RESUMOS/ABSTRACTS

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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.Lepr, 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 reasessed.

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 classitication 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.Lepr., 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.Lepr., 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. *Lepr.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 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 in be associated with bacterial load ($r=0.414$; $P< 0.01$) indicating that in Iepromatous 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 histopathoiogical 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. *lnd.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 cioning and characterization of contiguously located repetitive and single copy DNA sequences of *Mycobacterium tuberculosis* Development of PCR-based diagnostic assay. *lnt.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. kansasiiDNA.* 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 immunoreactivityto the antigen, which well *may* be associated with the local and/or systemic release of cytokines [tumor necrosis factor-a (TNFα) and interferon-gamma (IFNy)] 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. *lnd.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 ±.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-y). Clinically similar contralateral lesions injected with excipient served as controls. Lesional esterase-positive cells(suggestive of monocytes/macrophages) from rIFNy-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 O_2^- in 4 of 5 subjects. Such inhibition was not observed In rIFN-y- injected sites. From the present studies it was not possible to determine whether the above effects of rIFN-y were primarily on lesional mature macrophages or on newly migrated young monocytes. Erythemaand 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-y 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 muitidrug 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. *Ind.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 bom 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 soclo-eco nomic 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. 199204, 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 leve. *Ind.J.Lepr, 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 trainning centres.

SAHA, S.P. & DAS, K.K. Disability pattern amongst leprosy cases in an urban area (Calcutta). *Ind.J. Lepr., 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) signficantly 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 mediun 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 x 10^7 to 4.8 x 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$_1$ (AGM$_1$), 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.1.), 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 delipidifed 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_2Oy) 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 fort he 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_20_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_20_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 forfouryears 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^{-2} 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 fort he 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 intraderrnal 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 posiive. 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 an 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. lepraewas* 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 x 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. at. al. Cross-Sectional assesment of ELISA reactivity in leprosy patients, contacts, and normal population usinh 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 efficiecy of a leprosy control program.

CHIPLUNKAR, S.V. et. al. Immunoreactivity of Mycobacterial strain ICR C and Mycobacterium leprae antigens with polycional 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 monocional antibodies in a radioimmunoprecipitation assay. It was observed that polycional 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 monocional 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 harborT- 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 serafrom 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 (Dasypus 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 antileprosyvaccine, 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 trasnport activity across the tubular basement mebrane. 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 !eels 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 *Mycobacteriumlepraeantigens* 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 reportthe methods of the Karonga Prevention Trial, a doubleblind 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 10^7 killed Mycobacterium leprae, or BCG+6 x 10^8 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 10^8 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 I year.

SHINDE, S.R. et. al. Lymphocyte proliferation, IFN-yproduction and limiting dilution analysis of T-cell responses to ICRC and mycobacterium leprae antigens in leprosy patients. Int.J.Lepr., 61(1), p. 51-58, 1993.

Lymphocyte proliferative responses and interferon-gamma (IFN-y) 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-y 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-yproduction after stimulation with ICRC and PPD but not with *M. leprae* antigens. Tuberculoid leprosy patients showed higherT-cellfrequenciesto 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 SI-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.

ZAHEER, 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-I I 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 SMLAI 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 leprornatous 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 signifcantly 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 absorvance 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 formely 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.Lepr., 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, star-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/ii.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. *Lepr. 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 sensoryloss 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 Schuwann 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 sever; (4) the presence of active inflamation 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 distribued 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. *Lepr 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 continuously 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 PGLI; 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 lepras* in mice. *InLJ.Lepr., 61(1),* p. 66-69, 1993.

The comparative bactericidal activities of sparftoxacin and ofloxacin against *Mycobacterium leprae* in mice were determined using the proportional bactencidal test at doses of 12.5 mg/kg – 100 mg/kg. Significant bactericidal activity

was found at 12.5 mg/kg sparfloxacin and 25 mg/kg ofloxacin. Sparfloxacin was significantly more bactericidal than oftoxacin at all doses, and the results with 25 mg/kg sparfloxacin 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 sparftoxacin may have a higher therapeutic index than ofloxacin in leprosy, and that the tentative standard dosage of 200 mg sparfloxacin 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 DADDS 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 biopsed and suscepitibility 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., BHUTAN], 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. 0_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. Stimulalion 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 deami-nase (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 Ieprae for efficient killing.

LI, Huan-Ying. Problems of leprosy relapse in China, Int.J.Lepr., 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 after6 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. 136142, 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 slopped. Of these 26 patients, 19 had histological clearance at 6 months while the remaining 7cleared 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.Lepr., 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 stratifed according to the prevalence rale 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 v 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 mutidrug therapy in an open trial. Fifteen of them received the standard WHO multidrug regimen ie., rifampicin 600 mg and ciofazimine 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 fazer 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 I (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 benzoxazinorifamycin, KRM-1648. *Int.J.Lepr*., 61(2), p. 255-258, 1993.

The in vivo anti-Mycobacterium leprae activity of the newly synthesized benzoxazinorifamycin, 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 ciofazimine, 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 eiofazimine-resistant *M. smegmatis* strain.

VENKATESAN, K. et. al. Bioavailability of Dapsone on oral administration of dapsomine - A comparative evaluation, I*nd.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 statiscally significant differences in parameters such as peakdapsone 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 $_{0\text{-}8h}$) and $AUC_{0\text{-}24h}$) 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 immunopro-phylactic 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 immunopro-phylactic 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-resis-tant, 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-resis-tant and rifampin-resistant strains.