "Regular" after counselling. Regularity in drug compliance was better in patients on multidrug therapy than in those on monotherapy. It is suggested that periodic testing of urine for checking for regularity of drug intake and subsequent counselling of patients should be made a routine practice to maintain drug compliance at a high level.

N'DELI, L. et. al. Effectiveness of Pefloxacin in the Treatment of Lepromatous Leprosy. *Int.J.Lepr.*, 58(1), p.12-18, 1990.

As a first clinical trial of a fluoroquinolone derivative in leprosy, ten previously untreated lepromatous leprosy patients, about two fifths of them with primary dapsone resistance but all susceptible to rifampin, were treated with pefloxacin 400 mg twice daily for 6 months. Defi-

nite clinical improvement was observed in all ten patients as early as 2 months after beginning treatment, and the morphological index was also drastically decreased to the baseline during the same period. The rapid bactericidal effects, as measured by serial mouse foot-pad inoculations, were demonstrated to the extent that about 99% of the bacilli were killed during the first 2 months of treatment. However, the bacterial load, in terms of the bacterial index and the number of acid-fast bacilli per mg of tissue, of the patients was only moderately reduced. The side effects were mild, and the patients tolerated the treatment well.

PATTYN, S.R. et. al. Evaluation of five treatment regimens, using either dapsone monotherapy or several doses of rifampicin in the treatment of paucibacillary leprosy. *Leprosy Review*, 61(2), p.151-156, 1990.

The objective of the present study was to define short-course treatment regimens for PB leprosy and to compare them with the 'classical' dapsone treatment and the WHO-PB regimen. Five treatment regimens were studied and evaluated by the histologic evolution. The regimens were: (1) dapsone 100 mg daily, non-supervised for 3 years; (2) RMP 900 mg supervised, once weekly, 8 doses; (3) idem 12 doses; (4) RMP 600 mg, once monthly, supervised, 6 doses and during this treatment dapsone 100 mg daily unsupervised; (5) RMP 600 mg together with dapsone 100 mg daily, supervised for 6 days. For each of these regimens there were between 114 and 195 person-years of follow-up.

Results are comparable for the 5 treatment regimens, and reach 65-75% cure rates at 36 months and 80-90% at 48 months after the start of therapy. The relapse rate for all groups is about 0.5% per year. The difficulty for the diagnosis of relapse in PB leprosy discussed.

It is concluded that treatment of PB leprosy can be relatively simple but that a relatively long time is needed to evaluate its effect.

RAJAH, M.A. Eye in Multi Drug Therapy. *Ind.J.Lepr.*, 62(1), p.33-38, 1990.

Eyes of 237 multibacillary leprosy patients on Multi Drug Therapy were studied for a minimum period of 2 years and maximum period of 4 years. Ocular status remained unaltered in 75%, improved in 16% and there was worsening in 9% during the study period. The changes in those worsened were of microscopic nature and seen mostly among those with long duration of disease and among reactors.

THOMAS, A. et. ai. Controlled Clinical Trial of Two Multidrug Regimens with and without Rifampin in Highly Bacilliferous BULL South Indian Patients: A Five-year Report. *Int.J.Lepr.*, 58(2), p.273-280, 1990.

A controlled clinical trial of two multidrug regimens in multibacillary lepromatous and near-lepromatous patients with a bacterial index (BI) of 2.5 or more was conducted. Patients were randomly allocated to either a two-drug regimen of dapsone plus ciprofloxacin for 60 months or a four-drug regimen of rifampin, isoniazid, dapsone, and ciprofloxacin for the first 3 months and ciprofloxacin plus dapsone for the next 57 months. There was no difference between the rifampin and nonrifampin regimens with respect to the clinical improvement or bacteriological status of the patients at 60 months. Reactive states and neuritis were observed to be equal in the two patient groups.

ZEIS, B.M. et. al. The influence of structural modifications of dihydrophenazines on arachidonic acid mobilization and superoxide generation by human neutrophils. *Leprosy Review*, 61(2), p. 163-170, 1990.

In this study the effects of nine dihydrophenazine derivatives, relative to ciprofloxacin (B663), on the N-formyl-L-methionyl-L-leucyl-L-phenylalanine (FMLP) stimulated release of superoxide anion and on the spontaneous generation of arachidonic acid by human neutrophils were investigated. Previous findings that the pro-oxidative activity of the agents depended largely on the substitution in position 2 of the phenazine molecule and on chlorination in the paraposition of the phenyl and anilino rings were confirmed. Only

riminophenazines, but not aposafranone derivatives or the imidazophenazine B621, could enhance superoxide release from activated neutrophils. The lack of chlorination of the phenyl and anilino rings could be compensated for by chlorine substitution in position 7 of the phenazine core.

The priming effect of the agents on FMLP stimulated superoxide generation was completely prevented by the phospholipase A₂ inhibitor 4-*p*-bromophenacyl bromide. Furthermore pro-oxidative activities correlated closely with a stimulatory effect of the agents on arachidonic acid release. It was therefore concluded that dihydrophenazine derivatives with pro-oxidative properties can prime neutrophils for FMLP-stimulated superoxide release by modulation of phospholipase A₂ activity.

ABRAHAM, B. et. al. Rifampin in Drug-incorporated Diet: Effect of Duration and Temperature of Storage Relevance to Drug-susceptibility Testing in Mice Inoculated with *M.leprae*. *Int.J.Lepr.*, 59(1), p. 68-75, 1991.

This paper is in two parts. Plasma concentrations of rifampin were assayed at 11 time points in 24 hr in mice fed one of three dosages of rifampin, either by gavage or by dietary incorporation. The drug-mixed diets had been stored for a maximum of 3 weeks at 4°C or at room temperature (30°C-35°C). The peak concentration of rifampin produced by gavage was approximately 1 1/2 times higher than the maximum plasma concentration of the corresponding dosage in fresh diet. Plasma concentrations decreased with the increasing duration of storage of the drug-mixed diet, irrespective of whether the diet was stored at 4°C or at room temperature. This decrease was less when the diet was stored at 4°C than at room temperature.

Drug levels were also assayed in another set of mice selected from ongoing drug-susceptibility experiments; these mice were fed a rifampin-incorporated diet stored at room temperature. The plasma concentrations in these mice, assayed at the time of foot pad harvest, were generally higher than in the 24-hr experiment. The harvest results from these mice were compared

with the harvest results from a third set of mice, also from ongoing drug-susceptibility experiments, but fed a rifampin-mixed diet stored at 4°C. Multiplication of *Mycobacterium leprae* in mouse foot pads was prevented by rifampin mixed in the diet at a dosage of $\geq 0.003\%$, whether stored at room temperature or at 4°C.

This study defines the criteria for rifampin resistance of *M. leprae* in the mouse foot pad by discussing methods of rifampin administration, the plasma concentration curves that result, and the effect of these on the multiplication of the organisms in the mouse foot pad.

BECC-BLEUMINK, M. Allocation of Patients to Paucibacillary or Multibacillary Drug Regimens for the Treatment of Leprosy A Comparison of Methods Based Mainly on Skin Smears as Opposed to Clinical Methods-Alternative Clinical Methods for Classification of Patients. *Int.J.Lepr.*, 59(2), p.292-303, 1991.

This paper reports on the experience with classification of patients at the All-Africa Leprosy and Rehabilitation Training Centre (ALERT) in the Shoa Province in Ethiopia. Classification on clinical grounds is compared with classification which is primarily based on the result of skin-smear examinations. In addition, possible alternative clinical methods for the allocation of patients to the multidrug therapy (MDT) regimens are discussed.

The analysis includes 1525 new patients. In 730 patients classified clinically as paucibacillary (PB), this classification was not confirmed by skin-smear results in only 1.5%; whereas in 795 patients classified clinically as multibacillary (MB), the classification was not confirmed in 21.1%. Possible reasons, notably for the latter discrepancy, are discussed.

Based on an assessment of the correctness of the diagnosis and the most probable classification, it was found that if classification had been based on the skin-smear results, 9.3% of the 795 patients classified as MB would have been classified incorrectly as PB. Classification based on clinical signs resulted in incorrect classification, MB instead of PB, of 8.7% of the 795

patients. Over-classification of MB patients, which was found to be supervisor related, is open to improvement by a strict application of clinical criteria for classification. The experience in the ALERT leprosy control program shows that classification which is based on clinical signs may, in particular, result in some PB patients being classified as MB, while classification based on the results of skin-smear examinations is more likely to result in some MB patients being classified as PB. It was concluded that, provided a number of requirements aimed at limiting the number of misclassified patients are introduced, patients can be classified based on clinical signs and, hence, in the absence of skin-smear services for routine classification purposes.

BECX-BLEUMINK, M. Experience with WHO-recommended Multidrug Therapy (MDT) for Multibacillary (MB) Leprosy Patients in the Leprosy Control Program of the All Africa Leprosy and Rehabilitation Training Center in Ethiopia: Appraisal of the Recommended Duration of MDT for MB Patients. *Int. J. Lepr.*, 59(4), p. 558-568, 1991.

During 1981 a World Health Organization Study Group recommended that multibacillary (MB) leprosy patients should be given multidrug therapy (MDT) for at least 2 years and, wherever possible, until skin-smear negativity. This paper reports on the experience with MDT for MB patients under routine field conditions in the leprosy control program of the All Africa Leprosy and Rehabilitation Training Center (ALERT) in the Shoa Region of Ethiopia. The period of MDT to reach skin-smear negativity was evaluated for 348 new MB patients. Only 31.6% of these patients could be released after 26 four-weekly doses of MDT, and 19.8% needed over 5 years of MDT. The average period of MDT to reach skin-smear negativity was estimated at about 4 years. Of 3343 patients of cohorts which, almost exclusively, consisted of patients treated with dapsone before MDT, 72.8% were released after 26 four-weekly doses of MDT; whereas of 712 patients of cohorts which mainly included new patients, only 23.5% were released. It was estimated that if

MDT would be stopped, regardless of skin-smear results, after 26 four-weekly doses of the drugs collected within a period of 3 years, about 80% of the patients would complete treatment. The operational problems with continuation of MDT until skin-smear negativity are discussed.

Although as yet it has not been proven by study results that after 2 years of MDT the relapse rate will be low, the available knowledge indicates that this is likely to be the case. Based on a) probability, b) the finding that 2 years of MDT can be maintained in the majority of the patients, and c) the operational difficulties with the continuation of MDT until skin-smear negativity, it is recommended that MDT should be limited to 2 years. MDT of limited and fixed duration will facilitate the implementation and expansion of the treatment in parts of the world where most patients are not yet benefitting from this treatment.

BLOK, L.M. et. al. A retrospective study on seven years of multiple drug treatment for paucibacillary and multibacillary leprosy, in Bayara General Hospital, Nigeria. *Leprosy Review*, 62(2), p.193-200, 1991.

In Bauchi State, Nigeria, a retrospective study was carried out among 973 patients on multidrug therapy (MDT), multibacillary (MB) and paucibacillary (PB), and 118 patients on a dapsone-ciofazimine therapy. These patients were registered between January 1983 and September 1989. Clinical results and the problem of defaulting were investigated.

The most important conclusions drawn are: although relapses occur, MDT-PB can be a valuable treatment; health education, shorter duration of treatment and permission to come less often lower the default rate, but in spite of this, the distance between home clinic remains a problem.

BOERRIGTER, G. et. al. Four-Year Follow-up Results of a WHO -recommended Multiple-drug Regimen in Paucibacillary Leprosy Patients in Malawi. *Int.J.Leprosy*, 59(2), p. 255-261, 1991.

An evaluation of a World Health Organization-recommended multidrug therapy (WHO/MDT) in 499 paucibacillary leprosy patients is described. Patients were followed for 48 months after completion of treatment. Overall relapse rates after treatment were found to be 6.5 per 1000 person years (95% confidence interval 3.4-11.4). There were 12 relapses. A relative lack of cell-mediated immunity, as suggested by number of lesions, clinical classification and lepromin test results, and poor compliance with the dapsone component of WHO/MDT, appeared to be associated with a marginally increased risk of relapse. Severe type 1 reactions after completion of treatment occurred in 17 (3.5%) patients, 15/17 during the first 12 months of follow-up. Overall, 12 (2.5%) patients developed new disabilities during or after WHO/MDT.

BYRD, S.R. & GELBER, R.H. Effect of dapsone on haemoglobin concentration in patients with leprosy. *Leprosy Review*, 62(2), p.171-178, 1991.

Haemolysis and frank anaemia from dapsone therapy of leprosy has been long recognized. However, the frequency and severity of this side-effect have not been well documented. We report herein a retrospective analysis of the effect of daily dapsone (generally 100 mg/day) on the haemoglobin concentration of 100 leprosy patients undergoing initial chemotherapy. The average haemoglobin was found to fall significantly by almost 2 g/dl, from 14.25 ± 1.27 g/dl to a nadir of 12.31 ± 1.61 (P < 0.001). Eighty-three percent of patients had a fall of haemoglobin concentration of 1 g/dl or more, while in 16% of patients the haemoglobin fell ≥ 3 g/dl. Increasing age was found associated with an increased magnitude of dapsone-related haemolysis (P<0.004). Decreasing the daily dose of dapsone was associated with an increased haemoglobin concentration (P<

0.001%). We have concluded that dapsone commonly results in not only haemolysis but a significant decrease in haemoglobin concentration. This may have serious clinical implications, especially in endemic areas, where, owing to nutrition, malaria, and intestinal parasitism, the haemoglobin concentration is already compromised.

CARTEL, J-L. et. al. Longitudinal study on relapses of leprosy in Polynesian multibacillary patients on dapsone monotherapy between 1946 and 1970. *Leprosy Review*, 62(2), p.186-192, 1991.

Between 1946 and 1970, 295 new leprosy patients were detected in French Polynesia, of whom 145 were multibacillary. Of these 145, put on dapsone monotherapy, 131 reached bacteriological negativity in a period of time ranging from 2 to 12 years (average 4.72 years) and were followed-up for a period of time ranging from 19 to 43 years (median follow-up period after bacteriological negativity: 18 years). Among the 131 patients, 36 relapses were detected, the first one 4 years after bacteriological negativity and the last one 26 years after. The crude relapse rate was 27.5%, the risk of relapse was 1.39 per 100 patient years and the cumulative relapse probability, calculated using the lifetable method, reached 0.38 ± 11 by year 31 of the study. From these findings one may assume that at least in French Polynesia, one-third to one-half of multibacillary patients put on dapsone monotherapy would relapse if still present 36 years after bacteriological negativity. Such results re-emphasize the need for leprosy patients to be treated with multidrug therapy as recommended by WHO.

CHATURVEDI, V. et. al. On the Value of Sequential Serology with a *Mycobacterium leprae*-specific Antibody Competition ELISA in Monitoring Leprosy Chemotherapy. *Int.J.Leprosy*, 59(1), p.32-40, 1991.

The *Mycobacterium leprae*-specific antibody assays-a serum antibody competition test

(SACT-ELISA) for the epitope on the 35-kDa protein, and an enzyme immunoassay for the disaccharide epitope of phenolic glycolipid-I (PGDS-ELISA)- were evaluated as tools for the serological monitoring of chemotherapy in 20 lepromatous and 6 tuberculoid leprosy patients. In addition to estimates for *M. leprae*-specific antibodies, assessments of the bacterial index (BI) and clinical activity of the disease were also carried out prospectively in these patients on two to four occasions over a period of 19 months. In most cases, a decline in the BI, clinical scores, and antibody levels was observed during the course of treatment. The relative rate of decline was steepest and least variable with the SACT-ELISA, followed by the PGDS-ELISA and the BI. In some patients who showed a static or even an increased BI, despite marked clinical improvement, the antibody levels decreased. These data indicate that, unlike the BI, there is a greater dependence of specific antibody levels on the viability of *M. leprae*. This, combined with the fact that antibody titers would reflect the antigen load in the whole body, makes *M. leprae*-specific serology a promising tool for monitoring chemotherapy in leprosy patients.

CONSTANT-DESPORTES, M. et. al. A Case of Relapse with Drug-susceptible *M. leprae* after Multidrug Therapy. *Int.J.Lepr.*, 59(2), p. 242-247, 1991.

A male born in 1930 was diagnosed as smear-positive borderline leprosy in 1971, and was treated with dapsone and/or sulfamethoxy-pyridazine from 1972 to 1980 with clinical improvement. However, new skin lesions with smears strongly positive appeared in August 1980, and he was diagnosed as having down-graded to lepromatous (LL) leprosy, but the bacilli recovered from the skin biopsy were fully susceptible to both dapsone and rifampin by mouse foot pad technique. Between 1981 and 1983, the patient was treated with 24 months of rifampin 600 mg and dapsone 100 mg daily, supplemented with prothion-amide 500 mg daily during the initial 3 months, and his skin lesions gradually improved during treatment with the combined

regimen. Afterward, the patient was kept under surveillance without treatment. From 1984 to 1986, his skin smears were negative, and no bacilli could be found from a skin biopsy taken in 1985. Then in 1987, 52 months after stopping treatment, new skin lesions appeared with a high concentration of *Mycobacterium leprae* (2×10^6 /mg tissue). The drug-susceptibility test again demonstrated that the organisms were fully susceptible to both dapsone and rifampin. Apparently the relapse was due to remultiplication of drug-susceptible persisters.

DHOPLE, A.M. et. al. In vitro and in vivo interactions of drugs used in multidrug therapy in leprosy. *Ind.J.Lepr.*, 63(2), p.166-179,1991.

Interactions of different drugs commonly used in multiple drug therapy were evaluated using both in vitro culture (cell-free as well as macrophage) system and mouse footpad. No additive effects were obtained in the in vitro system when dapsone was combined with either rifampicin or clofazimine, while a strong antagonism was observed when clofazimine was combined with rifampicin but not with rifabutin. In the mouse footpad system, a strong synergism was obtained when clofazimine was combined with either rifampicin or rifabutin, but significant antagonism was observed with the combination of clofazimine and dapsone.

DIETZ, M. et. al. Intrabacterial Sodium-to-Potassium Ratios and ATP Contents of *Mycobacterium leprae* from Ofloxacin-treated Patients. *Int.J.Lepr.*,59(4), p. 548-557, 1991.

In a clinical trial including 17 multibacillary leprosy patients the in vivo effectiveness of ofloxacin on *Mycobacterium leprae* was tested via mass spectrometric determination of intrabacterial ratios of the concentrations of the sodium and potassium ions of individual organisms and of the ATP content per 10^6 bacteria isolated from skin biopsies. After 3 months of treatment, the in vivo drug effect could be determined with at least one of the two methods in 14 cases. Both methods revealed

that in two cases the bacteria definitely did not respond to a 3-month ofloxacin monotherapy (200 mg twice daily). In three further cases a nonresponse of the *M. leprae* organisms was suspected from the mass spectrometric measurements. In the responder cases, the *M. leprae* were severely impaired. From the intrabacterial cation ratios the percentage of viable organisms averaged over all untreated biopsies was determined to be 58% and the percentage-killing during the first 3 months of treatment was 72%.

EKAMBARAM, V. & RAO, M.K. Relapse rate in paucibacillary leprosy patients after multidrug therapy in north arcot district. *Ind.J.Lepr.*, 63(1), p. 34-42, 1991.

Surveillance data from 14,227 paucibacillary (PB) patients who had been released from treatment one year earlier, after completing multidrug therapy (PB regimen) for 6 to 12 months, were analysed to assess relapse rates and the influence of three variables, viz., number of lesions, nerve involvement and duration of treatment. The overall relapse rate at one year of surveillance was acceptably low at 0.34%. Relapse rates were about four times higher when there were many (4-9) lesions, or, when nerve was involved (0.80% cf 0.20%). Extending the duration of treatment beyond 6 months did not reduce the relapse rates significantly in the high risk groups. Detection of PB cases early, before these risk factors become operative, and treating them with MDT would appear to be the best strategy to minimize relapse rates.

FFYTCHÉ, T.J. Residual sight-threatening lesions in leprosy patients completing multidrug therapy and sulphone monotherapy. *Leprosy Review*, 62(1), p. 35-43, 1991.

An analysis of data derived from standardized surveys of the ocular findings in cross-sections of the leprosy population in 23 areas is presented. It shows that 24.3% of the patients completing multidrug therapy and 32.9% of those

completing sulphone monotherapy have ongoing eye problems which have the potential to lead to blindness or severe visual impairment. Most of the ocular complications involve the lids, cornea and anterior uveal tract, but a significant proportion of patients had cataract threatening vision.

If left unsupervised, many of these patients will develop major visual problems which could have been avoided. It is important that completion of systemic leprosy therapy should not be regarded as a guarantee that the eyes are safe, and that regular ocular supervision should be continued long after the patient has been classified as 'cured'.

KATOCH, K. et. al. Clinical and Bacteriological Progress of Highly Bacillated BL-LL Patients Discontinuing Treatment After Different Periods of MDT. *Int.J.Lepr.*, 59(2), p.248-254, 1991.

Highly bacillated lepromatous patients (BULL) with an initial bacterial index (BI) of 4 to 6 + are being treated with a modified World Health Organization-recommended multiple-drug therapy (WHO/MDT) regimen consisting of rifampin 600 mg once a month, clofazimine 100 mg on alternate days, and dapsone 100 mg daily. The clinical and bacteriological profiles of the patients who had discontinued treatment at different durations have been compared with patients who took the same treatment until attainment of smear negativity. All six of the patients who had discontinued treatment at 12-18 months had worsened clinically and bacteriologically, and viable bacilli could be demonstrated in those tested for ATP. In four patients who had stopped treatment at 24-30 months, the BI continued to fall and there was no clinical or bacteriological worsening in 1 to 2 years of follow-up. The fall in the BI in five cases who had discontinued treatment at 36-44 months was comparable to those on continuous treatment, and there was no worsening. These observations indicate that with the conventional MDT regimen it is not advisable to stop treatment at 12 and 18 months. It appears that treatment should be continued for at least 2 years, and longer in the untreated highly bacillated cases. Prospective

clinical trials with a sufficient number of cases and long-term follow-up need to be carried out to ascertain the optimum duration.

MATHAI, R. et. al. Fixed Duration MDT in Paucibacillary Leprosy. *Int.J.Leprosy*, 59(2), p.237-241, 1991.

The World Health Organization (WHO) has recommended a fixed duration of multidrug therapy (MDT) for paucibacillary leprosy which is currently widely implemented in India. A clinico-pathological study was initiated in 1984 to assess the efficacy of this regimen. The clinical and histological responses of the patients to MDT were assessed at the end of 6 months, when their treatment was stopped, and at 2 1/2 years, when they were released from surveillance, and compared with the responses of a matched patient group to conventional dapsone (DDS) monotherapy during the same period. Of 28 patients who completed the MDT schedule, there was less than 60% improvement in 33% of them when treatment was stopped at the end of 6 months and in 20% of them at the end of 2 1/2 years. Of 26 patients receiving DDS monotherapy, 37% showed less than 60% improvement at the end of 6 months but only 8.8% had less than 60% improvement at 2 1/2 years. It is concluded that MDT for paucibacillary leprosy as recommended by WHO may not have a major advantage over DDS monotherapy, since about 20% of those patients on MDT continue to have evidence of active disease when discharged from surveillance.

PANDIAN, T.D. et. al. Risk of relapse among non-lepromatous patients released from treatment after dapsone monotherapy. *Leprosy Review*, 62(3), p. 288-296, 1991.

Information on 14,625 non-lepromatous patients released from treatment after dapsone monotherapy and followed up to a maximum of 15 years at the ILEP project. Dharmapuri, India, was analysed to study the pattern of relapses. The overall relapse rate was 5/1000 person years.

Males had a higher relapse rate than females. The risk of relapse increased with age, number of lesions and duration of treatment. The risk for relapse remained constant over several years after release from treatment. Even through the absolute risk for relapse after MDT may be different, the pattern of relapses and the factors affecting it may be similar to what has been shown in this study.

PATTYN, S.R. *Anti-Mycobacterium leprae* Activity of Several Quinolones Studied in the Mouse. *Int.J.Leprosy*, 59(4), p. 613-617, 1991.

The *anti-Mycobacterium leprae* activity of several fluoroquinolones (A-56619, A-56620, ofloxacin, fleroxacin, lomefloxacin, temafloxacin, tosufofloxacin, and PD-117596) was studied in the mouse. In a dosage of 150 mg/kg administered daily, A-56619 is active and A-56620 is inactive against *M. leprae*. Ofloxacin administered daily for 2 weeks at 300 mg/kg is bactericidal. The minimal effective dose of PD-117596, lomefloxacin and temafloxacin is less than 37.5 mg/kg. When administered at 300 mg/kg at monthly intervals temafloxacin, PD-117596, and ofloxacin are bacteriostatic; while fleroxacin and lomefloxacin are bactericidal. Tosufofloxacin is less active than the other quinolones included in the present study.

PATTYN, S.R. et. al. A controlled therapeutic trial in paucibacillary leprosy comparing a single dose of rifampicin with a single dose of rifampicin followed by one year of daily dapsone. *Leprosy Review*, 62(2), p. 179185, 1991.

The cure rates of two treatment regimens in PB leprosy were compared in a prospective randomized trial: treatment U consisting of a single dose of rifampicin 40 mg/K bodyweight, and treatment A of rifampicin 1500 mg in a single dose, followed by one year of daily dapsone 100 mg. In patients with a BI=0, the cure rates evaluated on the basis of histopathology of skin biopsies, were identical for the two regimens but in patients with a BI=1, cure and relapse rates were unacceptable.

For this reason and particularly the need to separate patients on the basis of the BI in skin biopsies, the single dose regimen does not appear to be suited wide-scale application.

RAMESH, V. et. al. Multibacillary Leprosy Presenting as a Solitary Skin Lesion; Report of Three Cases and Its Significance in Control Programs. *Int. J. Lepr.*, 59(1) p.1-4, 1991.

Three patients with solitary skin lesions showing the cardinal signs of leprosy were seen and clinically classified among the paucibacillary cases. Initially, they were treated with two drugs (rifampin and dapsone) as recommended by the WHO Expert Committee. On the first visit of their follow-up, they were seen to be histopathologically either in the borderline (BB) or borderline lepromatous (BL) group, and acid-fast bacilli were demonstrated in the sections. Later they were put on three drugs (rifampin, dapsone and clofazimine) as given for multibacillary cases, and therapeutically they also behaved like bacilliferous leprosy. Such cases are rare and the reasons for the occurrence are not clear. Further studies on the subtle relationship between the local host factors and the virulence of the organisms grown from these lesions may offer an explanation. In light of these cases and previous reports of even lepromatous leprosy presenting as a single skin lesion, field workers-including both medical and paramedical workers-should carefully perform and interpret slit-skin smears from clinically diagnosed paucibacillary cases so that such unusual presentations of the disease are treated appropriately and not missed.

REDDY, P.K. & CHERIAN, A. Relapse in leprosy after multidrug therapy and its differential diagnosis with reversal reaction. *Ind. J. Lepr.*, 63(1), p. 61-69, 1991.

Relapse may be caused either by persists or through reinfection in a patient released from treatment after MDT. Differentiating relapse from reversal reaction is not always easy, on histological and clinical grounds. A therapeutic

trial with steroids for 2-4 weeks can be used to differentiate relapse from reversal reaction occurring in the skins. However, if a patient develops nerve function deficit after release from treatment, it is best to initiate antileprosy treatment along with a long course of steroids.

REVANKAR, C.R. et. al. Reduction in caseload after multidrug therapy in an urban leprosy control programme-a retrospective study in Bombay. *Leprosy Review*, 62(1), p. 44-48, 1991.

A fall in the active registered case prevalence rate together with a fall in the active caseload per worker after the introduction of multidrug therapy (MDT) is becoming a managerial issue in leprosy control. A retrospective analysis was undertaken to assess the caseload per paramedical worker with reference to active cases for treatment (3341), cases for surveillance (2227) and cases for care after cure (165) at the end of December 1989. All these cases were under the care of 24 paramedical workers.

The analysis showed that the caseload per worker was 239 (active cases 139, plus surveillance cases 93, plus care after cure cases 7), through active registered case prevalence rate declined from 1.82/1000 (before starting MDT) to 0.79/1000 by the end of December 1989. The case detection rate was 0.49/1000 by the end of 1989. so, although the active registered case prevalence rate declines, the worker will have enough to do because of the need for surveillance and the detection of relapses, early neuritis, early disabilities and care after cure. Simultaneously, new case detection and treatment must be continued.

All these aspects need to be considered when programme managers are reviewing leprosy control strategy.

TANAKA, M. et. al. Effects of Cyclosporin A on Bacterial Growth and Immunological Responsiveness in BALB/c Mice Infected with *Mycobacterium Leprae*. *Int. J. Lepr.* 59(4), p. 598-604, 1991.

When BALB/c mice were infected with *Mycobacterium leprae* and orally treated 6 times weekly with a dose of 8 mg/kg cyclosporin A (CsA) for 19 months, the number of organisms was slightly higher at 19 months as compared with mice in which the dose of CsA was gradually decreased after 6 months and discontinued at the 8th month ($p < 0.01$ for the 15th and 19th months). Lymphocyte blast transformation (LBT) showed that spleen cells from CsA-treated mice 4 weeks after infection with *M. leprae* and 3 weeks after CsA treatment was stopped responded to the sonicated supernatant of *M. leprae* suspension (SS), *M. leprae* (MI), and concanavalin A (ConA) less than those cells from mice not treated with CsA. This response was dose-dependent. At week 15, 14 weeks after CsA administration was stopped, the LBT response to SS and MI by cells from *M. leprae*-infected mice exceeded that of mice without CsA treatment, and the response to ConA in *M. leprae*-infected mice was less than that in uninfected mice without CsA-treatment. Thus, if CsA was administered, the T-cell functions were suppressed. However, when CsA treatment was discontinued for longer periods, the T-cell function was activated. From these results, we speculate that *M. leprae* would have the capability of growing more abundantly in mice treated with CsA 100 mg/kg for 1 week every month.

VACHULA, M. et. al. Effect of Glucocorticoids and Interferon- γ on the Oxidative Responses of Monocytes from Leprosy Patients and Normal Donors. *Int. J. Lepr.*, 59(1), p. 41-48, 1991.

Leprosy patients suffering from erythema nodosum leprosum are frequently treated with glucocorticosteroids. The role glucocorticosteroids and interferon-gamma (IFN- γ) play in regulating the interaction of phagocytic

cells with *Mycobacterium leprae* was examined. Monocytes from leprosy patients receiving prednisone therapy responded to lower concentrations of IFN- γ *in vitro* with enhanced superoxide anion release when challenged with *M. leprae* or *M. bovis* BCG than did monocytes from healthy subjects and other leprosy patients. Although the number of patients was small and the population heterogeneous, the data suggested that prednisone could affect IFN- γ efficacy and led to the examination of the effect of glucocorticosteroids on IFN- γ activation of monocytes. IFN- γ treatment following *in vitro* dexamethasone pretreatment of monocytes from healthy subjects resulted in a greater enhancement of superoxide anion generation than that observed with IFN- γ treatment alone. These findings are important considerations in evaluating patient immune function because IFN- γ is being used in a number of clinical trials with leprosy patients.

VAN TRIER, Y.D.M. & SOLDENHOFF, R. de. Self-administered dapsone compliance of leprosy patients in Eastern Nepal. *Leprosy Review*, 62(1), p. 53-57, 1991.

Self-administered dapsone intake by leprosy patients in Eastern Nepal was monitored with a urine spot test. Of 341 outpatients 55 (16.1%) were found to be noncompliant. A significant relationship was found between noncompliance and age and between noncompliance and caste. Sex, disease classification, type of treatment, duration of treatment, history of leprosy reactions and travel time to the clinic did not influence the compliance.

In remote areas the urine spot test can be useful in leprosy control programmes.

YODER, L.J. et. al. The activity of rifabutin against *Mycobacterium leprae*. *Leprosy Review*, 62(3), p. 280-287, 1991.

Minimal effective doses of rifampicin were determined in *Mycobacterium leprae* isolated from skin biopsies of newly diagnosed, previously untreated lepromatous leprosy patients. Rifabutin was more potent than rifampicin. Our previous

report that rifabutin was fully active against rifampicin-resistant *M. leprae* could not be confirmed. Examination of two strains of rifampicin-resistant *M. leprae* from elsewhere, and a repeat experiment on our original strain of rifampicin-resistant bacilli, showed full cross-resistance between rifampicin and rifabutin. A clinical trial in three newly diagnosed, previously untreated lepromatous patients showed that rifabutin has rapid bactericidal activity.

ZAHEER, S.A. et. al. Immunological upgrading with combined immunotherapy and chemotherapy in a lepromatous leprosy patient: a case report. *Leprosy Review*, 62(3), p. 297-302, 1991.

Immunotherapy with *Mycobacterium w* was given, in addition to standard multidrug therapy (MDT) to a lepromatous leprosy (LL) patient with a bacteriological index (BI) of 6. After 15 months of treatment this patient attained bacteriological negativity and clinical inactivity. Histopathologically the patient upgraded to borderline-tuberculoid at 12 months, and at 15 months showed features of nonspecific infiltration in the dermis. The rapid immunological upgrading seen in the patient is highlighted in this paper.

BECX-BLEUMINK, M. Duration of Multidrug Therapy in Paucibacillary Leprosy Patients; Experience in the Leprosy Control Program of the All Africa Leprosy and Rehabilitation Training Center (ALERT) in Ethiopia. *Int.J.Leprosy*, 60(3), p. 436-444, 1992.

Multidrug therapy (MDT), according to the recommendations of a WHO Study Group of 1982, was introduced in the leprosy control program of the All Africa Leprosy and Rehabilitation Training Center (ALERT), Ethiopia, in January 1983. Of 6042 paucibacillary patients who were put on MDT during a period of 7 years, 5485 patients (90.8%) completed the course of MDT; 437 patients (7.2%) did not fulfill the requirement for clinic attendance and either discontinued MDT

themselves or the treatment was discontinued by the service. The remaining 120 patients (2.0%) either died, were transferred, left the control area or continued MDT after 9 months. The urine spot for the presence of dapsone showed a significantly higher proportion of positive results for patients on MDT than for patients on dapsone.

The analysis of the compliance with the prescribed doses of MDT showed that of 963 patients, 81.9% received six doses of MDT and 18.1%, more than six doses; 82.6% of these 963 patients attended with 100% regularity, 12.7%, 3.6%, and 1.1% missed one, two, or three clinic appointments, respectively, while fulfilling the requirement for overall clinic attendance. Of the 429 patients who had not been treated with dapsone before MDT, the skin lesions were clinically active at the time of stopping MDT in 130 patients (30.3%). In all, except one of the 114 patients (0.9%) who attended for follow-up examination, the skin lesions had become clinically inactive within 2 years after stopping MDT. The recommended duration of MDT is discussed based on findings in the ALERT leprosy control programs and observations by others.

BECX-BLEUMINK & BERHE, D. Occurrence of Reactions, Their Diagnosis and Management in Leprosy Patients Treated with Multidrug Therapy; Experience in the Leprosy Control Program of the All Africa Leprosy and Rehabilitation Training Center (ALERT) in Ethiopia. *Int.J.Leprosy*, 60(2), p. 173-184, 1992.

This paper reports on reactions in leprosy patients who were treated with multidrug therapy (MDT) in the leprosy control program of the All Africa Leprosy and Rehabilitation Training Center (ALERT) in Ethiopia. Only those reactions which occurred in patients who had not been treated with dapsone before MDT and which required treatment with prednisolone were included. Until the end of the second year of MDT a reversal reaction had been diagnosed in 43.6% of 266 borderline lepromatous (BL) patients and in 19.2% of 109 lepromatous leprosy (LL) patients, and an erythema nodosum leprosum (ENL) reaction

in 2.7% and 11.1% of the patients, respectively. The reversal reactions were observed in 4.9% of the BL patients and in 0% of the LL patients at the time of diagnosis of leprosy, in 26.3% and 12.8% of the patients during the first year of MDT, and in 12.4% and 6.4% during the second year of MDT. ENL reactions were seen in 0.8% of BL patients at diagnosis, 1.1% in the first year and 0.8% in the second year and 2.8% at diagnosis, 5.5% in the first year, and 2.8% in the second year for LL patients.

During a 3 $\frac{1}{2}$ -year period, a total of 405 reactions were diagnosed among multibacillary (MB) patients on MDT; 365 of these reactions (90.1%) were reversal reactions and only 40 (9.9%) were ENL reactions. The point in time of the reversal reactions showed that the risk of several reactions is highest during the first year of MDT. Thereafter there is a gradual decline, although reactions were still observed during the fifth year of MDT.

A reversal reaction was diagnosed in 21.0% of 438 BT patients; in 3.4% of the patients the reaction was present at the time of diagnosis of leprosy; in 10.3% it occurred during MDT, and in 7.3% during the first year after release from MDT. During a period of 3 $\frac{1}{2}$ years a total of 183 reversal reactions were diagnosed among BT patients. The point in time showed a declining trend in the risk of reversal reaction after starting MDT. The risk is highest during MDT, followed by the first 6 months after stopping MDT. However, reactions, although few, still occurred during the fourth year after stopping MDT.

The analysis of the results of prednisolone treatment in 161 patients who were treated for nerve function loss in the field showed that 142 patients (88.2%) regained complete or partial recovery of the nerve function(s), while no improvement was observed in 19 patients (11.8%). With the criteria defined for field treatment of reactions, about 85% of the patients could be treated with standard courses of prednisolone in the field. The main reasons for referral to the hospital were severe ENL reactions, associated medical problems whether or not related to leprosy, examination for a possible relapse, recurrent reactions, and deterioration of nerve function. It was estimated that during the period in

which all patients who needed prednisolone were required to be hospitalized, less than one third of the patients who developed a reaction were treated for it.

In addition to the finding that substantially more patients will be treated for their reactions if prednisolone is given in the field, other advantages of field treatment over hospital treatment are: a) it is much more convenient and economical for the patients, b) it has a positive effect on the credibility of the leprosy control services, c) it motivates the staff to do regular sensory and voluntary test and d) it is substantially less expensive.

BECX-BLEUMINK, M. Relapses Among Leprosy Patients Treated with Multidrug Therapy: Experience in the Leprosy Control Program of the All Africa Leprosy and Rehabilitation Training Center (ALERT) in Ethiopia; Practical Difficulties with Diagnosing Relapses; Operational Procedures and Criteria for Diagnosing Relapses. *Int.J.Lepros.*, 60(3), p. 421-435. 1992.

Multidrug therapy (MDT), according to the recommendations of a WHO Study Group of 1982, was introduced in the leprosy control program of the All Africa Leprosy and Rehabilitation Training Center (ALERT), Ethiopia, in January 1983. Paucibacillary (PB) patients are treated with 6 months of MDT. Multibacillary (MB) patients are treated with at least 2 years of MDT and until skin-smear negativity. An analysis was made of the relapses which had been diagnosed among self-reporting patients in four rural districts and Addis Ababa. Among 3065 PB patients, 34 relapses (1.1%) were diagnosed during an average period of 6.1 years after stopping MDT (range 2 $\frac{1}{2}$ to 7 $\frac{1}{2}$ years). Among 2379 MB patients, 24 relapses (1.0%) were diagnosed during an average period of 4.7 years after stopping MDT (range 2 $\frac{1}{2}$ to 6 years). The estimated relapse rate per 1000 patient-years after release from MDT was 2.1 for PB patients and 2.4 for MB patients

From the analysis of the clinical, bacteriological, and histopathological findings, it was concluded that there was strong positive evidence for

the diagnosis for 16 of the 34 relapses in the PB patients and for 0 of the 24 relapses in the MB patients. The main cause for overdiagnosis of MB relapses was that too much reliance had been put on skin-smear results, without a careful comparison of the results with those from before, during, and at completion of MDT; the diagnosis was based on the finding of positive smears in one set of smears only; insufficient attention was given to finding solid-staining bacilli; and findings in biopsies, if these were examined, did not confirm the diagnosis. The main cause of overdiagnosis of PB relapses was that too much reliance was put on histological findings, while these are often inconclusive for differentiating between a relapse and late reversal reaction.

Recommendations are made on how to limit overdiagnosis of relapses. Operational procedures and criteria for making the diagnosis under conditions where facilities for back-up histological and mouse foot pad investigations are not available are proposed.

BECX-BLEUMINK, M. Relapses in Leprosy patients After Release from Dapsone Monotherapy; Experience in the Leprosy Control Program of the All Africa Leprosy and Rehabilitation Training Center (ALERT) in Ethiopia. *Int.J.Leprosy*, 60(2), p. 161-172, 1992.

Before implementation of multidrug therapy (MDT), leprosy patients who were clinically inactive, skin-smear negative and had been treated with dapsone monotherapy for at least 5 years (paucibacillary patients) or for at least 10 years (multibacillary patients) were released from treatment.

An analysis was made of self-reporting relapses in 1081 paucibacillary (PB) patients and 1123 multibacillary (MB) patients who had been released in Addis Ababa and two rural districts of the leprosy control program of the All Africa Leprosy and Rehabilitation Training Center (ALERT). During average period of 6.6 years after stopping dapsone, 44 relapses were diagnosed among the PB patients and 148 relapses among the MB patients. The overall relapse rate was 4.1% or 7.2

per 1000 patient-years after release from treatment for PB patients and 13.2% and 24.8, respectively, for MB patients. The annual relapse rate in PB patients did not differ significantly from year to year. However the relapse rate for MB patients was significantly lower during the fifth to seventh years after stopping treatment compared with the first 4 years. Based on clinical findings there was a strong suspicion of relapse with dapsone-resistant bacilli in 40.4% of MB relapses. It is concluded that the relapse rate for PB patients is acceptable. However, the relapse rate for MB patients is considered too high. It is strongly recommended to administer to all MB patients, including those who have been on long-term treatment with dapsone and have become clinically and bacteriologically inactive, a 2-year course of MDT.

BHATKI, W.S. & CHULAWALA, R.G. Immunotherapeutic potential of ICRC vaccine: a case control study. *Leprosy Rev.*, 63(4), p. 358-364, 1992.

A bacteriological follow-up of 16 leproatous patients with a high initial Bacteriological Index (BI) showed that in 8 randomly selected patients who received single doses of ICRC Vaccine (C44) at the onset of multidrug therapy, the average reduction of BI was from 4.4+ to 1+ in 2 years - 3 of these patients became negative and 3 showed BI 1+ or less. Comparable bacteriological assessments in 8 non-vaccinated but otherwise similar patients showed an average reduction of BI from 4.7+ to 2.6+ i.e., consistent with the expected response to MDT in lepromatous patients. Here we discuss the role of immunotherapy and the selection of a desirable antileprosy vaccine in the context of fixed-duration MDT.

CARTEL, J.L. et. al. Leprosy in French Polynesia. The possible impact of multidrug therapy on epidemiological trends. *Leprosy Review*, 63(3), p. 223-230, 1992.

In 1982, following the recommendations of a WHO study group, multidrug therapy (MDT)

was introduced into French Polynesia to treat all patients suffering from active leprosy, and - only on request - those still on dapsone monotherapy. After 5 years, a clear-cut decrease of prevalence and mean annual detection rates for leprosy (except for detection rates among children aged less than 15 years, many of such cases being detected early by increased household contact training) has been observed. There was also a decrease in the proportion of newly detected cases with disabilities. During the 21-year period preceding the introduction of MDT into the control programme, mean annual detection rates for leprosy had remained stable, and this led to the consideration that such a decrease was due neither to the natural decline of the disease nor to the economic improvement of the country. Our results, together with the fact that, to date, the relapse rate was nil in the Polynesian patients put on MDT, strongly suggest that the implementation of MDT has resulted in a decrease of detection rates for leprosy which may be a consequence of a decrease in the transmission of the disease.

CHIN-A-LIEN, R.A.M. et. al. Follow up of multibacillary leprosy patients using a phenolic glycolipid-1-based ELISA. Do Increasing ELISA-values after discontinuation of treatment indicate relapse? *Lepr. Rev.*, 63(1), p. 21-27, 1992.

With the introduction of reproducible serological tests it was hoped that relapses in leprosy patients, after discontinuing treatment, could be detected before damaging reactions occurred and before the patients became infections. The possible value of an ELISA using a semisynthetic analogue of phenolic glycolipit-I to detect antibodies to this antigen in order to predict a relapse in multibacillary patients was investigated. In contrast to that reported for paucibacillary patients, this test was useful to detect early relapses in multibacillary patients. In 3 out of 4 multibacillary patients who relapsed, the ELISA-values were increased. The decreased ELISA-values in the one relapsed patient could be attributed to the corticosteroid therapy. In the

multibacillary patients who did not relapse after RFT, the ELISA-values were consistently low or decreased. In only one patient did the ELISA-values increase following his release from treatment as this patient was clinically suspected of developing a relapse.

FRANKEL, R.I. et. al. Resolution of Type 1 Reaction in Multibacillary Hansen's Disease as a Result of Treatment with Cyclosporine. *Int.J.Lepr.*, 60(1), p. 8-12, 1992.

Type 1 Hansen's disease reaction (reversal reaction) is believed to result from a change in the immune response in patients with borderline Hansen's disease. The only effective therapy for significant type 1 reactions has been systemic corticosteroid therapy. Cyclosporine is an immunosuppressive drug which has been widely used in organ transplantation. We report a case of type 1 reaction complicating borderline lepromatous Hansen's disease. Cyclosporine therapy resulted in prompt and sustained resolution of the reaction. The possible mechanism of action of cyclosporine and the implications regarding the immunopathogenesis of type 1 reaction are discussed.

FRANZBLAU, S.G. et. al. Doubleblind evaluation of BACTEC and Buddemeyer-type radiorespirometric assays for in vitro screening of antileprosy agents. *Leprosy Review*, 63(2), 1992, p. 125-133.

Two radiorespirometric assays, the BACTEC 460 and Buddemeyer-type $^{14}\text{CO}_2$ detection systems, were evaluated in a double-blind manner for their ability to discriminate between authentic antileprosy agents and inactive compounds. Freshly harvested, nude-mouse derived *Mycobacterium Ieprae* were incubated in axenic media in the presence of coded test solutions prepared in a remote laboratory. Activity was assessed by comparing the rate of ^{14}CO evolution from [^{14}C] palmitic acid to controls. Breaking the code revealed that both systems demonstrated a dose response to ethionamide, pefloxacin and

rifampicin as well as sensitivity to dapsone. Most of the water, ethanol, sucrose, dabsyl chloride and riboflavin negative-control samples failed to effect a significant reduction in radiorespirometric activity. This study confirms the ability of the radiorespirometric assays to function as a primary drug screening system in leprosy.

GIDOH, M. & TSUTSUMI, S. Activity of sparfloxacin against *Mycobacterium leprae* inoculated into footpads of nude mice. *Leprosy Review*, 63(2), p. 108-116, 1992.

The antileprosy activity of a new quinolone, sparfloxacin, was examined in the nude mouse footpad model. By serial dosing (once a day, 5 or 6 times per week, during the 3rd-5th months postinoculation), 10 mg/kg of sparfloxacin displayed bactericidal-type activity and bacteriostatic activity was present at daily doses of 5 and 2 mg/kg. By intermittent dosing (once a day, twice weekly at daily doses of 10 and 20 mg/kg or once weekly at a daily dose of 30 mg/kg, during the 3rd-5th months postinoculation), sparfloxacin markedly inhibited the growth of leprosy bacilli with slight remultiplication at later stages. Sparfloxacin seems to be worth studying clinically as a novel antileprosy drug.

GIDOH, M. et. al. Bactericidal action at low doses of a new rifamycin derivative, 3-hydroxy-5-(4-isobutyl-1-piperazinyl) benzoxazinorifamycin (KRM-1648) on *Mycobacterium leprae* inoculated into footpads of nude mice. *Leprosy Review*, 63(4), p. 319-328, 1992.

Among series of newly-synthesized benzoxazinorifamycins, 2 of the 3'-hydroxy-5'-(4-alkyl-1-piperazinyl) derivatives, named KRM-1648 and KRM-2312, whose respective alkyl residues are isobutyl and isopropyl, were examined for efficacy against nude mouse-model leprosy. KRM-1648 completely inhibited the growth of leprosy bacilli inoculated into nude mouse footpads, even 6 months after the medication had been stopped, when given orally at a daily dose of 0.6 mg/kg, 5 or 6 times weekly, during 3-5 months postinocula-

tion. In comparison, the growth inhibition by KRM-2312 was incomplete under the same conditions, though it was still stronger than that by rifampicin. Complete growth inhibition by KRM-1648 was also observed when it was given orally at a dose of 1 or 3 mg/kg twice weekly during the same period. In contrast, the growth inhibition by rifampicin was only slight at 1 mg/kg and partial at 3 mg/kg under the same condition.

GIRDHAR, A. et. al. Red discoloration of the sputum by ciprofloxacin simulating haemoptysis - A case report. *Leprosy Review*, 63(1), p. 47-50, 1992.

A patient of lepromatous leprosy, who received a high dose of clofazimine as part of multidrug therapy, for chronic erythema nodosum leprosum (ENL) had frequent 'haemoptysis'. The haemoptysis was later found to be due to expectoration of ciprofloxacin. This interesting, and perhaps first cases of such an occurrence, is reported.

GUPTA, A. et. al. Intravascular Hemolysis and Acute Renal Failure Following Intermittent Rifampin Therapy. *Int.J.Leprosy*, 60(2), p.185-188, 1992.

Renal failure is a rare complication associated with the use of rifampin. Intravascular hemolysis leading to acute renal failure following rifampin therapy is extremely rare. Two patients with leprosy who developed hemolysis and acute renal failure following rifampin are reported.

JADHAV, V.H. et. al. Comparison of two multidrug regimens in multibacillary leprosy. *Ind.J.Leprosy*, 64(4), p. 501-504, 1992.

One of the technical problems relating to the multidrug therapy of leprosy is the slow decrease in the bacteriological index (BI) in multibacillary patients. In this study we have compared a regimen containing rifampicin given daily for 9 months with the standard WHO multidrug regimen for

multibacillary leprosy. We have found, at the end of two years, a significantly greater fall of BI in patients who had received the regimen containing daily rifampicin as compared to those who had received pulsed doses of rifampicin. The doses of dapsone and clofazimine were similar in these two groups. It appears that daily administration of rifampicin may be useful in treating multibacillary patients in whom reduction in the BI is slower than expected. However, in view of its high cost and the very much increased incidence of type-2 reactions and hepatitis, daily rifampicin therapy cannot be recommended for a control programme.

KAR, P.K. et. al. Indeterminate leprosy: A therapeutic evaluation. *Ind.J.Lepr.*, 64(2), p.163-168, 1992.

Out of 50 cases of indeterminate leprosy, 46 were male and 4 were female. The only clinical finding was a single hypopigmented macule in 38 (76%) cases. Nine (18%) patients had two and three (6%) cases had three hypopigmented macules. All patients were treated with multidrug therapy for one year. At the end of six months, the lesions were still active in 12 (24%) cases. At the end of one year of treatment it was found that 33 (66%) patients became inactive and 3 (6%) cases were still to be active. The study shows that all indeterminate leprosy cases must be treated with multidrug therapy till all signs of activity are subsided.

KATOCH, K. et. al. Treatment of paucibacillary leprosy with a regimen containing rifampicin, dapsone and prothionamide. *Ind.J.Lepr.*, 64(3), p. 303-312, 1992.

Ninety paucibacillary leprosy patients having indeterminate (I) tuberculoid (TT) and borderline tuberculoid (BT) type of leprosy with bacterial index (BI) of less than two on the Ridley scale were treated with rifampicin (RFM) 600 mg once a month, dapsone (DDS) 100 mg daily and prothionamide (PTH) 250 mg daily. Treatment was stopped at the end of six months. The pa-

tients tolerated the drugs fairly well and in only two patients the drugs had to be stopped (in one due to Jaundice and in the other due to gastric intolerance). About 6% of patients had early reactions which subsided with additional steroid therapy. The inactivity rate was 60% at six months and this improved to 96% at 12 months. No cases of late reactions and relapses were encountered in the limited follow-up period of six months; and a longer follow-up is necessary for ascertaining the relapse rates. The preliminary results however suggest that the addition of prothionamide to the standard WHO paucibacillary regimen is well-tolerated with increased inactivity rate and fewer instances of late reactions.

KAUR, S. et. al. Paucibacillary multidrug therapy in leprosy 7th years experience. *Ind.J.Lepr.*, 64(2), p. 153-162, 1992.

Three hundred and twenty-three paucibacillary (PB) leprosy patients were treated with WHO, recommended multidrug therapy (MDT) and followed up for over 7^{1/2} years. The paucibacillary MDT regimen (PBR) was well accepted and tolerated. Complete clinical regression was attained in 61.2% patients after 6 doses of PBR. Persistence of clinical activity after 6 months of therapy was associated with occurrence of type I upgrading reaction, presence of six or more patches and more than two thickened major nerve trunks. Reversal reactions were encountered in 15.9% patients, one third of which were accompanied by severe neuritis. Delayed upgrading reaction occurred in six patients, two patients had relapse one and two years after stopping of PBR.

The WHO recommended MDT regimen for paucibacillary cases needs careful evaluation and it may be necessary to extend the treatment beyond six months in certain situations.

MUKHERJEE, A. et. al. Histopathological Monitoring of an Immunotherapeutic Trial with *Mycobacterium w.* *Int J. Lepr.*, 60(1), p. 28-35, 1992.

Immunotherapeutic trials with *Mycobacterium w.* (*M. w.*) on multibacillary patients are in progress at two large hospitals in New Delhi. A total of 380 patients so far have been inducted into the trial. The histopathological profile of the initial 87 patients had MDT with starch injections as a placebo. Skin biopsies were taken at induction and thereafter at every 6 months. The results show a significantly higher proportion of biopsies with histopathological upgrading and/or clearance of dermal granuloma among the vaccinated cases. The number of patients becoming bacteriologically negative was higher in the vaccine group. There was no increase in the degree of neural inflammation in the biopsies showing upgrading. The lepromin site biopsy in patients who converted to positivity after vaccination showed epithelioid cell granulomas as did the biopsies from the nodules developing at the vaccination sites. The histopathological observations confirm the additional immunotherapeutic effect of *M. w.* used along with standard MDT therapy.

PATIL, M.A. et. al. Correlation between inhibitory effect of quinolones and mycolic acid metabolism in mycobacteria. *Ind. J. Lepr.*, 64(3), p. 331-340, 1992.

Mycolic acids are important components having a significant role in maintaining the rigidity of mycobacterial cell wall. They could also be the barrier for penetration of certain drugs into the bacterial cell. A novel in vitro model system was established for assessing the effect of Ciprofloxacin on mycolic acid metabolism in pathogenic mycobacteria *M. Kansasii* (which has similar mycolic acid pattern to that from *M. leprae*) and the effect of norfloxacin in *M. intracellulare*. These test mycobacteria were exposed in their midlogarithmic phase of growth to 0.5, 1, 2, 3, 4, 5 and 6 µg/ml of ciprofloxacin and norfloxacin respectively for 1, 2 and 24 hours. Ciprofloxacin completely inhibited the synthesis of mycolated in

M. kansasii at 3, 4 and 5 µg/ml; whereas norfloxacin exhibited its maximum inhibitory action on mycolic acids in *M. intracellulare* at 6 µg/ml for all the durations of exposure. Inhibition of mycolates directly correlated with bacterial viability which was estimated by colony forming units. The effect of quinolones on mycolic acid metabolism appears to be direct and not secondary to DNA gyrase. The results obtained from this study and our previous findings show that mycolic acid metabolism is affected by various groups of drugs, whose primary sites of activity may be different. The findings of the present study may have significant therapeutic implications in leprosy and other mycobacterial diseases.

PATTYN, S.R. et. al. Ambulatory treatment of Multibacillary leprosy with a regimen of 8 months duration. *Lepr. Rev.*, 63(1), p. 36-40, 1992.

An ambulatory treatment regimen for multibacillary leprosy, of 34 weeks duration composed of 8 weeks daily supervised rifampicin, ethionamide (ETH), dapsone (DDS) and clofazimine (CLO) followed by 26 weeks of unsupervised ETH, DDS and CLO, introduced in 1983 has been evaluated; 268 patients were followed for a mean of 4.4 years and a total of 1188 patient years. The relapse rate was 0.33 per 100 patient years of follow up. The reduction of the duration of the combined administration of RMP + ETH reduced the hepatotoxicity to 1.4%. It is possible that both phases of the regimen studied could still be reduced, however in the near future ETH will be replaced by alternative bactericidal drugs, avoiding the hepatotoxicity.

PATTYN, S. R. et. al. Treatment of multibacillary leprosy with a regimen of 13 weeks duration. *Lepr. Rev.* 63(1), p. 41-46, 1992.

In a prospective study 559 multibacillary patients in Zaire were treated for 13 weeks with twice weekly rifampicin (600 mg) and daily ethionamide (500 mg) and dapsone (100 mg), 13-RED, or clofazimine (100 mg), 13-REC. The patients were followed for a total of 1418 person

years, mean 3.2 years. The incidence of hepatitis was 3.3%. The incidence of relapses was 0.28 per 100 person years. Relapses were due to drug-sensitive organisms.

In patients who received the same drug regimens but with a reduced dosage of ethionamide to 5 mg/kg bodyweight, the incidence of hepatitis was significantly lower but the relapse rate was 7.8 per 100 person years of follow-up in the RED group, no relapses were diagnosed in the REC group.

It is concluded that by the use of potent antileprosy drugs in suitable combinations and dosages it will be possible to shorten the duration of antibacterial treatment in multibacillary leprosy to 3 months.

RAMESH, V. et. al. Multidrug Therapy in Multibacillary Leprosy; Experience in an Urban Leprosy Center. *Int.J.Lep.*, 60(1), p. 13-17, 1992.

The article records the experience of treating multibacillary (BB, BL, and LL) leprosy with multidrug therapy (MDT) in an urban leprosy center. The problem of leprosy is to be properly assessed throughout the Indian subcontinent because most of the epidemiological data from the areas labeled low-endemic have to be updated. The regularity of therapy must be ensured and monitored constantly but in spite of our efforts to do so some factors were beyond our control!, such as providing a means of livelihood for the migrants from other places. In addition, the intake of drugs also has to be periodically checked from the history and discoloration of skin and, most importantly, confirmed by performing random spot tests for dapsone in the urine. The main problems discussed are the difficulty in demonstrating acid-fast bacilli in slit-skin smears from the macular form of borderline leprosy (also called dimorphous macular) and, secondly, whether the duration of multibacillary therapy was adequate since only approximately 50% of our patients achieved smear negativity after taking MDT for the stipulated period of 24 months. Experiences from other centers have suggested that the duration of MDT should be prolonged in multibacillary pa-

tients to achieve smear-negative status. Yet another group notes that smear negativity is gradually achieved during the period of surveillance following stoppage of MDT after 24 months. These questions await more information from good centers with controlled field studies.

RAO, P.S. et. al. Initial intensive therapy for multibacillary leprosy patients - in retrospect. *Lepr.Rev.*, 63(4), p. 350-357, 1992.

We analysed the results of 4845 multibacillary (MB) patients being treated with multidrug treatment (MDT) in the Srikakulam District of Andhra Pradesh, India. Of these, 2309 (47.7%) patients were given an initial 14-day intensive therapy with rifampicin, clofazimine and dapsone, followed by the recommended pulse therapy. The rest of the cases were given only pulse therapy. The improvement in terms of bacteriological clearance and the proportion of cases declared released from treatment (R FT) was found to be significantly higher among patients treated with only pulse therapy. Clinic attendance was found to be better and more regular in patients treated with intensive therapy, and no relapses were seen with either therapy. The implications of these findings on the operational aspects of programme implementation were discussed.

SHANNON, E.J. et. al. Thalidomide's effectiveness in erythema nodosum leprosum is associated with a decrease in CDH-cells in the peripheral blood. *Lepr.Rev.*, 63(1), p. 5-11, 1992.

Thalidomide is well documented as being an effective drug in the treatment of erythema nodosum leprosum (ENL). The mechanism of action of thalidomide in ENL, as well as the pathogenesis of ENL are yet to be fully determined.

Lepromatous leprosy patients experiencing ENL have been reported to have an increase in the ratio of CD4+ to CD8+ cells in their blood and ENL skin lesions. Thalidomide has been shown to cause a decrease in the ratio of CD4+ to CD8+ lymphocytes in the blood of healthy males. This

decrease was due to a significant reduction in the numbers of CD4+ lymphocytes and an apparent increase in the numbers of CD8+ lymphocytes.

In this study, thalidomine's effectiveness in halting chronic ENL and arresting a relapse into ENL, was consistently associated with a decrease in the numbers of CD4+ lymphocytes in the blood of 2 male lepromatous leprosy patients.

SHETTY, V.P. et. al. Persistence of *Mycobacterium leprae* in the peripheral nerve as compared to the skin of multidrug-treated leprosy patients. *Lepr.Rev.*, 63(4), p. 329-336, 1992.

Skin and nerve biopsies obtained from 18 multibacillary (MB) and 16 paucibacillary (PB) cases of leprosy who had been fully treated by the WHO regimen were assessed for bacterial load using different staining techniques. In addition skin and nerve homogenates of 10 MB cases were tested for 'persistor' *Mycobacterium leprae* using immuno suppressed mice.

While significant amounts of integral bacilli and BCG cross-reactive antigen of *M. leprae* were detected both in skin and nerve tissue of all the MB cases (100%), 56% of skin and 62% of nerve biopsies of PB cases also showed the presence of BCG cross-reactive antigen.

Detection of 'persistor' *M. leprae* in 2/10 skin biopsies (20%) and 3/10 nerve biopsies (30%) of MB cases was thought to be unexpectedly high after 2 years of MDT.

VAN BRAKEL, W.H. et. al. The allocation of leprosy patients into paucibacillary and multibacillary groups for multidrug therapy, taking into account the number of body areas affected by skin, or skin and nerve lesions. *Lepr.Rev.*, 63(3), p.231-246,1992.

In Nepal, the setting up and maintaining of reliable services for slit-skin smears has proven difficult. A clinical classification system for leprosy has therefore been developed to assist in the allocation of patients to either paucibacillary or multibacillary groups for the purposes of multiple

drug therapy (MDT), using 9 body areas: head (1), arms (2), legs (2), trunk (4). Patients with more than two areas of the body affected are grouped as multibacillary (MB) and those with only one or two areas affected are paucibacillary (PB). Using a computer simulation model and the data of 53 patients registered at Green Pastures Hospital (GPH) in Pokhara and 703 field patients from the Western Region, different clinical classification systems were evaluated with regard to their sensitivity, specificity, and predictive value for MB or PB classification, as compared with the histological classification for the GPH cases and the bacteriological classification for the field patients. The sensitivity and specificity of the body area system in present use were 93% and 39%, respectively. The low specificity is due to MB overclassification. The sensitivity of the WHO classification system without skin smear facilities is 73% (the difference with the body area system is significant: $p < 0.05$, McNemar's test). Our histology findings confirm previous publications indicating that, while some borderline tuberculoid (BT) patients may outwardly have a 'PB appearance' and be skin-negative, their nerve biopsy and sometimes skin biopsy may show a 'MB' picture. This is the first publication discussing a 'body area system' for the purpose described, including diagrams of the areas used. In Nepal it has proved easy to use and teach and its use may be justified in other control programmes which implement MDT, particularly if slit-skin smear services are unreliable or nonexistent.

VENKATESWARLU, B. et. al. Role of Rifampin and Clofazimine Ointments in the Treatment of Leprosy. *Int.J.Lep.*, 60(2), p. 269-270, 1992.

The use of rifampin and clofazimine ointments alone and in combination over the patches of tuberculoid patients has a beneficial effect. In combination (rifampin and clofazimine), erythema, inflammation, and edema are considerably reduced. For some of the cases with a recent appearance of a patch, the patch completely disappeared. It is suggested that topical therapy with rifampin and clofazimine ointments would be economical and beneficial in tuberculoid leprosy.

RESUMOS/ABSTRACTS

Indian Journal of Leprosy
International Journal of Leprosy
Leprosy Review

PERÍODO CONSIDERADO

Indian Journal of Leprosy e
International Journal of Leprosy
Janeiro a Setembro de 1993 .
Leprosy Review
Janeiro a Dezembro de 1993.

CLÍNICA

AWOFESO, N. Inventory of skin smear practices in 6 leprosy control programmes in Nigeria *Lepr.Rev.*, 64(2), p. 150-156, 1993.

A study of slit skin smear (SSS) examination practices in 6 Nigerian Leprosy Control Programmes was undertaken to assess the quality of smearing, staining and reading. Results indicated that the standard of SSS practices fall below the ideal. There is a great need for training as well as supervision and support of laboratory staff if this deplorable situation is to be improved.

BHATIA, A.S. et. al. Clinical and histopathological correlation in the classification of leprosy. *Int.J.Lep.*, 61(3), p. 433-438, 1993.

This study reports our observations on the correlation between clinical and histopathological diagnoses of the classification of leprosy. The histopathological classification of leprosy in 1351 cases was done per Ridley-Jopling criteria and was compared with the clinical diagnoses of the same cases. These 1351 cases included 79 cases diagnosed clinically as having a "reaction". However, the

histopathologists could not detect any evidence of reaction in 16 of these 79 cases (20%).

Of the remaining 1272 cases, 68(5%) were reported as "no evidence of leprosy" by the histopathologists; 37 of these 68 were found to be from the clinically indeterminate type of leprosy. Histopathological and clinical diagnoses of the classification of leprosy coincided in 69% of the cases. Concordance between the clinical and histopathological diagnoses for different types of leprosy was: indeterminate (I) = 36% tuberculoid (TT) = 50%, borderline tuberculoid (BT) = 77%, borderline (BB) = 26%, borderline lepromatous (BL) = 43%, and lepromatous (LL) = 91%. When some of the types were combined (BT with TT, BL with LL), the overall concordance figure was 76%; concordance for the TT/BT group was 80%, for the BULL group it was 93%. Since both TT and BT are considered paucibacillary and LL or BL are considered multibacillary for treatment purposes, differentiating TT from BT or BL from LL is, perhaps, therapeutically irrelevant. However, for classification purposes it appears that the weight given to different signs and/or histopathological parameters for classifying leprosy cases (especially TT, BB and I) needs to be reassessed.

BLUM, L. et. al. Leprosy reversal reaction in HIV-positive patients. *Int.J.Lepr.*, 61(2), p. 214-217, 1993.

We report two cases of leprosy in HIV-infected patients who, by their clinical, histological and immunological features, enhance the evidence that HIV-positive leprosy does not differ from nonHIV-positive leprosy. Moreover, extensive studies of reversal reactions in HIV-positive patients might be of great interest in determining the exact pathogenesis of this leprosy reactional state.

BOBHATE, S.K. et. al. Malignant transformation of plantar ulcers in leprosy. *Ind.J.Lepr.*, 65(3), p.297-303, 1993.

Malignant transformation of plantar ulcers in leprosy is not uncommon. The apparent rarity of these neoplasms could be because many observed cases are not reported. To determine the extent of the problem, 133 consecutive cases of plantar ulcers seen over two years were studied clinically as well as histologically. Plantar ulcers were more common in the distal third of foot (64.67%) but malignant transformation was seen more often in plantar ulcers of proximal third of foot (64.29%). Malignant transformation was more common in plantar ulcers of long duration.

Histologically, most of the lesions were benign, being instances of pseudo-epitheliomatous hyperplasia (57.89%) or atypical pseudo-epitheliomatous hyperplasia (13.53%). However, squamous cell carcinoma was observed in 10.53% cases. Thus it may be that more cases with this complication will be detected if it is borne in mind that malignant change may be encountered in such ulcers.

BRANDT, F. et. al. A histological study of the eye lesions in 12 leprosy patients with tuberculoid lesion in 4 eyes. *Lepr.Rev.* 64(1), p.44-52, 1993.

The histological reactions in 12 eyes of 12 leprosy patients were studied (5 BT, 1 BB, 1 BL, and 5 LL). Granuloma lesions composed of

epithelioid cells, Langerhans giant cells, macrophages and lymphocytes were found in various intraocular tissues, e.g. cornea, sclera, iris, ciliary body or retina in 4 patients (1 BT and 3 LL). Of the 3 LL patients, according to the records, 2 were cured and in the other patient the outcome of the treatment was not mentioned. In view of the finding of the granulomatous lesions in the clinically cured patients and tuberculoid granuloma in the intraocular tissues in the LL patients, could there be some peculiarities in the intraocular sites? Or perhaps the tuberculoid reaction is just a manifestation of an upgrading reaction? More examinations on human leprosy eye specimens will be needed to answer these questions.

EL HASSAN, A.M. et. al. Distinguishing post-kala-azar dermal leishmaniasis from leprosy: experience in the Sudan. *Lepr.Rev.*, 64(1), p. 53-59, 1993.

In this study 4 patients were post-kala-azar dermal leishmaniasis (PKDL), whose lesions were similar to those of lepromatous and borderline leprosy, are described. In 2 patients there was no previous history of kala-azar but they were residents of an area of known endemic kala-azar. Lack of proper clinical and laboratory assessment was behind the failure to diagnose PKDL. Consequently the patients were treated with antileprosy drugs without proof of leprosy. The 3rd and 4th patients, though suspected clinically of leprosy, were correctly diagnosed as PKDL with adequate history, clinical assessment and appropriate laboratory investigations.

The salient points in distinguishing PKDL from leprosy are described and discussed.

FINE, P.E.M. et. al. Extent, origin and implications of observer variation in the histopathological diagnosis of suspected leprosy. *Int J.Lepr.*, 61(2), p.270-282,1993.

Identical slides from 100 biopsies obtained from individuals suspected of having leprosy, ascertained in a total population survey in Malawi, were examined twice, independently, by

three histopathologists. Results were reported in a standard protocol, and were compared among themselves and with a standardized clinical assessment of each 'suspect'. The proportion of biopsies considered to show definite evidence of leprosy ranged from 29 to 55 among the six evaluations (twice by each of three histopathologists). Comparisons of variations within and between histopathologists revealed three different patterns. Two of the pathologists were very consistent as individuals, but differed markedly between themselves in that one was the least inclined and the other the most inclined to report definite evidence of leprosy. The third pathologist was less consistent, reporting appreciably more definite leprosy on the first.

FOSS, N.T., et. al. Correlation between TNF production, increase of plasma C-reactive protein level and suppression of T lymphocyte response to concanavalin A during erythema nodosum leprosum. *Int.J.Lepr.* 61(2), p. 218-226, 1993,

The complex symptoms observed in lepromatous leprosy patients with reactive episodes of the erythema nodosum leprosum (ENL) type are associated with different serum components actively participating in the acute inflammatory reaction. Among them are the tumor necrosis factor (TNF) and the acute-phase protein C-reactive protein (CRP). TNF and CRP were found at significantly more elevated concentrations in the serum of patients with ENL with a positive correlation of about 95% when compared with patients with nonreactive lepromatous leprosy (L) or tuberculoid leprosy (T) or with control individuals. Furthermore, in another series of experiments CRP had a specific and significant suppressive action on concanavalin A (ConA)-induced lymphoproliferation in cultures from patients and controls, the reduction being more marked (75%) in patients with ENL. By extrapolation from its known actions, production of TNF may have a number of potential consequences for the immunobiology of ENL. Thus, TNF may cause direct injury to compromised cells, facilitating mononuclear cell activation and production of

cytokines such as interleukin-1 and interleukin-6, and upregulating hepatocyte expression of CRP. Both CRP and TNF in high serum concentrations have the ability to enhance the acute inflammatory process in ENL, favoring increased macrophage activation and phagocytosis, and contributing to the elimination of damaged cells and bacilli, as well as in the reduction of T-suppressor cells, with a consequent improvement in the immunologic response of ENL patients.

GHEI, S.K. et. al. Group specific component (Gc) in erythema nodosum leprosum (ENL). *Ind.J.Lepr.*, 65(3), p. 323-326, 1993.

The distribution of phenotypes of group specific component (Gc) was examined in 71 lepromatous leprosy (LL) patients without any history of ENL reaction and 65 LL patients with history of frequent episodes of ENL reaction. The distribution of none of the phenotypes of Gc (Gc 1-1, Gc 21, Gc 2-2) was statistically significant among these groups.

EPIDEMIOLOGIA

GIRDHAR, B.K., et. al. Borderline-tuberculoid relapse in lepromatous leprosy. *Lepr.Rev.*, 64(2), p,157-163, 1993.

We report details of 2 patients who had been treated for a long time by dapsone monotherapy and who had remained smear negative for over 10 years, but were found to have relapsed with borderline-tuberculoid (BT) leprosy.

KAUR, S. et. al. Concurrent skin and nerve histology in leprosy and its role in the classification of leprosy. *Lepr. Rev.*, 64(2), p. 110-116, 1993.

Concurrent skin and nerve histology was evaluated in 60 leprosy patients (25 BT, 28 BL and 7 LL). The twin aims were to study the comparative

histology and the usefulness of nerve histology in the classification of the disease. In BT patients, clinical and histological classification was in agreement in 11 (44%) skin and 17 (68%) nerve biopsies. Concurrent skin and nerve histology was in consonance in 14 (56%) BT patients, while in 6 (24%) patients, only nerve histology was helpful in the classification of the disease, the skin histology being non-specific. Nerve histology was classified as BL in 3 (12%) BT patients, the skin histology was non-specific.

In the BL group, the histology of 23 (82.4%) nerve biopsies correlated with the clinical classification, In contrast to skin histology which correlated with clinical assessment in 19 (68%) patients only. In the LL patients, the histology of nerve correlated with the clinical classification in 5 patients (71.4%), compared to histology of the skin in 4 (57%) patients only. The GF was higher in the nerves than in the skin throughout the leprosy spectrum (BT, BL, LL); the difference was, however, marginal in BL leprosy. The average bacteriological Index (BI) was higher in nerves (4+) compared to that of skin histology and slit skin smears (3+) in BL leprosy. There was, however, no difference in the BI of the slit skin smears, skin and nerve biopsies in lepromatous leprosy. It is inferred that the neural histology is often more useful than skin histology in the classification of leprosy patients ($p < 0.01$) and it correlates better with clinical classification, particularly in the borderline tuberculoid disease. The neural histology gave a better idea about the bacterial load in the BT, BL patients. It is proposed that bacteriologically negative patients clinically and histologically classified as BT, but with nerve histology more consistent with BL, should be considered multibacillary for purposes of therapy.

LOCKWOOD, D.N.J. et. al. Clinical features and outcome of reversal (type 1) reactions in Hyderabad, India. *Int.J.Lep.*, 61(1), p. 8-15, 1993.

A retrospective survey of the notes on all patients attending Dhoolpet Leprosy Research Center, India, during 1985 was done to establish the frequency, timing, and clinical features of

reversal (type 1) reactions; 494 cases notes were examined and clinical evidence of a reversal reaction was found in 44 cases (10.9%). Reactions were most common in borderline patients, with 11.4% and 14.8% of borderline tuberculoid (BT) and borderline lepromatous (BL) patients developing reactions, respectively. Presentation in reaction was frequent with 47.5% of reactional patients having signs of a reversal reaction at the time of their first visit to the Dhoolpet clinic; 50% of skin reactions developing in patients on antileprosy treatment occur within the first month of treatment. Neurological reactions occur later and over a longer time course. Late reactions may occur up to 61/2 years after the start of treatment. Further reactional episodes occurred in 31.8% of the patients, and may be repeated. Steroid treatment produced improvement of both skin lesions and neuritis, but improvement in clinical signs and symptoms occurred in only 50% of the neuritic episodes.

McAULEY, D.M. et. al. Effect of hand soaking on sensory testing. *Int.J.Lep.*, 61(1), p. 1619, 1993.

This study investigates the effect of hand soaking on sensory testing scores in 58 patients with leprosy. Sensation was tested with Semmes-Weinstein monofilaments and scored. Patients were tested before and after soaking their hands in water for 30 minutes. A statistically significant improvement in sensory testing scores for individual nerve territories was noted. The importance of these findings should be considered when using sensory testing as an evaluative tool for nerve damage in leprosy.

MISHRA, B. et. al. Evolution of early lesions in leprosy. *Lep.Rev.*, 64(3), p.259-266,1993.

We observed 29 patients presenting with vague peripheral neurological symptoms for 6 months or more. During this period, 16 developed clinical leprosy, 3 developed borderline tuberculoid leprosy and the other 13 developed neuritic leprosy. Of these 13 cases 11 subsequently devel-

oped skin lesions similar to those seen in indeterminate and in borderline tuberculoid leprosy. Based on the above observations, an attempt has been made to explain the evolution of early lesions of leprosy.

MISHRA, B. et. al. Paralysis of occipitofrontalis in a borderline case of leprosy. *Lepr.Rev.*, 64(1), p. 60-63, 1993.

A patient with neuritic leprosy developed borderline skin lesions. Later, another skin lesion developed on the left side of the forehead with clinical involvement of the supraorbital branch of the ophthalmic division of the trigeminal nerve. Simultaneously, paralysis of the occipitofrontalis and mild paresis of orbicularis oculi occurred.

MISHRA, B. et. al. Trigeminal neuralgia-a presenting feature of facial leprosy. *Lepr. Rev.*, 64(3), p.255-258, 1993.

Trigeminal neuralgia is a well recognized clinical entity. However, it has not been reported to mimic leprosy or vice versa. Of the 3 cases reported here, 2 initially presented with neuralgia symptoms similar to that seen in trigeminal neuralgia and later developed borderline lesions on the face. The 3rd case demonstrated a tingling sensation along with firm and palpable supraorbital nerve (a branch of trigeminal nerve), and a very early skin lesion on the face pointed to the need to consider neuritic type leprosy before concluding the final diagnosis of a disease like trigeminal neuralgia which calls for a different therapeutic approach.

NEGESSE, Y. et. al. In leprosy the presence of mycobacteria in the nerve is an essential factor in the cycle and spectrum of *Mycobacterium leprae* infection. *Lepr.Rev.*, 64(2), p. 104-109, 1993.

A total of 220 untreated leprosy patients who underwent parallel skin and nerve biopsies are included in this study, which is intended to

evaluate the extent of previously reported differences in bacillary load between skin and nerve lesions in leprosy and to describe the response of peripheral blood lymphocytes to *Mycobacterium leprae* antigens in such patients.

In 161 patients out of the 220, the skin and nerve biopsies were diagnostic for leprosy. When patients were grouped according to their skin and nerve lesions, the 3 groups observed were (1) paucibacillary skin and nerve lesions; (2) multibacillary skin and nerve lesions, and (3) paucibacillary skin and multibacillary nerve lesions. There was no observation of a group of patients with multibacillary skin and paucibacillary nerve lesions. In all patients with multibacillary nerve lesions, regardless of the type of skin lesions, a low response of peripheral blood lymphocytes to *M. leprae* was consistently noted. These results suggest that the bacillary load in the nerve is certainly one of the factors determining the immunological spectrum observed in leprosy.

PARKASH, O.M., GIRDHAR, B.K. & SENGUPTA, U. Serum lactoferrin in lepromatous leprosy patients. *Lepr.Rev.*, 64(4), p.295-301, 1993.

The serum concentrations of lactoferrin were determined by competitive enzyme immunoassay in the sera of 38 lepromatous leprosy patients and 16 healthy volunteers. Of the 38 lepromatous patients, 25 were without any sign of reactions while 13 were suffering from ENL type of reactions. The lactoferrin levels, in both types of patients, were observed to be significantly higher ($P < 0.01$ and < 0.001 , respectively) than in that of healthy volunteers. The rise in lactoferrin level in reactive patients was also higher ($P < 0.05$) when compared to those without reactions. The serum lactoferrin levels were also found to be associated with bacterial load ($r=0.414$; $P < 0.01$) indicating that in lepromatous leprosy patients, lactoferrin may not be very effective in preventing the growth of *Mycobacterium leprae*. Further studies to improve the understanding of the role of elevated levels of lactoferrin in pathogenesis of lepromatous leprosy patients and in establishing its possible use in predicting the occurrence of ENL type of reactions would be worthwhile pursuing.

PATTYN, S.R. et. al. Detection of *Mycobacterium leprae* by the polymerase chain reaction in nasal swabs of leprosy patients and their contacts. *Int.J.Lepr.*, 61(3), p. 389-393, 1993.

Nose swabs from 4 paucibacillary (PB) and 8 multibacillary (MB) leprosy patients and their contacts were tested for the presence of *Mycobacterium leprae* by two polymerase chain reactions (PCR); 30% of the samples contained inhibitors for the PCR, 1 of 52 (1.9%) swabs and 13 of 164 (7.9%) swabs were positive for *M. leprae* among contacts of PB and MB patients, respectively. Since this difference is not significant, and some positives were found among contacts of MB patients treated and cured of their infection, it is concluded that the observed infections are community acquired.

PONNIGHAUS, J.M. et. al. Long-term active surveillance of leprosy suspects - what are the likely returns? *Lep.Rev.*, 64(1), p. 25-35, 1993.

Data are presented from the Karonga District in Northern Malawi on the long-term follow up of 277 leprosy suspects who were not given antileprosy treatment or kept on active surveillance. Individuals who were started on antileprosy treatment within a year after leprosy was first suspected, usually on the basis of histopathology results, are excluded from this analysis, because their active surveillance would not usually cause an organizational or financial problem for leprosy control projects. After an average follow-up period of 4-5 years 35 of the 277 suspects included in the analysis (13%) were diagnosed with what we consider to be unequivocal leprosy, and 3 of the 35 had developed disabilities. In 211/277 (76%) all signs of leprosy had disappeared completely.

Comparing clinical certainties at first and last examinations and comparing clinical with histopathological certainties at last examinations it is estimated that up to 50% of the 35 cases of unequivocal leprosy which 'arose' in this group were attributable to misdiagnosis at the 1st or 2nd

examination rather than to genuine progression of the disease. This estimate is compatible with an overall sensitivity of 90% and an overall specificity of 95%, at each examination. Leprosy suspects with 1 cardinal sign of leprosy, either a typical lesion without loss of sensation, or loss of sensation in an otherwise untypical lesion, should be considered a high-risk group in that approximately 25% of such suspects (19/78) were later found with unequivocal leprosy. Policies towards such suspects should be formulated by leprosy control projects.

PORICHHA, D. et. al. Ambiguities in leprosy histopathology. *Int.J.Lepr.* 61(3), p. 428-432, 1993.

This paper presents the percentage of definite or suggestive evidence present in 482 biopsies from different types of leprosy. The presence of acid-fast bacilli (AFB) and nerve involvement were taken as definite features for a diagnosis of leprosy, and infiltration of the dermal appendages, neurovascular bundles and dermis by granuloma cells and lymphocytes were regarded as suggestive signs of leprosy. Using these criteria, all cases were categorized into three groups having definite, suggestive, or no signs of leprosy. The results showed definite and suggestive features in 72.2% and 14.1% of the cases respectively. The remaining 13.7% had none of these signs. These cases were mostly healed lesions. Large, epithelioid cell granulomas without any nerve element present and healed cases proved difficult for a definite diagnosis. Emphasis is placed on searching for residual nerve elements in AFB- negative sections because this increases the certainty level of the diagnosis. Also, it is suggested that for uniformity of understanding and reporting, terminologies need to be narrowed down and restricted to only definite, suggestive, or no diagnosis of leprosy.

RAO, S.P. & BHARAMBE, M.S. Electro neuro physiological studies in early tuberculoid leprosy. *Ind.J.Lepr.*, 65(2), p. 181-187, 1993.

Electro physiological studies were carried out in early tuberculoid type of leprosy in order to study their utility in detecting nerve damage before the onset of obvious functional deficit. Fifty-three cases showing one mixed nerve thickening in one limb were selected. Nerve conduction studies (both motor and sensory) were done using single blind technique. There was no statistically significant difference between the findings obtained from clinically thickened and non-thickened nerves. There was also no direct relationship between clinical sensory deficit and electro physiological abnormality. Clinical motor power loss was well correlated with electro physiological abnormalities.

REDDI, P.P., TALWAR, G.P. & KHANDEKAR, P.S. Molecular cloning and characterization of contiguously located repetitive and single copy DNA sequences of *Mycobacterium tuberculosis* Development of PCR-based diagnostic assay. *Int.J.Lepr.*, 61(2), p. 227-235, 1993.

Screening of a Xgt11 genomic library has been used as an approach for molecular cloning of the *Mycobacterium tuberculosis* repetitive DNA shown to be present on a previously described 5.6-kb Alu I genomic fragment. The recombinant clone R18.8.2, which strongly hybridized with the radio-labeled 5.7-kb Alu fragment, carried two Eco RI inserts of 2 kb and 1.4 kb in size. Southern hybridization of each of these fragments to restriction endonuclease-cleaved *M. tuberculosis* DNA clearly demonstrated the 2 kb to contain the repetitive DNA sequence, while the 1.4 kb is represented in a single copy. When replica plaque lifts from the genomic library were probed, the 5.6-kb genomic fragment and the cloned 2-kb repetitive insert hybridized to an identical number of plaques, indicating the similarity and the high copy number of the repeating unit shared by the two fragments. Restriction

mapping and Southern hybridization patterns indicated that the 2-kb repetitive and the 1.4-kb single-copy DNA sequences originated from a contiguous piece of genomic DNA. Both fragments were found to be unique to members of the *M. tuberculosis* complex, except that the 2-kb insert exhibited a weak hybridization with *M. kansasii* DNA. Finally, a 169-bp region from one end of the single-copy sequence has been amplified by polymerase chain reaction (PCR) in a manner specific to members of the *M. tuberculosis* complex. The sensitivity of the PCR was such that as few as 9-10 bacilli could be detected.

SAMPAIO, E.P. et. al. Development of giant reaction in response to PPD skin test in lepromatous leprosy patients, *Int.J.Lepr.*, 61(2), 1993.

The present study analyzes some clinical and immunological aspects of the giant reaction (GR) in lepromatous leprosy. Sixteen out of a total of 147 (10.9%) lepromatous patients developed the clinical features of GR upon the intradermal administration of PPD; most (14 of 16) GRs occurred in bacteriologically positive cases. GR precipitated an episode of erythema nodosum leprosum (ENL) in three patients. In addition, patients with GR showed enhanced in vitro response to PPD, by the lymphoproliferation test and interferon-gamma assay, as compared to either PPD-negative individuals or PPD-positive patients without GR. Therefore, cell-mediated-immune response to mycobacterial antigens is present in lepromatous patients with GR. It is suggested that the exacerbated in vivo response to PPD in lepromatous leprosy is the result of an increased immunoreactivity to the antigen, which well may be associated with the local and/or systemic release of cytokines [tumor necrosis factor- α (TNF α) and interferon-gamma (IFN γ)] by the inflammatory cells. These episodes may, in fact, play an important role in determining the development of disabilities and reactional states, thereby interfering with the prognosis of leprosy disease.

SCHEEPERS, A. et. al. Oral manifestations of leprosy. *Lepr.Rev.*, 64(1), p. 37-43, 1993,

A total of 37 out of 187 patients with leprosy had oral lesions. All were biopsied. Oral lesions were found most frequently in patients with lepromatous leprosy. Prevalence of lesions was higher in males than in females (73%:27%). Oral lesions were recorded on the WHO topographical map, and in most cases (92%) several topographical locations were affected, including hard palate in all cases. Topographical locations affected increase with age; males are more extensively affected than females ($p=0.001$); and patients with oral lesions who reported affected family members (11 out of 37) had more extensive oral lesions than those who did not. In 27 cases with oral lesions histopathological diagnosis was possible.

SHENDE, R.K. et. al. Adenosine deaminase activity in leprosy. *Ind.J.Lepr.*, 65(2), p. 201-205, 1993.

Serum adenosine deaminase (ADA) was studied in 60 patients of different types of leprosy and 50 healthy control subjects. ADA levels in patients with tuberculoid (50.50 ± 5.22 U/L), borderline (41.14 ± 3.89 U/L) and lepromatous leprosy (30.10 ± 0.03 U/L) were higher than that in controls (17.84 ± 2.78 U/L), thus correlating with the immunological status of patients. Patients with lepra reaction showed decreased ADA levels and higher grade of lepromin test; positivity was associated with increased ADA activity.

SIDDALINGASWAMY, M.K. & RAO, K.S. Nerve abscess in leprosy: a retrospective study. *Lepr.Rev.*, 64(4), p. 357-361, 1993.

Nerve abscesses occur, both in tuberculoid and lepromatous leprosy. We studied 20 patients who had undergone surgery for nerve abscess in mixed peripheral and cutaneous nerves. Details of these cases and the controversial question as to how long the question PB regimen should be continued are discussed.

SIVASAI, K.S.R. et. al, Effect of recombinant interferon gamma administration on lesional monocytes/macrophages in lepromatous leprosy patients. *Int.J.Lepr.*, 61(2), p. 259-269, 1993.

Hydrogen peroxide (H_2O_2) and superoxide anion (O_2^-) were estimated in lesional cells from 10 lepromatous leprosy patients injected intralesionally with recombinant interferon-gamma (rIFN- γ). Clinically similar contralateral lesions injected with excipient served as controls. Lesional esterase-positive cells (suggestive of monocytes/macrophages) from rIFN- γ -injected sites of many subjects showed net increments in the H_2O_2 and o_2 levels compared to controls. When these cells were exposed to *Mycobacterium leprae in vitro*, there was a down-regulation of 0 in 4 of 5 subjects. Such inhibition was not observed in rIFN- γ -injected sites. From the present studies it was not possible to determine whether the above effects of rIFN- γ were primarily on lesional mature macrophages or on newly migrated young monocytes. Erythema and induration were observed at the cytokine-injected site but not at the control site between 24 and 72 hr. A monthly slit-skin smear examination of the former site showed a bacterial index (BI) reduction compared to the controls in 4 of 10 patients this reduction occurring as early as 4 to 8 weeks. Histopathology of the biopsies of 6 of 10 subjects between 9 and 10 months showed a further BI decrease attributable to rIFN- γ and not to the subsequently instituted chemotherapy.

BHARTI, R. & SAINI, R. Improving NLEP performance in a low endemic area. *Ind.J.Lepr.*, 65(3), p. 327-332, 1993.

New innovative strategies of the medical officer of an upgraded urban leprosy centre of a low endemic state (Punjab) resulted in an increase in new case detection by seventy-four percent. Indigenous patients were much more regular than immigrant patients in colonies. The number of new indigenous punjabi patients has not shown any decline in last one decade, probably because of deficiencies in the functioning of

NLEP. It is suggested that improved case detection by adapting strategies used by the authors and restricting free migration of untreated and partially treated patients would help in achieving the goals of NLEP.

BWIRE, R. & KAWUMA, H.J.S. Hospital-based epidemiological study of reactions, Buluba Hospital, 1985-89. *Lepr. Rev.*, 64(4), p. 325-329, 1993.

A retrospective study of 256 reactional episodes, both reversal reaction and erythema nodosum leprosum (ENL), seen in Buluba Hospital over a 5-year period (1985-89) was made. Over 90% of these episodes were due to reversal reaction, with ENL being encountered infrequently. About 80% of reversal reactions occurred during chemotherapy but all the episodes of ENL occurred during this period. Over 70% of both reversal and ENL episodes presented with clinically apparent nerve and skin involvement.

The need to assess the effect of multidrug therapy on the incidence of reactions and to develop more sensitive diagnostic tools to detect early neuritis is emphasized. It is also necessary to study those patients who develop recurrent reactional episodes.

ÇAKINER, T. et. al. Women and leprosy In Turkey. *Int.J.Lepr.*, 65(1), p. 59-67, 1993.

Women in Turkey have many social, cultural and economical problems. Women with leprosy have problems in common with other women as well as those related to physical and social consequences of leprosy.

There are 2,414 patients with leprosy in Turkey, registered to Istanbul Leprosy Hospital and 829 of them are females. The mean age and duration of disease of our female leprosy patients are high. Most women with leprosy were born in eastern part of Turkey where prevalence of leprosy is higher and most have moved to western regions. The proportion of women who have some kind of social security is very low. Their economic status is also not good and 79% of

patients had stigma about their disease. Three fourths of these cases have been hospitalized some time, for different reasons. Most of them (97.2%) have inactive disease at present.

Disability degrees of patients are high.

Patients with disability degrees over one constitute 54% of total for eyes, 55% for hands and 51% for feet. High percentage of multibacillary form and long duration of disease, delayed diagnosis, insufficient self cure of patients due to low socio-economic and cultural status and failure of health personnel to control patients periodically may be among the reasons for such high ratios of moderate and severe disabilities. In the light of the data obtained in our study, some measure to alleviate the problems of patients resulting from their socio-economic, cultural and social status have been suggested.

FRUCHT-PERY, J. & FELDMAN, S.T. Cataract surgery in a leprosy population in Liberia. *Int.J.Lepr.*, 61(1), p. 20-24, 1993.

In Liberia, 43 eyes of 30 patients with ocular leprosy underwent cataract extraction; 33 eyes had extracapsular cataract extraction (ECCE) and 10 eyes had intracapsular cataract extraction (ICCE). ICCE was performed in eyes with poor visualization of the anterior chamber. In 95% of the eyes, the postoperative vision improved by 2 Snellen lines or more, but functional visual acuity (better than 20/200) was achieved in only 65% (82% post-ECCE and 10% post-ICCE). Fewer postoperative complications were observed after ECCE. These findings may have been related to less ocular involvement by leprosy preoperatively. ECCE should be attempted when the visualization of the anterior chamber is fair.

GLAZIOU, P. et. al. Tuberculosis in leprosy patients detected between 1902 and 1991 in French Polynesia. *Int.J.Lepr.*, 61(2), p. 199-204, 1993.

From 1902 onward, notification and follow up of leprosy patients has been systematic in French Polynesia. Since 1960, a tuberculosis con-

trot program and a register has also been implemented. From 1902 to 1959, 673 cases of leprosy were detected [346 multibacillary (MB), 138 paucibacillary (PB), and 179 unclassified due to the loss of medical files by the time of classification which was done during the 1980s]. Of these 673 cases, 89 (13.2%) died from tuberculosis, giving a mean annual death rate of tuberculosis in leprosy patients of 232 per 100,000. Mortality from tuberculosis in leprosy patients detected between 1901 and 1930 was 20.7%, and decreased to 8.04% in patients detected from 1931 to 1959. In total, it was estimated that 26.4% of the leprosy cases had developed tuberculosis. From 1960 to 1991, 350 new cases of leprosy were detected (141 MB, 209 PB). Of them, 12 (3.4%) developed tuberculosis (7 before detection of leprosy, 5 after detection of leprosy). The dramatic decrease of the proportion of leprosy patients who developed tuberculosis between the periods 1902-1959 (26.4%) and 1960-1991 (3.4%) might be related to the important decline of the tuberculosis situation since 1960. From 1902 to 1959, mortality from tuberculosis occurred significantly more frequently in MB patients (13%) than in PB patients [4%, relative risk (RR) = 3.21 p=0.003]. From 1960 to 1991, the incidence of tuberculosis seemed more frequent in MB patients (RR= 2.96, p = 0.07) whatever the sequence of detection of the two diseases. Our study suggests that lepromatous patients could share factors of susceptibility to mycobacterial diseases with patients developing tuberculosis.

REDDY, J.V.S., Health and human resource mobilization: an assessment of staffing pattern in NLEP at operational level. *Ind.J.Leptr*, 65(1), p. 81-93, 1993.

In this paper the staffing pattern, training and infrastructural facilities of the National Leprosy Eradication Programme (NLEP) at operational level as well as the attendant problems in mobilising human resources are discussed. The study shows that the major portion of the work of the NLEP is being shared by the PMWs (72%), followed by NMS (14%) and Medical Officers (5%). The population served by the PMW in all the

high and moderate endemic regions is more than the prescribed limit except in Nagaland and Sikkim. In the some areas the Medical Officer serves a population more than the norm in Andhra Pradesh, West Bengal, Maharashtra, Karnataka and Bihar. Regarding case load, in no state the M.O. serves more than 2500 cases except in Bihar and Kerala, in moderate endemic and low endemic regions respectively. The PMW in Haryana and Punjab states attends more than 250 cases. In NLEP every one out of four sanctioned posts is vacant. There is also an urgent need to rationalize the training programme so that there is optimal utilization of the training centres.

SAHA, S.P. & DAS, K.K. Disability pattern amongst leprosy cases in an urban area (Calcutta). *Ind.J. Leptr*, 65(3), p. 305-314, 1993.

In a retrospective study of 1,264 leprosy cases, registered during 1987-1992, 282 were found to have disabilities giving a disability rate (DR) 22.31% and 150 of them were also found to have deformities, giving a deformity rate 11.9%. Mean disability index (DI), was found to be 1.17. Disability rate (DR) significantly increased with age and the highest rate was 52.75% in lepromatous (L) cases, followed by 27.51% in borderline (N?L) and only 4.53% in nonlepromatous (N) cases. L cases had the highest deformity rate (22.25%) and N cases had the lowest DR (2.23%). DI was highest (1.46) in L, and lowest (0.52) in N cases. Males had significantly higher DR (27.2%) compared to females (13.0%). Deformity in hands (42.55%) was more common than in feet (22.70%). Increasing trend of DI was noticed with increasing duration of disease in L and N?L types. The number of nerves involved was high (4.72) in L cases compared to other types. DI was highest (1.25) in patients engaged in occupations involving hard work.

HANSENÍASE EXPERIMENTAL

BHATIA, V.N. & THAWANI, G. Observations on attempted leprosy cultures in two media. *Ind.J.Lepr.*, 65(2), p. 163-171, 1993.

Suspensions of skin tissue material collected from lepromatous leprosy patients and material from mouse foot-pad harvests were inoculated into two media, viz., a biphasic medium and a minimal basal medium. The cultures were incubated at 37°C and 15°C. Small oval (or round) cells appeared in these cultures around the tenth day along with a few cystic structures; and they increased in number later, reaching the maximum around six - seven weeks. The above cells appeared acid-fast in some cultures and some of them appeared to split into pairs of acid-fast bacilli. The cells were most often seen in the biphasic medium at 37°C. The identity of these structures is not known at this stage.

CHO, S.N. et. al. Serologic responses to nerve antigens in sooty mangabey monkeys with experimental leprosy, *Int J.Lepr.*, 61(2), p. 236-244, 1993.

Eight sooty mangabey monkeys were inoculated intravenously and intradermally with varying doses of *Mycobacterium leprae* from 4.8×10^7 to 4.8×10^{10} . Serum samples were obtained from the animals at intervals of about 3 months for 90 months, and were examined for IgM and IgG antibodies to nerve antigens, including ceramide, galactocerebroside (GC), and asialo-GM. (AGM), using an enzyme-linked immunosorbent assay (ELISA). The serological results were then compared with clinical findings, particularly nerve involvement. Of 8 mangabey monkeys inoculated with *M. leprae*, 7 animals had clinical leprosy; 6 of them had nerve damage, including neurologic deformities in 4 monkeys and nerve enlargement in 2. Median time for the initial signs of leprosy was 10 months postinoculation (p.i.), a

range from 4 to 35 months. In contrast, nerve damage was noted rather late, about 35 to 86 months p.i. (median 54 months). The major immunoglobulin class to ceramide, GC, and AGM1 antigens was IgM, and the antibody responses to the nerve antigens appeared from 15 to 63 months p.i. (median 37 months). Antineural antibodies were thus detectable about 18 months (range -2 to 60 months) prior to observable nerve damage. In addition, elevation of antineural antibody levels were predictive of clinical exacerbation of the disease and neuritic damage. This study suggests that antineural antibodies are produced during the course of *M. leprae* infection and may be indicative of nerve damage, such as neurological deformities or nerve enlargement, in leprosy patients.

DAMLE, A. & MAHADEVAN, P.R. In vivo effect of delipidified cell component of *Mycobacterium leprae* in relation to infection with leprosy bacteria in mice. *Ind.J.Lepr.*, 65(3), p. 271-282, 1993.

The delipidified cell component (DCC) of *Mycobacterium leprae* was used as an immunomodulatory agent in Swiss white mice. The peritoneal macrophages of these mice were activated to produce increased amount of reactive oxygen intermediates like hydrogen peroxide (H_2O_2) and superoxide. These macrophages also attained the ability to kill *M. leprae* in vitro as shown by several assay systems including the conventional mouse foot-pad technique. The increased levels of superoxide seem to be responsible for the killing of *M. leprae* in addition of the enzyme superoxide dismutase, which breaks down O_2 , resulted in survival of these bacilli inside the macrophages. The increased production of H_2O_2 does not seem to be responsible for killing *M. leprae*. The results indicate that the DCC of *M. leprae* acts as an effective immunomodulator in mice leading to the activation of macrophages with increased production of H_2O_2 and superoxide as well as enabling them to kill *M. leprae* via the action of superoxide anions.

KOHSAKA, K. et. al. Preservation of *Mycobacterium leprae* in vitro for four years by lyophilization. *Int.J.Lepr.*, 61(3), p. 415-420, 1993.

Although the viability of *Mycobacterium leprae* suspended in distilled water with or without 10% fetal calf serum was reduced approximately 10^3 to 10^4 from that of the starting material during the process of lyophilization, bacilli capable of multiplication in nude mouse foot pads were found in the lyophilized samples stored for 4 years at 4°C. The multiplication rate of the lyophilized bacilli which were suspended in 10% serum-water was much higher than that of the bacilli suspended in water only. On the other hand, no reduction of the viability of *M. leprae* suspended in 10% skim milk-water was demonstrated during the process of lyophilization as well as storage for 2 years at 4°C. From the results obtained here, it could be suggested that *M. leprae* might be preserved in vitro by means of lyophilization. In particular, the viability of lyophilized *M. leprae* was extremely stable during cryopreservation when the bacilli were suspended in 10% skim milk-water. Therefore, the composition of the solution for suspending the bacilli is definitely critical for the maintenance of *M. leprae* viability by means of lyophilization.

KRISHNAMURTHY, P. et. al. *Mycobacterium leprae* soluble antigen (REES) skin test responses in an endemic population in India. *Ind.J.Lepr.*, 65(1), p. 49-57, 1993.

The response to intradermal administration of Rees soluble skin test antigen was studied in 12,142 randomly selected individuals living in a highly endemic area in South India. Taking a cutoff point of 12mm induration as the criterion for 'positivity', 73% of PB cases, 45% of MB cases and 63% of noncase population (67% in contacts and 63% in non-contacts) were found to be positive. Age-specific positivity rates were higher in males than in females and in adults than in children. The difference in age-adjusted positivity rates between cases, contacts and noncontacts in the female population was found to be significant.

However, the differences in reaction response were not sufficient to identify the sub-populations of cases, contacts and noncontacts and as such this antigen is not likely to be useful in epidemiological studies of infection and evolution of clinical disease in high endemic populations.

PESSOLANI, M.C.V., HUNTER, S.W. & BRENNAN, P.J. Relationship between host histones and armadillo-derived *Mycobacterium leprae*. *Int.J.Lepr.*, 61(3), p. 381-388, 1993.

A major protein previously recognized as being primarily associated with the cell walls of *Mycobacterium leprae*, major wall protein (MWP), is now identified as histoprotein H2b based on N-terminal amino-acid sequencing, electrophoretic comparisons, and several other properties. An avid association between several host/armadillo-derived histones and *M. leprae* was demonstrated. Since such armadillo-derived *M. leprae* are the basis of several ongoing vaccine trials, a simple procedure that permits the prompt solubilization and quantification of histones in *M. leprae* preparations is described. The quantity of histones associated with *M. leprae* is significant, ranging from 0.6 to 4.8 µg of histoprotein H2b per mg of bacteria.

SHETTY, V.P. Animal model to study the mechanism of nerve damage in leprosy - A preliminary report. *Int.J.Lepr.*, 61(1), p. 70-75, 1993.

Intraneural injection of $10-20 \times 10^6$ viable *Mycobacterium leprae* into the sciatic nerve of normal, unsensitized, Swiss white mice gives rise to a tuberculoid type of granulomatous response in 2 weeks. The same dose of viable *M. leprae* when injected into the sciatic nerves of unsensitized immunosuppressed mice (T200 x 5R) elicited a macrophage response. When macrophages were systemically immobilized using an intraperitoneal injection of silica quartz dust in normal mice, the lesion produced was of the lepromatous type, suggesting a role for the

macrophage in the induction of the tuberculoid type of granulomatous response. In all of these *In situ* experiments, *M. leprae* failed to enter the Schwann cells.

IMUNOLOGIA

AZOUAOU, N. et. al. Reconstitution of *Mycobacterium leprae* immunity in severe combined immunodeficient mice using a T-cell line. *Int.J.Lepr.*, 61(3), p. 398-405, 1993.

To test whether *Mycobacterium leprae*-immune T cells can confer protection against infection with leprosy bacilli, severe combined immunodeficient (SCID) mice were reconstituted with a BALB/c-derived, *M. leprae*-responsive, T-cell line. Flow cytometric analysis of spleen and peripheral blood cells confirmed reconstitution with T cells. *In vitro* lymphokine production and the proliferation of spleen cells from the reconstituted animals established that the donor cells had maintained their functional activity for the duration of the study (275 days). The transfer of immune T cells 24 hr before foot pad infection with leprosy bacilli resulted in a profound reduction in *M. leprae* multiplication, as compared to the non-reconstituted SCID mice. The yield of acid-fast bacilli in the foot pads of SCID mice reconstituted with the *M. leprae*-immune T cells also was significantly lower than that found in naive BALB/c mice, and at levels previously found only in BALB/c mice that had been immunized effectively. These experiments demonstrate that *M. leprae*-immune T cells home effectively and control *M. leprae* infection in SCID mice.

CELLONA, R.V. et. al. Cross-Sectional assesment of ELISA reactivity in leprosy patients, contacts, and normal population usin the semisynthetic antigen natural disaccharide octyl bovine serum albumin (ND-O-BSA) in Cebu, the Philippines. *Int.J.Lepr.*, 61(2), p. 192-198, 1993.

An Indirect enzyme-linked immunosorbent assay (ELISA) using natural disaccharide octyl bovine serum albumin (ND-O-BSA) as antigen was used in testing leprosy patients, contacts and a normal population in Cebu. The Philippines, from 1985 to 1989. A total of 1413 persons were studied. The results suggested that ELISA reactivity and the bacterial Index (BI) correlate in a general way. In multibacillary (MB) leprosy positivity ranges from 54.2% to 92.3% among patients with a BI of < 2+ to > 4+ on the Ridley scale, with an overall average of 84.5% Paucibacillary (PB) leprosy patients have a low degree of reactivity, with only 15.0% ELISA positive. The test is more efficient in detecting MB than PB leprosy. The contacts of MB leprosy showed 6.5% positivity; contacts of PB leprosy, 7.0% positivity. The normal population showed 11% positive ELISA or 17 per thousand population, which is very much less than that of the household contacts. However, because the normal population is a much larger population than the household contact population in a community, more new leprosy cases would emanate from it. Leprosy workers are concerned about the transmission of the disease to household contacts. However, for the reason stated above, we should be more concerned with the silent spread of the disease to the normal population in the community. Further studies are required along this line: One to determine whether there is a correlation between prevalence rates of ELISA positivity in the normal population, the other is to find out if the rate of ELISA positivity in the normal population of a community can be used to monitor the efficiency of a leprosy control program.

CHIPLUNKAR, S.V. et. al. Immunoreactivity of *Mycobacterium* strain ICR C and *Mycobacterium leprae* antigens with polyclonal and monoclonal antibodies. *Int.J.Lepr.*, 61(3), p. 421-427, 1993.

ICRC, a cultivable mycobacterium, is undergoing clinical trials as an antileprosy vaccine in India. In the present study, we have investigated the crossreactivity between antigens of the mycobacterial strains of ICRC and *Mycobacterium*

leprae using polyclonal and monoclonal antibodies in a radioimmunoprecipitation assay. It was observed that polyclonal anti-ICRC and anti-*M. leprae* antibodies showed predominant reactivity to a 21-kDa protein of the mycobacterial strains ICRC and the 21-and 14-kDa proteins of *M. leprae*. Crossreactivity between the antigens of the mycobacterial strains ICRC and *M. leprae* was established further by using *M. leprae*-specific monoclonal antibody WML06 (reacting with the 14-kDa protein of *M. leprae*), which identified the 21 - and 14-kDa proteins of the mycobacterial strain ICRC. Thus, our studies demonstrate that the 14-kDa protein of *M. leprae*, which is known to harbor T- and B-cell epitopes, shares crossreactive antigenic determinants with the 21-and 14-kDa proteins of the mycobacterial strain ICRC. We believe that such proteins may provide important reagents for designing subunit vaccines and for determining skin-test reagents.

CONVIT, J. et. al, BCG Vaccination protects against leprosy in Venezuela: A case-control study. *Int.J.Lepr.*, 61(2), p. 185-191, 1993.

A total of 64,570 household and other close contacts of about 2000 leprosy cases were screened for eligibility for entry into a trial of a new leprosy vaccine. The screening procedure included a clinical examination for leprosy and for the presence of BCG and lepromin scars. Ninety-five new cases of leprosy were identified, and the prevalence of BCG and lepromin scars among them was compared with similar data from matched controls selected from among those with no evidence of leprosy. The difference in the prevalence of BCG scars in the two groups was used to estimate the protection against leprosy conferred by BCG vaccination. One or more BCG scars was associated with a protective efficacy of 56% (95% confidence limits 27% to 74%). There was a trend of increasing protection with four or more BCG scars, but this was not statistically significant. There was no evidence that the efficacy of BCG varied with age or according to whether or not the contact lived in the same household as a case. The protective effect was significantly higher

among males, and was significantly greater for multibacillary than for paucibacillary leprosy.

ISLAS-RODRIGUEZ, A.E. et. al. Recognition of *Mycobacterium leprae* antigens with antibodies present in sera from patients with lepromatous leprosy. *Int.J.Lepr.* 61(2), p. 245-249, 1993.

A great diversity of antigens from *Mycobacterium leprae* have been described. One practical approach should be to utilize them as markers to indicate when a household contact is at risk of becoming infected and then moving to an active form of leprosy. For this purpose, sonic extracts of *M. leprae* were fractionated in 10% SDS-PAGE under reducing conditions. The fractionated proteins were then transferred to nitrocellulose sheets and incubated with sera from lepromatous leprosy cases, their contacts, and normal subjects in order to reveal the frequency of antigen recognition of each set of sera. The results showed that sera from lepromatous leprosy patients frequently recognized two proteins, one of approximately 28 kDa and the other of approximately 65 kDa, when compared with the sera from normal subjects. The contacts frequently recognized an approximately 16-kDa antigenic band, while sera from normal subjects recognized one protein of approximately 18 kDa. According to the results, the four recognized proteins from *M. leprae* can be considered markers of the above conditions (approximately 65 kDa, approximately 28 kDa for lepromatous leprosy, approximate: 16 kDa for contacts, and approximately 19 kDa for normal subjects). From these, an easy serological test, such as an ELISA, can be developed to predict if a contact is moving toward lepromatous leprosy before detection of the actual clinical signs or symptoms.

JOB, C.K. et. al. Armadillos (*Dasyus novemcinctus*) as a model to test antileprosy vaccines; a preliminary report. *Int.J.Lepr.*, 61(3), p. 394-397, 1993.

The efficacy of two candidate leprosy vaccines, BCG and a mixture of BCG and killed

Mycobacterium leprae, was tested in 62 armadillos caught in the wild. The abilities of the vaccines to convert lepromin-negative armadillos to a positive reaction were compared with a group of control animals. Both vaccines upgraded subsequent lepromin skin-test histopathology. The conversion results parallel the protection values obtained in some BCG vaccine trials against leprosy in humans. Before conducting expensive human trials with new antileprosy vaccines, it would be worthwhile first to evaluate them in the armadillo model.

KAR, H.K. et. al. Reversal reaction in multibacillary leprosy patients following MDT with and without immunotherapy with a candidate for an antileprosy vaccine, *Mycobacterium w*. *Lepr.Rev.*, 64(3), p.219-225, 1993.

Immunotherapy with a candidate for an antileprosy vaccine, *Mycobacterium w*, was given in addition to standard multidrug therapy (MDT) to 53 multibacillary lepromin negative patients belonging to BB, BL and LL types of leprosy (vaccine group). An equal control group received MDT and injections of micronized starch as placebo. Both the vaccine and placebo were administered intradermally every 3 months. The patients were evaluated at determined intervals by clinical, bacteriological and histopathological parameters and lepromin testing. Reactional episodes were analysed with reference to incidence, onset, frequency and severity during and after release from treatment (RFT). Incidence of reversal reaction (RR) was marginally higher in the vaccine group (22.6% vaccine group vs 15% control group). All cases with a history of downgrading type 1 reaction developed RR during therapy. Most episodes occurred within the 1 st year of the commencement of therapy - 50% developing within 3 months. Late reversal reaction (after RFT) were observed in 3.8% of cases in both groups, and 50% of the reactors in the control group and 33% in the vaccine group had repeated reactional episodes. Incidence of neuritis associated with RR as well as isolated neuritis was similar in both groups.

KAUR, I. et. al. Bacillaemia and *Mycobacterium leprae* cell wall antigen in paucibacillary leprosy. *Ind.J.Lepr.*, 65(3), p.283-288,1993.

A study was undertaken to estimate bacillaemia and *M. leprae* antigen detection in 54 paucibacillary leprosy patients (TT, BT). Acid-fast bacilli were detected in the blood of 14.8% patients of borderline tuberculoid (BT) leprosy. *M. leprae* antigen was demonstrated in 48.2% patients of BT leprosy. Slit-skin smears were negative in all these patients. At the end of treatment (6 months of WHO-MDT) all the follow-up blood samples were negative for both bacillaemia and *M. leprae* antigen in the serum.

KOHLI, M. et. al. Transport of aminoácido across renal brush border membrane vesicles In. *Mycobacterium leprae* infected Swiss albino mice-effect of Convit vaccine. *Lepr. Rev.*, 64(4), p. 316-324, 1993.

Brush border membrane vesicles prepared from kidneys of *Mycobacterium leprae* infected (non-vaccinated) and vaccinated-infected Swiss albino mice were used to assess the effect of Convit's combined vaccine (BCG + *M. leprae*) on amino acid transport activity across the tubular basement membrane. The protective effect of Convit's vaccine was more pronounced with respect to the uptake of L-alanine than L-aspartate. Uptake of L-lysine showed no significant difference in the different groups. Footpad counts followed characteristic growth curves in the non- vaccinated infected group but showed a lag in the development of peak leels in the vaccinated group. Further Convit's vaccine appeared to have a protective effect on renal impairment in the mouse model of leprosy in the initial stages of Infection only, as indicated by the transient reversal of amino acid uptake and a diminution in the footpad counts induced by *M. leprae* infection. No significant ($P>0.05$) protective effect of the vaccine was found in the advanced disease state.

KROUMPOUZOS, G. et al. Evaluation of the autoimmune response in leprosy. *Lepr. Rev.*, 64(3), p. 199-206, 1993.

Immunological responses to a panel of antigens were evaluated in 27 patients with lepromatous and 20 patients with tuberculoid leprosy and compared with 24 pulmonary tuberculosis patients, 25 systemic lupus erythematosus patients and 41 healthy blood donors. Some autoantibody specificities were extensively studied for the first time in mycobacterial infections. Striking immunoserological abnormalities were found in patients with lepromatous leprosy, particularly in those presenting with relapse. Inhibition assays were performed, providing a tool for further analysis of the binding range of specific anti-N.D.O. BSA antibodies and strengthening the suggestion of molecular mimicry reactions between cytoskeletal proteins, host stress proteins and *Mycobacterium leprae* antigens or stress proteins. A significant serological overlap between lepromatous leprosy and autoimmune diseases is indicated.

PONNIGHAUS, J.M. et al. The Karonga prevention trial: a leprosy and tuberculosis vaccine trial in Northern Malawi. I. Methods of the vaccination phase. *Lepr. Rev.*, 64(4), p. 338-356, 1993.

In this report the methods of the Karonga Prevention Trial, a double-blind leprosy and tuberculosis vaccine trial in Karonga District, Northern Malawi, are described in detail. During a total population house-to-house survey, which lasted from November 1985 until August 1989, 121,008 people (57,892 males and 63,116 females) were vaccinated. A further 5835 people refused vaccination and 5757 were ineligible for vaccination, 2652 of them because they had a history or signs of leprosy, or because they were suspected to have early leprosy. A total 66,145 individuals, without evidence of prior BCG vaccination, received one of the following: BCG, BCG+5 x 10⁷ killed *Mycobacterium leprae*, or BCG+6 x 10⁸ killed *M. leprae*; 54,863 individuals found with a typical or a doubtful BCG scar received either

placebo or BCG, or (from mid-1987 onwards) BCG+6 x 10⁸ killed *M. leprae*. Side-effects were not looked for systematically, but 4 individuals self-reported with glandular abscesses, 9 with large post-vaccination ulcers (> 25 mm in diameter) and 2 with ulcers which persisted for more than 1 year.

SHINDE, S.R. et al. Lymphocyte proliferation, IFN- γ production and limiting dilution analysis of T-cell responses to ICRC and mycobacterium leprae antigens in leprosy patients. *Int.J.Lep.*, 61(1), p. 51-58, 1993.

Lymphocyte proliferative responses and interferon-gamma (IFN- γ) production after stimulation with antigens of ICRC, *Mycobacterium leprae*, and purified protein derivative (PPD) were assessed in leprosy patients and healthy donors. The patients studied were newly diagnosed as having lepromatous leprosy (LL), multidrug therapy (MDT) responders (MDT-R LL), MDT nonresponders (MDT-NR LL), borderline lepromatous (BL), and borderline tuberculoid/tuberculoid (BT/TT) leprosy. The tuberculoid leprosy patients showed increased lymphocyte proliferation and IFN- γ production in response to stimulation with ICRC, *M. leprae*, and PPD antigens compared to other groups of LL patients and healthy donors. Although lymphocytes from LL patients showed low responses to ICRC and *M. leprae* antigens, their responses to PPD were not grossly affected. MDT-R LL patients showed higher lymphocyte proliferative responses and IFN- γ production after stimulation with ICRC and PPD but not with *M. leprae* antigens. Tuberculoid leprosy patients showed higher T-cell frequency to ICRC and *M. leprae* antigens compared to MDT-R LL and MDT-NR LL patients. The increased lymphocyte proliferative responses to ICRC observed in the MDT-R LL patients was reflected in the increased T-cell frequency to ICRC compared to *M. leprae*.

YAMASHITA, J.T. et. al. Circulating immune complexes in leprosy sera: demonstration of antibodies against mycobacterial glycolipidic antigens in isolated immune complexes. *InLJ.Lepr.*, 61(1), p. 44-50, 1993.

Circulating immune complexes (CIC) were assayed in sera of leprosy patients. Using an immunoassay for two mycobacterial antigens - phenolic glycolipid-I (PGL-I) and glycolipid IV (SL-IV) sera from 65 patients with leprosy (38 lepromatous, 18 borderline, and 9 tuberculoid) were studied. The CIC were isolated by polyethylene glycol (PEG) precipitation, washed, treated with and acid buffer, neutralized, and tested using an enzyme-linked immunosorbent assay (ELISA). We demonstrated that CIC could contain IgG and IgM antibodies reacting against PGL-I and SL-IV. The high levels of antibodies in the precipitable CIC showed concordance with high levels in the original sera, although some patients presented high levels of precipitable CIC in the absence of high titers of antibodies in their sera. It was concluded that some of the CIC observed in patients with leprosy were composed of IgG and IgM immunoglobulins against specific mycobacterial antigens.

ZAHNER, S.A. et. al. Immunotherapy with *Mycobacterium w* vaccine decreases the incidence and severity of Type 2 (ENL) reactions. *Lepr.Rev.*, 64(1), p. 7-14, 1993.

Immunotherapy with *Mycobacterium w* (*M. w.*) vaccine was given to 45 patients with multibacillary (MB) leprosy; 41 similarly classified patients served as controls. All patients received standard multidrug therapy (MDT). Incidence, severity and frequency of type 2 (ENL) reactional episodes were monitored in both groups in a follow-up extending up to 4 years. Reactions were seen in fewer vaccinated (10/37) BL and LL patients than in the control group (12/34). A total of 20 episodes were recorded in the vaccine group as against 29 in the controls, 75% of reactions were mild in vaccinated and 51.72% were mild in the control group patients, and 3

patients in the control group had more than 3 reactional episodes. None of the vaccinated patients showed this. No additional incidence of neuritis were seen among vaccinated individuals during reactional episodes.

ZAI-LING, C. et. al. Pilot study to determine acceptability and ability of heat-killed *Mycobacterium leprae* plus BCG (HKML+BCG) vaccine to induce skin test conversion. *Lepr. Rev.*, 64(2), p. 117-127, 1993.

Although local reactions, including erythema, induration and ulcers, appeared in every patient after the injection of the combined HKML+BCG vaccine, they were accepted by the patients. There was no tendency for the local reaction to become aggravated after repeated vaccination. However, systemic reactions, mainly iridocyclitis and complaint of numbness of the fingers and toes, became quite common after the 5th vaccination and therefore significantly reduced the acceptability of vaccine by injection. It seems that repeated vaccination might activate the iridocyclitis, but the relationship between the complaint of numbness and vaccination has not been well established. Neither typical ENL nor reversal reaction had been observed throughout the trial.

A significant proportion of patients converted to SMLA positivity after repeated vaccination. However, it seems the positive status was not stable as many of them reverted to negative after the following vaccination. After the 7th vaccination, the positive conversion rate to SMLA-I was 45% and to SMLA-II was 35%. After the 8th vaccination, 66.7% of patients converted to Mitsuda reaction positive, which has been confirmed by histopathological examination. Nevertheless, further follow-up is required in order to determine whether or not such conversion will be of a long duration.

The reactions to SMLA-I and SMLA-II were associated but only correlated at a moderate level. Overall, the positive conversion rate to SMLA-I was significantly higher than that to SMLA-II after repeated vaccination. Neither the early reaction nor the late (Mitsuda) reaction of the lepromin test were correlated to either SMLA reaction.

The repeated vaccination of HKML+BCG vaccine did not affect the weakly-positive anti-PGL-I *Mycobacterium leprae* antibody level seen in the skin-smear negative lepromatous patients participating in this study.

MICROBIOLOGIA

LAL, H. et. al. Detection of antibodies to phenolic glycolipid by alisa in leprosy patients. *Ind.J.Lepr.*, 65(1), p. 95-99, 1993.

Antibody (IgM) response to PGL-I, a surface glycolipid unique to *Mycobacterium leprae* has been studied in 25 cases each of lepromatous and tuberculoid leprosy and in 25 healthy controls. The absorbance value at 488 nm was expressed as antibody titre. Serum antibody titre was found to be significantly higher in patients than controls. Results confirm that antibody response in leprosy patients depend upon bacterial load.

OUTROS EXAMES LABORATORIAIS

BHATIA, V.N. et. al. Application of filter paper method for collection of blood for MLPA test. *Ind.J.Lepr.*, 65(2), p. 207-210, 1993.

The results of MLPA test using serum and filter paper eluate have been compared in this paper. Testing 64 patient samples at 1:32 dilution, 31 were negative by both serum and eluate, 20 were positive by both, six were positive only by serum and one was positive only eluate. In six other cases eluate gave equivocal results while serum result was clearly positive. Some eluates negative at 1:32 dilution gave weak positive agglutination at 1:16 dilution.

SEKAR, B. et. al. Serological response of leprosy

patients to *Mycobacterium leprae* specific and mycobacteria specific antigens: possibility of using these assays in combinations, *Lepr.Rev.* 64(1), p. 15-23, 1993.

The serological response of 147 leprosy patients to 3 mycobacterial antigens, PGL-I, 35 kDa (*Mycobacterium leprae*-specific) and LAM (which is a common mycobacterial antigen) were analysed. A stronger serological response was seen amongst the MB patients than the PB patients in all the assays. The 3 antibody levels correlated positively with each other in both MB and PB cases. An overlap of seropositivity was seen between anti-PGL-I and anti-LAM ($p > 0.05$). A progressive increase in seropositivity and a significant difference of absorbance or titre in antibody levels in all 3 assays over increasing grades of BI were seen in the MB patients ($p < 0.05$). A significant difference in seropositivity between untreated and treated groups of patients was observed for anti-PGL-I ($p < 0.05$) and antiLAM ($p < 0.01$) antibodies. The sensitivity, specificity and efficiency of antiPGL-I (50%; 99%; 70%), antiLAM (43%; 95%; 64%) and antiga kDa (66%; 100%; 80%) assays taken individually were less than that of combinations of antiPGL-I/anti-35 kDa (74%; 99%; 84%) or antiPGL-I/anti-35 kDa/ antiLam (80%; 94%; 86%). The difference in the efficiency of both sets of combination of assays were not statistically significant ($p < 0.05$).

REABILITAÇÃO

GUOCHENG, Z. et. al. An epidemiological survey of deformities and disabilities among 14,257 cases of leprosy in 11 counties. *Lepr.Rev.*, 64(2), p. 143-149, 1993.

This study was planned and conducted in Yang Zhou Prefecture, covering 11 counties that were formerly areas with a high prevalence of leprosy. Out of 14,257 leprosy patients, 8122 (56.97%) cases with deformities and disabilities were found. The disability rate is much higher in patients with MB leprosy (81.15%) than in PB

leprosy (53.04%). The statistical data and the type of deformities and disabilities are presented. The influences of various host factors and disease factor which cause disability and deformity are discussed.

JAGANNATHAN, S.A. et. al. A pilot project on community based rehabilitation in south India - a preliminary report. *Ind.J.Lep.*, 65(3), p. 315-322, 1993.

A pilot project on Community Based Rehabilitation was launched by the Hind Kusht Nivaran Sangh in South Arcot District of Tamil Nadu with the help of the Hemerijckx Rural Centre, Rawttakuppam on an experimental basis to assess the cost effectiveness and suitability of its application in other districts. Twenty cured disabled leprosy patients with grades 1 and 2 deformities from 17 villages were given training in trades like cycle repairing, tailoring, pesticides spraying, doll making, cane work, cigar making, fish net knitting and incense stick making.

The duration of the training varied from two to six months depending upon the trade. Local artisans and craftsmen from among the community members were identified, motivated, and utilised as trainers. The travel and maintenance costs paid to the trainees was an incentive to learn the trade and the honorarium paid to the trainers motivated them to spare their time to impart the skill within the specific period. On completion of training, start-up funds needed for purchase of tools and accessories required for pursuing the vocation were arranged through banks under DRI scheme, IRDP schemes from BDO office and from other voluntary agencies. The total expenditure incurred for training 20 cured disabled leprosy patients worked out to only Rs. 25,350/i.e., approximately Rs. 1,250/- per patient. Out of the 20 patients trained, 17 have already started earning through the skills imparted to them.

MIKO, T.L. et. al. Regeneration at the predilective damage sites of nerve trunks in treated leprosy. *Lep. Rev.*, 64(4), p. 330-337,

1993.

Superficially located large and medium sized peripheral limb nerves in active leprosy have previously been shown to have well-recognized fusiform swellings. It is generally agreed that these are the sites of predictive nerve involvement where the severest degeneration and fibrosis occur. A semiquantitative histopathological study on one of these sites, the flexor retinaculum region of the posterior tibial nerve, has been carried out on 14 treated leprosy patients who suffered from total sensory loss to the foot for between 2 and 40 years. The following observations were made: (1) large-scale nerve regeneration was presented as characterized by numerous Schwann cells and unmyelinated axons which formed regeneration clusters; (2) thick myelinated axons were either absent or present only in very low numbers; (3) the intraneurial fibrosis was usually not severe; (4) the presence of active inflammation probably interfered with nerve regeneration; (5) it appeared that this regeneration started shortly after the onset of therapy and persisted for decades; (6) lepromatous cases were characterized by evenly distributed pathology, whereas borderline tuberculoid cases had an unevenly distributed pathology; (7) the massive nerve regeneration observed was functionally ineffective - these findings indicate that the total nerve damage may affect the more peripheral nerve branches.

TERAPÊUTICA

BOERRIGTER, G. & PONNIGHAUS, J.M. Does the introduction of WHO-MDT influence trends in the incidence of leprosy? - the Malawian experience. *Lep. Rev.*, 64(3), p. 227-235, 1993.

There has been an average annual decline in detection rates of all types of leprosy in Malawi of around 11.6% between 1977 and 1991. There was no obvious acceleration or slowing down of this decline following the introduction of WHO/MDT in 1983-84. Disability ratios stayed at the same level of about 11% during the 15 years

covered by this paper suggesting that patients did not self report earlier after 1983-84 which might have masked an underlying accelerated decline in detection rates. Thus it is concluded that the influence of WHO/MDT on the pattern of leprosy over a period of time, in a country like Malawi, is so far not noticeably different from any influence dapsone monotherapy might have had.

BWIRE, R. & KAWUMA, H.J.S. Human immunodeficiency virus and leprosy-type 1 reactions, nerve damage and steroid therapy: "a case report". *Lepr.Rev.*, 64(3), p. 267-269, 1993.

In this study a 28-year-old female with both BL leprosy and HIV infections is discussed. Her clinical progress was followed until she completed MDT. During this period she developed recurrent reactional episodes, nerve damage and intercurrent illnesses - some of which might have been due to steroids.

CORNWALL, J., CAMERON, G. & ELLIS-PEGLER, R.B. The effects of World Health Organization chemotherapy on imported leprosy in Auckland, New Zealand, 1983-90. *Lepr.Rev.*, 64(3), p. 236-248, 1993.

Between January 1983 and December 1990 in Auckland, New Zealand, 87 patients (28 paucibacillary disease (PBD) and 59 multibacillary disease (MBD)) commenced WHO multidrug therapy (MDT).

All were immigrants from the Pacific Islands (65) or Asia (22). A total of 57 patients had already received non-WHO regimens, some continuously, but often intermittently, for many years; 30 patients received WHO MDT only. By December 1990, 50 had completed treatment, with 1 relapse and 1 late reaction, both in patients with PBD treated with WHO MDT only. There have been no relapses in those treated with WHO MDT after prior leprosy treatment.

In those with MBD, type II leprosy reactions were less common (16%) in those treated only with WHO MDT than in those treated continu-

ously before 1983 with older regimens (64%). Type I leprosy reactions occurred in about 20% of both these groups. The bacterial index fell faster in those who had had a prolonged prior treatment beginning WHO MDT than in those starting WHO MDT as their initial leprosy chemotherapy.

Overall we found WHO MDT was well accepted and the compliance good, but 13 patients (15%) left Auckland before treatment was completed and 6(7%) during follow up.

DROWART, A. et. al, Effects of chemotherapy on antibody levels directed against PGL-I and 85A and 85B protein antigens in lepromatous patients. *InLJ.Lepr.*, 61(1), p. 29-34, 1993.

IgG antibodies against antigens 85A and 85B from *Mycobacterium bovis* BCG, IgM antibodies against phenolic glycolipid-I (PGL-I) and circulating PGL-I antigen were measured in the serum of 11 patients with lepromatous leprosy receiving multidrug therapy (MDT). Before treatment, 6 patients were reactive to antigen 85A, 10 patients to antigen 85B, and 11 patients to PGL-I; circulating PGL-I was detected in the sera of all of them. After 2 years of MDT PGL-I antigen could no longer be detected in all of the patients, except for two who were not compliant with treatment. IgG antibodies directed against the 85A and 85B antigens and IgM antibodies against the PGL-I antigen also decreased significantly during treatment but more slowly. The determination of circulating PGL-I antigen remains the most appropriate tool for monitoring lepromatous leprosy under MDT.

FRANZBLAU, S.G. et. al. Sparfloxacin is more bactericidal than ofloxacin against *Mycobacterium leprae* in mice. *InLJ.Lepr.*, 61(1), p. 66-69, 1993.

The comparative bactericidal activities of sparfloxacin and ofloxacin against *Mycobacterium leprae* in mice were determined using the proportional bactericidal test at doses of 12.5 mg/kg - 100 mg/kg. Significant bactericidal activity

was found at 12.5 mg/kg sparfloracin and 25 mg/kg ofloxacin. Sparfloracin was significantly more bactericidal than ofloxacin at all doses, and the results with 25 mg/kg sparfloracin were nearly identical to those obtained with 100 mg/kg ofloxacin. These results, together with pharmacokinetic and toxicological data in mice and man, suggest that sparfloracin may have a higher therapeutic index than ofloxacin in leprosy, and that the tentative standard dosage of 200 mg sparfloracin daily should be appropriate for a clinical trial.

GONZÁLEZ, A.B. et. al. Survey for secondary dapsone and rifampicin resistance in Cuba. *Lepr.Rev.*, 64(2), p. 128-135, 1993,

A total of 1211 Cuban multibacillary leprosy patients treated for at least 5 years were clinically and bacteriologically examined. They were being treated according to a 2-phase monotherapy regimen with RMP first and DDDS afterwards. On skin-smear examination 50 patients were found positive, of which 9 showed a BI of 3+ or higher at any site. With regard to the clinical status the only cases found with clinical signs of relapse were 5 out of 7 longstanding patients with BI of 4+ and 5+. A 6th patient of this high BI group who showed a good clinical condition, except for a heavy infiltration of both earlobes, was receiving a second RMP course when examined and biopsied for this research. These 9 patients were biopsied and susceptibility tests to RMP and DDS performed. The results showed that in 1 case the *Mycobacterium leprae* were resistant to both drugs; the organisms from 2 other patients were susceptible to RMP but low-grade resistant to DDS. Those from another patient were susceptible to RMP and fully resistant to DDS. In 3 other cases the bacilli did not multiply in any of mice but 1 of these strains was from the patient taking a second RMP course, therefore this strain might also be susceptible to RMP and resistant to DDS. In the last 2 cases multiplication was only observed in 2 of the controls and in 1 of the 0.0001% DDS treated mice; therefore, these experiments were not conclusive, and the AFB recovered were inoculated into fresh mice to

repeat the tests but these failed to multiply.

HABTE-MARIAM, H.S. & GUEBRE-XABIER, M.

Loss of viability of *Mycobacterium leprae* isolated from nasal secretions of lepromatous leprosy patients following daily rifampicin and DDS therapy. *Lepr.Rev.*, 64(4), p. 312-315, 1993.

Excreta from blowing their noses was collected from 4 previously untreated multibacillary (LL) patients in the ALERT hospital, immediately before and during daily treatment with 600 mg rifampicin and 100 mg dapsone (DDS). The *Mycobacterium leprae* recovered from the nasal secretions were enumerated and inoculated into the footpads of normal mice. Bacilli recovered from 2 of the patients failed to infect mice after 1 day's treatment, and all infectivity of the bacilli from the other 2 patients was lost after 2 days' treatment. These findings demonstrate the rapidity with which rifampicin-containing multidrug treatment is likely to reduce a patient's level of infection to their contacts.

KHARE, S., BHUTANJ, L.K. & RAO, D.N. Modulation of peripheral blood derived monocytes/macrophages from leprosy patients using "tuftsin" for production of reactive oxygen intermediates. *Lepr.Rev.*, 64(3), p. 208-218, 1993.

Phagocytic cells respond to a variety of membrane stimulants by producing reactive oxygen intermediates (ROI), i.e. O_2 , H_2O_2 and OH. metabolites. Plasma membrane activation is associated with superoxide generating NADPH oxidase, thereby causing the production of these toxic species. Stimulation of phagocytic cells also results in activation of purine catabolism, which directs the metabolic flux through xanthine oxidase to produce the superoxide anion. We previously observed that BULL macrophages (MO) exhibited a premature inability to undergo tuftsin stimulated phagocytosis and microbicidal activity. The present study was undertaken to measure ROI levels in the absence and presence of 'tuftsin'

pulsing as a function of in vitro culture age and also correlated these levels with adenosine deaminase (ADA) activity. The latter is known to be a contributor of OZ generation and is also involved in the maturation of the monocyte/macrophage system. The behaviour of normal and tuberculoid monocytes/macrophages were more or less the same, either in the presence or absence of tuftsin, i.e. they showed a progressive increase in ROI production until day 3, then tapered off in older cultures by day 7. In contrast, after day 1, the lepromatous macrophages were unable to undergo tuftsin mediated stimulation for the production of ROI and ADA activity. These findings indicate a defective MO function in lepromatous patients towards tuftsin pulsing, thereby supporting our earlier observations. Thus BL/LL MΦ behaved as if they were aged after 1 day of in vitro culture, which may account for an inability to handle *Mycobacterium leprae* for efficient killing.

LI, Huan-Ying. Problems of leprosy relapse in China, *Int.J.Lep.*, 61(1), p,1-7, 1993.

The proportion of relapses among all patients detected each year increased steadily since the initiation of the national leprosy control program in China with dapsone monotherapy in 1955, reaching 18% - 24% in the more leprosy-endemic provinces along the coast. Relapses were also reported in the formerly rifampin-plus-dapsone-treated patients. So far, only three paucibacillary relapses after 6 months of multidrug therapy (MDT) have been reported, and these were due to misclassification at the time of diagnosis.

A short course of MDT should be given to all formerly dapsone- and/or rifampin-plus-dapsone-cured patients for the prevention of relapse. If not, they should be screened every 1 to 2 years for any possible signs of relapse, and MDT given when needed.

LIM, J.T. & TAN, T. Efficacy and safety of multidrug therapy in paucibacillary leprosy in Singapore. *Lepr. Rev.*, 64(2), p. 136-142, 1993.

A total of 49 patients with paucibacillary leprosy (PB) who completed multidrug therapy (MDT) between 1985 and 1990 were analysed retrospectively for efficacy and complications; 20 (40.8%) patients had borderline-tuberculoid (BT), 13 (26.5%) had tuberculoid (TT), 1 (2.1%) had indeterminate (I) and 15 (30.0%) had pure neural (N) leprosy; 26 patients (76.5% of 34 non-neural leprosy) were skin biopsied for histological cure before MDT was stopped. Of these 26 patients, 19 had histological clearance at 6 months while the remaining 7 cleared beyond 1 year (18-36 months). The remaining 8 non-neural patients who refused rebiopsy had MDT for 6-8 months and the MDT was stopped when there was clinical clearance. Of the 15 neural (N) leprosy patients, 11 were given MDT for 6 months while the rest had 12-18 months of treatment; 1 patient with neural leprosy, who was treated for 6 months, relapsed with BT leprosy 18 months post-treatment.

There were few complications among the 49 patients - 4 (8.2%) patients developed reaction to dapsone, 1 (2.0%) had the dapsone syndrome, 2 (4.1%) had haemolytic anaemia and 1 (2.0%) had dapsone hepatitis; 7 (14.3%) patients had type I reaction.

NADKARNI, N.J., GRUGNI, A. & KINI, M.S. Fixed duration MDT in paucibacillary leprosy (classical and Modified), *Int. J.Lep.*, 61(1), p. 25-28, 1993.

We analyzed the records of 1022 patients of paucibacillary leprosy who had received either 6 doses of WHO-MDT alone ("classical" MDT, 668 patients) or had post-MDT dapsone for at least 6 months ("modified" MDT, 354 patients). The duration of post-therapy surveillance ranged from 6 months to 7 years (mean 20.4 months). We found that the incidence of unfavorable events was significantly higher with the classical regimen when patients were graded as active at the end of the fixed duration regimen, especially when patients with > 2 lesions were considered. In the patients who were graded as inactive at the end of 6 doses, there was a slight excess of unfavorable events in the modified regimen, although not statistically significant. No correlation was found

between unfavorable events and the regularity of treatment or the lepromin status. Overall, the incidence of adverse events was higher in patients with multiple lesions, and more than 90% of the adverse events occurred during the first 2 years of follow up. It is felt that 6 doses of MDT is adequate in the majority of patients who have few lesions or who have become inactive at the end of the treatment period. However, caution should be exercised in those with multiple lesions or in those considered active at the end of 6 doses.

NARAYAN, N.P.S. et. al. Sample survey of leprosy after three years of MDT in Bhavani Taluk of Periyar District, Tamilnadu. *Ind.J.Lepr.*, 65(3), p. 289-295, 1993.

A sample survey of Bhavani taluk was undertaken in March 1992 three years after the introduction of MDT. Ten percent of the population was taken for the sample. A population of 45,781 was enumerated and 41,554 was examined. The three sectors were stratified according to the prevalence rate and classifying the villages by the size of the population. Villages were selected by random sampling. The sample survey detected 288 new cases of leprosy of which 16 (5.55%) were bacteriologically positive for acid-fast bacilli. The child rate was 13.54% among new cases. According to the sample survey the current prevalence rate per 1000 population was 9.07 (with a new case detection rate of 6.93/1000 population), much higher than that derived from programme data (prevalence rate 3.45) and the expected ten fold reduction of prevalence under MDT. Independent sample surveys of NLEP units after three to five years of implementation of MDT will help to assess deficiencies in the programme and enable us to take remedial measures.

REVANKAR, C.R. et. al. Further observations on MDT blister-calendar packs in vertical leprosy eradication programmes—a multicentre study (Phase II). *Lepr.Rev.*, 64(3), p. 250-254, 1993.

To improve operational efficiency as

well as to improve patient compliance in leprosy programmes, DANIDA introduced blister-calendar packs (BCP) to deliver MDT in 4 MDT districts in India in 1987. An objective study (Phase II) involving 343 patients in a trial group (BCP group) and 253 patients in a control group (loose drug group) showed no significant difference in compliance rates for self-administered doses between the 2 groups.

Hence, while assessing the use of BCP's in leprosy programmes, other operational benefits like safe storage, easy transportation, easy drug accounting and safe preservation at home are to be considered. These aspects were followed up from Phase I of the study.

RICHARDUS, J.H. & SMITH, T.C. Squamous cell carcinoma in plantar ulcers in leprosy. A case control study. *Lepr. Rev*, 64(3), p. 270-273, 1993.

The objective of this case-control study was to identify factors associated with the development of squamous cell carcinoma (SCC) in plantar ulcers of leprosy patients. We examined 2 matched groups consisting of leprosy patients with and without SCC in a plantar ulcer.

No correlations were found between the development of SCC and race, profession, place of origin, duration of leprosy, the type and duration of leprosy chemotherapy, presence of bone involvement and type of ulcer care treatment given. The only statistically valid finding was that the duration of the ulcer was significantly lower in the group with malignant change. In this group there was an apparently higher use of pesticides, the difference being not of statistical significance.

It is concluded that factors other than ulcer duration need to be looked for, in order to identify factors influencing malignant change in plantar ulcers of leprosy patients.

ROCHE, P.W. et. al. Serological monitoring of the response to chemotherapy in leprosy patients. *Int.J.Lepr*, 61(1), p.35-43, 1993.

Sixty-five patients initially seropositive for

IgM anti-phenolic glycolipid-I (PGL-I) antibodies were tested for antibody levels to PGL-I, lipoarabinomannan (LAM), and the 35-kDa protein of *Mycobacterium leprae* at regular intervals for up to 30 months following the commencement of multidrug therapy (MDT). There was a steady decline in IgM anti-PGL-I and anti-35-kDa antibody levels to a mean of 17% and 14%, respectively, of the starting level at 24 months. The development of type 1 and type 2 reactions or the presence of drug resistant organisms in a small number of patients had no significant influence on the changes in antibody level. The rate of decline was similar in different disease categories, but a higher proportion of lepromatous patients remained seropositive at the end of 2 years of treatment than borderline tuberculoid patients. By contrast, the mean IgG anti-LAM antibody levels remained stable or increased. Again the occurrence of type 1 or type 2 reactions had no significant effect on antibody level over 2 years. Falls in the IgM anti-PGL-I anti-body levels mirrored the falls in the bacterial index in individual patients and provide an additional parameter for monitoring the response to chemotherapy.

SINGH, R.P. TIWARI, V.D. & CHATTOPADHYAY, S.P. Comparative study of short term results in two multidrug regimens in multibacillary leprosy. *Ind. J. Lepr.*, 65(2), p. 173-180, 1993.

Thirty lepromatous and Boderline lepromatous leprosy patients were treated with multidrug therapy in an open trial. Fifteen of them received the standard WHO multidrug regimen ie., rifampicin 600 mg and clofazimine 300 mg monthly, supervised, and dapsone 100 mg daily and clofazimine 100 mg on alternate days as self administered; the other 15 received a modified multidrug therapy regimen comprising of rifampicin 600 mg, clofazimine 100 mg and dapsone 100 mg daily for 21 days as suggested by the Indian Association of Leprologists, followed by the standard WHO regimen. The observation period was six months. Clinical, bacteriological, histological and immunological parameters were studied. The fall in morphological index was much faster in

patients receiving modified multidrug therapy regimen compared to those receiving the standard WHO regimen. Otherwise, there was no difference between the two groups of patients.

Five patients developed type 1 (upgrading) reaction with one developing (ulnar nerve paralysis). No untoward effects of drugs were noted in the study subjects except for darkening of skin colour of all the patients.

TOMIOKA, H. & SAITO, H. In vivo antileprosy activity of the Newly synthesized benzoxazonorifamycin, KRM-1648. *Int. J. Lepr.*, 61(2), p. 255-258, 1993.

The in vivo anti-*Mycobacterium leprae* activity of the newly synthesized benzoxazonorifamycin, KRM-1648, was studied. KRM-1648 was given orally to athymic, nude mice infected subcutaneously with *M. leprae* in the hindfoot pad, at doses between 0.001 and 0.01 mg of the drug/mouse/day six times per week, from day 31 to day 80. KRM-1648 administration markedly suppressed bacterial growth in the foot pads for 360 days. KRM-1648 given daily at the dose of 0.01 mg/mouse elicited a 2-4-log decrease in the number of acid-fast bacilli. The therapeutic effects of KRM-1648 were significantly higher than that of rifampin when (both drugs were given in the same dosage. Moreover, when mice were fed a KRM-1648-containing diet (0.00004%-0.0004%), the drug displayed an even higher efficacy against *M. leprae* infection, causing an almost 4-log decrease in the number of leprosy bacilli in the infected foot pad compared to untreated controls.

TOMIOKA, H. & SAITO, H. Therapeutic efficacy of some new quinolones and a combination of ofloxacin with rifampin against mycobacterium leprae infection induced in athymic nude mice. *Int. J. Lepr.*, 61(2), p. 250-254, 1993.

Ofloxacin (OFLX), having superior antileprosy activity among the various quinolones, was studied for its combined therapeutic efficacy

with rifampin (RMP) against *Mycobacterium leprae* infection induced in nude mice. When OFLX (3 mg/mouse) was given to infected mice in combination with RMP (0.01 mg/mouse) by gavage once daily six times per week, from day 31 to day 80 postinfection, a significant combined effect was observed. This study demonstrates the possibility of using OFLX in multidrug regimens for the clinical control of bacilliferous leprosy patients.

VAN LANDINGHAM, R.M. et. al. Activity of phenazine analogs against *Mycobacterium leprae* infections in mice. *Int.J.Lepr.*, 61(3), p. 406-414, 1993.

Twenty-five compounds structurally related to clofazimine were tested for their ability to inhibit the growth of *Mycobacterium leprae* using the kinetic method of drug evaluation in the mouse foot pad model of leprosy. Seven of the phenazine derivatives displayed anti-*M. leprae* activity comparable to that of clofazimine when administered at a concentration of 0.01% (w/w) in the diet. Three of the compounds, B746, B4087, and B4101, were active when administered at 0.001% in the diet. At a dietary concentration of 0.0001%, B4087 and B4101 were slightly more active than clofazimine, while B746 was less active. In the kinetic method of drug evaluation, greater anti-*M. leprae* activity of phenazine derivatives was generally associated with greater pigmentation of abdominal fat. Of the compounds which did not cause pigmentation when fed at a concentration of 0.01% in the diet, B4090 was the most active. This compound also inhibits the growth of a clofazimine-resistant *M. smegmatis* strain.

VENKATESAN, K. et. al. Bioavailability of Dapsone on oral administration of dapsomine - A comparative evaluation, *Ind.J.Lepr.*, 65(2), p. 157-161, 1993.

This study describes a comparative evaluation of dapsone kinetics in humans on administration of Dapsomine®, a capsule containing dapsone 100 mg dispersed in oily-base

suspension of clofazimine 50 mg. Seven untreated lepromatous leprosy patients were given one capsule of Dapsomine® a day for seven days and the pharmacokinetics parameters in this group was compared with those from another group of seven patients who received dapsone 100 mg and clofazimine 50 mg separately. There were no statistically significant differences in parameters such as peak dapsone plasma concentration (C_{max}), basal plasma level (C_{24h}), time to peak level (t_{max}), absorption half-life ($t_{1/2\alpha}$), elimination half-life ($t_{1/2\beta}$) and areas under plasma concentration-time curves (AUC_{0-8h}) and AUC_{0-24h}) between the two groups.

WALIA, R. et. al. Field trials on the use of *Mycobacterium w* vaccine in conjunction with multidrug therapy in leprosy patients for immunotherapeutic and immunoprophylactic purposes. *Lepr.Rev.*, 64(4), p.302-311, 1993.

A double blind field trial was started with a candidate anti-leprosy vaccine, *Mycobacterium w* as an immunotherapeutic and immunoprophylactic agent against leprosy in a highly endemic region with a prevalence rate of over 18 per 1000 population. By 31 August 1992, 224 villages have been surveyed, covering a population of 307,981 (1981 census). A total of 979 MB patients and 2801 PB patients have been registered. A total of 19,453 household contacts of leprosy patients have been examined for clinical signs of disease, of which 16,519 have received the initial dose while 10,434 have also received the booster dose of vaccine/placebo. The aims and objectives, study design of the trial, present status as well as the socio-cultural aspect involved are highlighted in this paper.

WALKER, L.L. et. al. Clarithromycin is bactericidal against strains of *Mycobacterium leprae* resistant and susceptible to dapsone and rifampin. *Int.J.Lepr.*, 61(1), p. 59-65, 1993.

The anti-*Mycobacterium leprae* activity; of clarithromycin when administered alone and in combination with rifampin and dapsone in the diet

was determined using the kinetic method of drug evaluation in mice. Clarithromycin when administered at a concentration of 0.1% (w/w) in the diet completely prevented growth of 2 pan-susceptible, 3 dapsone-resistant, 2 rifampin-resistant, and 2 rifampin and dapsone double resistant strains of *M. leprae*. A 0.03% (w/w) concentration also completely prevented growth of *M. leprae* in all mice infected with 2 of 7 strains tested, but in

only some of the mice infected with the remaining 5 strains. No antagonistic drug interactions were observed between clarithromycin and dapsone or rifampin. The addition of clarithromycin to the currently recommended multidrug regimen should improve the rate of killing of *M. leprae* and help to prevent the growth of dapsone-resistant and rifampin-resistant strains.