RESUMOS/ABSTRACTS

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ASPECTOS SOCIAIS

PREMKUMAR, R., KUMAR, K. S., DAVE, S.L. Understanding the attitude of multidisciplinary teams working in leprosy. Leprosy Rev., 65, n.1, p. 66-77, March, 1994.

This study investigated the attitude of health personnel who were working for the National Leprosy Eradication Programme (NLEP) in India to their leprosy patients. These personnel were studied individually and as homogeneous groups so that comparisons were possible within and among the groups, and between the groups in different regions who were conducting similar health programmes, with a difference in length of between 1 and 5 years.

The sample population was the NLEP employees of 2 state governments, consisting of 8 health professional groups. A questionnaire was developed for each of these groups to elicit information on 5 aspects of the relationships with their patients.

The main outcome of the study was that two-thirds of the personnel tested possessed the 'minimun desirable' interaction with their patients. The quality of their relationship differed only among work specialities, but was consistent within the same speciality in different regions; this pattern was unchanged after 5 years of a multidrug (MDT) programme. A further analysis showed that although they possessed a caring attitude towards patients from low socioeconomic classes, a domineering attitude towards these same patients was also prevalent. Analysis according to speciality revealed that laboratory technicians had the highest 'desirable attitude' (74-67%) and health educators had the lowest (57-5%), while the rest of the team members fell in between. The stigma shown towards leprosy was higher among doctors when compared to the rest of the team members.

Discussion is based on the performance, overall and in each of its 5 facets, of each the professional groups with reference to their job descriptions and with similar studies undertaken earlier.

SOMMERFELD, P. Voluntary donor agencies in antileprosy work: present contribution and probable future /EditoriaV. *Leprosy Rev., 65,* n. 1, p. 1-8, March, 1994.

For 10 years or more, those engaged in antileprosy work have been aware of the possibilities offered by multi-drug therapy (MDT). It has been commonplace to speak in the abstract of rapid change. Now the reality of that change, with both its successes and its limitations, is becoming evident.

Today we are faced by a debate which,

although at times tendentious, at least results from success. Just what are the tasks remaining in leprosy, and what are their scale? What is the time-frame in wich we need to think? And who will support and undertake the continuing work?

Voluntary donor agencies, such as those in membership of ILEP, the International Federation of Anti-leprosy Associations; come to that discussion with a particular perspective, the traditional vision of not-for-profit charitable organizations in liberal democracies: to seek support for the needy, and to fill gaps in provison.

It must be stressed that this article discusses only the role of voluntary donor agencies, and does not deal with the extremely important contribution made by local associations in endemic countries. They are often the local partners of the donor agencies discussed here; and it is frequently they who do the real work in the field.

CLÍNICA

DANIEL, A.E. ARUNTHATHI, S., BHAT, L. et. al. Intraocularpressure in leprosy patients without clinically apparent anterior segment pathology. *Indian J. Leprosy,* 66, n. 2, p. 165-172, Apr. - June, 1994.

Awidely prevalent notion is that intraocular pressures are generally lower in leprosy pattients than in normal individuals. Applanation intraocular pressures were recorded in one hundred sixty-six leprosy patients who had no clinically visible anterior segment in pathology and n one hundred and eleven healthy controls. Mean (SD) intraocular pressures in leprosy patients (13.6 (3.0) mm Hg) did not differ significantly from that of controls (13.1 (2.7) mm Hg). Eyes of only 1.5% of the leprosy patients had pressures of 7 mm Hg or less. Correlation coefficients (r) between age, sex and intraocular pressures were not statistically significant both in leprosy patients and in controls. No statistically significant differences in mean intraocular pressures were noted when leprosy patients were grouped according to the Ridley and Jopling classification. Duration of disease also did not affect the intraocular pressures. Neither did smear positivity or differing bacterial indices. This study questions the widely held belief that low intraocular pressures are a common feature in leprosy and contends that in the era of MDT where ocular complications associated with low intraocular pressures are thought to be less, the occurrence of low intraocular pressure may not be as common a phenomenon as it is believed to be.

LIENHARDT, C., FINE, P.E.M. Type 1 reaction, neuritis and disability in leprosy. What is the current epidemiological situation? *Leprosy Rev., 65,* n. 1, p. 9-33, March, 1994.

Type 1 reaction is one of the major causes of nerve damage in leprosy patients leading to disabilities of varying severity. Though this complication of leprosy has been extensively described, we still know very little of its natural history and of the factors which may predispose to it. This paper examines the descriptive and analytic epidemiology of these reactions in leprosy. We find that they vary greatly in clinical expression, time of onset, duration and severity, which has important implications for the way they are handled in the context of leprosy control programmes. We review the various risk factors that have been suggested over the last 30 years and the evidence of their utility in identifying 'high- risk' patients is assessed. We then review the specific aspects of neuritis and disability in leprosy and examine the contribution of Type 1 reaction to leprosy-associated disabilities. The prospects for early detection and prevention of Type 1 reaction are examined in *the* light of current knowledge, both at research and at the leprosy control level.

LUBBERS, W.J., SCHIPPER, A., HOGEWEG, M. et al. Paralysis of facial muscles in leprosy patients with lagaphtalmos. *Mt. J. Leprosy, 62,* n.2, p. 220-224, 1994.

The objective of the study was to determine the pattern of involvement of facial muscles in lagophtalmos. Fifty-seven patients with lagophtalmos were examined to assess the degree of paralysis of facial muscles. Eighty-one percent of the patients with lagophtalmos had involvement of at least one other muscle group. In patients with lagophtalmos with a gap at mild closure of 5 mm or more, 27 of 30 (90%) had involvement of at least one other facial muscle. In lepromatous leprosy the pattern of involvement was symmetrical and "patchy", the right and left sides being affected equally. In tuberculoid leprosy, the ipsilateral muscles were more often involved, which is the pattern of involvement of a nerve trunk. The upper and lower facial muscles were affected in the same proportion. Hence, on clinical grounds, there is little support for the often postulated statement that the superficial course of the facial nerve above the zygomatic bone is decisive for exclusive paralysis of the zygomatic branch of the facial nerve.

PANDYA, S.S., BHATKI, W.S. Severe pan-sensory neuropathy in leprosy. *Mt. J. Leprosy, 62,* n. 1, p. 24-31, March, 1994.

The sensory loss which occurs in leprosy is essentially cutaneous, resulting from centripetally ascending infection, the host cellular response and fibrosis, from dermal to certain mixed nerves. The hallmarks is pain/temperature and touch/pressure loss. Muscle denervation is a byproduct of mixed nerve involvement. Leprous sensory and motor neuropathy presents a stereotyped picture, with preservation of position sense, noninvolvement of the large girdle muscles, and retained deep tendon reflexes. We report clinical and investigative details of 7 patients (3 males, 4 females) with mild-tomoderate polyneuritic leprosy who manifested severe proprioceptive loss in the upper limbs; the lower limbs were similarly affected in 4 of them. Tendon reflexes were absent in the ataxic limbs. No other cause was found for the ataxia. Electrophysiological studies confirmed damage to large cutaneous and muscle afferents, and a normal EMG pattern in hip and shoulder muscles. Of great interest was the histology of a lumbar sensory ganglion biopsied in a severely disabled patient. There was extensive neuron loss and degeneration and reactive proliferation of capsular cells ("nodules of Nageotte"), an inflammatory focus of lymphocytes, and no bacilli. This suggests to us that the proprioceptive loss in these patients could well be the result of an unusual "leprous ganglionitis." Further clarification of the mechanism of ganglion degeneration and the frequency of inflammation could come from immunohistology of tissues from African green monkeys with experimental polyneuritic leprosy.

SHANNON, E.J., FROMMEL, D., GUEBRE-XABIER, M., HAILE-MARIAM, H.S. Titration of numbers of human-derived Mycobacterium leprae required to progressively oxidize 1dC-palmitic acid and release $^{14}CO^{2}$. Lepr. Rev., 65, n. 2, p. 100-105, June, 1994.

Mycobacterium lepraewas isolated from skin-punch biopsies of 2 untreated lepromatous leprosy patients. The bacteria were enumerated, diluted 10-fold and cultured in Middlebrook 7H9 medium supplemented with albumin, dextrose, catalase and ^{14}C-palmitic acid. The cultures were incubated at 33°C in a modified Buddemeyer radiorespiratory detection vessel. Those cultures containing at least 10^{7} mycobacteria demonstrated a progressive evolution of $^{74}CO^{2}$.

SONI, N.K. Eustachian tube functions in lepromatosus leprosy: A tympanometric study. Indian J. Leprosy, 66, n. 1, p. 45-49. Jan - Mar, 1994.

Tympanometry was performed in 20 patients with lepromatous leprosy. About 30%

showed tympanogram B type indicating middle ear pathology which was shown to be related to the stage of lepromatous rhinitis. The pathogenesis of middle ear malfunction In lepromatous leprosy is discussed.

SUBRAMANIAM, K., NAH, S.H., MARKS, S.C. A longitudinal study of alveolar bone loss around maxillary central incisors in patients with leprosy in Malaysia. *Lepr. Rev.,* 65, n. 2, p. 137-142, June, 1994.

The loss of alveolar bone supporting the maxillary central incisors and the general periodontal conditions were evaluated after 14 years In the 12 patients remaining from an original group of 47 under treatment in Malaysia. Alveolar bone loss was minimal during this period even in the presence of periodontal inflammation. These data suggest that treatment protects patients with leprosy from alveolar bone loss and suggests that other skeletal deformities might respond similarly.

DIAGNÓSTICO

KRISHNAMURTHY, P., RAO, P.S., SUBRAMANIAN, M., INDERPARKASH. The influence of operational factors in the profile of monolesional leprosy cases in South India. *Lepr. Rev.,* 65, n. 2, p.130-136, June, 1994.

A comparison of the profile of monoleslonal cases among new PB cases detected in a Government Leprosy Control Unit (GLCU) and the field area of Central Leprosy Teaching and Research Institute (CLTRI), both located in South India, demonstrates that the proportion of monolesional cases among new cases detected between 1987 and 1991 was higher in children than adults, higher In females than males (only in the CLTRI) - over 95% were the tuberculoid type. A significantly increasing trend in this proportion could be seen In the GLCU but not in the CLTRI; an explanation of this is based on the difference in operational aspects in case detection methodology adopted by the 2 areas - e.g. intersurvey interval and mode of case detection. Such studies, focusing on single skin lesions, help us in understanding the role of various possible operational factors in influencing the behaviour of the disease.

SINGH, N., ARORA, V.K., RAMAN, M. et. aI. An evaluation of the S-100 stain in the histological diagnosis of tuberculoid leprosy and other granulomas dermatoses. *Mt. J. Leprosy, 62,* n. 2, p. 263-267, June, 1994.

Forty biopsies of granulomatous dermatoses, 12 of which were tuberculoid leprosy (TL), were studied for patterns of nerve twig distribution using an immunoperoxidase technique for S-100 protein. Four distinct patterns of nerve twigs were identified: 1) within granulomas. 2) between granulomas, 3) within and between granulomas, and 4) undetectable nerve twigs in an adequate biopsy. Pattern 4 was seen exclusively in TL ($p < 0.5$). The other patterns occurred in nonleprosy dermatoses as well, suggesting that pattern 4 is the best indicator toward a diagnosis of TL. The granules of mycetoma and *Mycobacterium leprae* also stained positively with the S-100 stain.

VAN BRAKEL, W.H., SHUTE, J., DIXON, J.A., ARZET, H. Evaluation of sensibility in leprosy-comparison of various clinical methods. *Lepr. Rev.,* 65, n. 2, p. 106-121, June, 1994.

In order to determine whether various sensibility tests, not in common use at our hospital, are appropriate for the neurological screening of leprosy patients, an extended nerve function assessment (NFA) was done on 50 in - and outpatients who had been diagnosed as suffering from leprosy (100 hands and feet). The nerve function assessment battery consisted of Semmes-Weinstein monofilament testing

(SWMT), moving 2-point discrimination (M2PD), Pinprick (PP), position sense (PS), vibration sense (VS) and voluntary muscle testing (VMT). In addition the SWMT was performed on 637 hands and 634 feet of 'field patients' in order to get a better indication of the prevalence of sensory impairment as measured with the SWMT. The SWMT has been shown to be a sensitive test of peripheral nerve function, therefore the other tests were compared with the SWMT. Results are reported separately for the ulnar, median and posterior tibial nerve. Test sites were the pulp of the distal phalanx of the index finger, the little finger and the big toe. Correlation between the SWMT and each of the other tests proved statistically significant; the closest correlations were between the SWMT, M2PD and PP for both ulnar and median nerves ($r > 0.7$, F test > 100, $p < 0.0001$). It is argued that the first tests to show nerve function impairment (NFI) are the M2PD and the SWMT. VS and PS were also absent in a significant proportion of patients. Arguments are presented that this may indicate advanced NFI. Results are compared with other data currently avaiable in the literature.

EPIDEMIOLOGIA

ILANGUMARAN, S., SHANKERNARAYAN, N., GOPAL, R. et al. Antibody response to recombinat 65-kDa, 70-kDa and 18-kDa mycobacterial antigens in leprosy patients and healthy contacts in a lepro y-endemic population. Mt. J. Leprosy, 62, n. 2, p. 245255, June, 1994.

Antibody responses to recombinant Mycobacterium leprae 64-kDa (rML65) and 18-kDa (rML18), M. bovis BCG 65-kDa (rMB65) and M. tube rculosis 70-kDa (rMT70) antigens were measured by indirect ELISA in sera from leprosy patients and healthy contacts in a leprosy-endemic area in southem India. Antibody responses to M. leprae-specific epitopes on phenolic glycolipid-I (PGL-I) and a 35-kDa protein antigens also were measured simultaneously by PGL-I ELISA and the serum antibody competition test (SACT), respectively. Signifficantly higher levels of antibodies of the IgG isotype to rML65 and rMB65 were observed in bacterial index (BI)positive, lepromatous (LBI+) patients but not in other groups of leprosy patients and endemic controls [healthy family contacts (HFC), healthy hospital contacts (HHC), and healthy non-contacts (HNC)]. LBI+ patients could be distinguished from LBI- patients on the basis of their higher levels of IgG antibodies to rML65, rMB65 and rMT70; lower levels of IgM antibodies to these antigens and higher levels of anti-PGL-I IgM levels. In the former group, 84%were SACT positive in contrast to 39% in the latter groups. Among lepromatous patients good positive correlations were observed between IgG antibody responses to rML65 and rMB65 and anti-PGL-I IgM levels, SACT ID5, titers ass well as Bls. Among healthy controls, HFC had higher levels of IgG antibodies to rML65, but lower levels to rMB65 than did HNC. Thirty-nine percent of the HFC were seropositive to anti-PGL-I IgM antibodies in contrast to 4% in the HNC. On the basis of these criteria, the immune profile of the HFC appears to be distinctly different from that of the HNC, even though both groups are from the same endemic area. It is therefore possible that antibody response to defined protein antigens of mycobacteria is influenced by the lesional bacterial load in leprosy patients and by exposure to homologous proteins of M. leprae and/or related environmental mycobacteria in the case of healthy contacts and noncontacts. The above results are discussed in relation to T-and B-cell activity toward M. leprae antigens and the immunoregulatory mechanisms of antibody production in leprosy.

PONNIGHAUS, J.M., FINE, P.E.M., STERNE, J.A.C. et al. Incidence rates of leprosy in Karonga District, Northern Malawi: patterns by age, sex, BCG status classification. Int. J. Leprosy, 62, n. 1, p. 10-23, March, 1994.

This paper describes incidence rates by age, sex, prior BCG status and classification in Karonga District, northern Malawi. New cases

(489) were identified among 83,500 individuals followed for an average of 5 years (1.12 cases per 1000 person years). Only 29 (6%) of the incident cases were multibacillary. Incidence rates generally were higher among females than males, and increased steadily with age. Although the highest incidence rates of disease were recorded among young adults without BCG scars (males 15-19; females 20-24), these peaks were less dramatic than those reported among young adults in The Philippines and Norway. In the absence of historical data and data on infection status, it is not possible to assess to what extent these peaks may reflect either greater exposure or greater susceptibility to disease among adolescents or young adults.

The incidence rates of leprosy among individuals with a prior recorded BCG scar were approximately half those of individuals lacking a scar, at all ages. Since BCG had been introduced into this population only during the 1970s, this provides strong evidence for the effectiveness of BCG when given to adults. It was estimated that past vaccination of approximately 40% of the district population had reduced the overall incidence rate of leprosy by 18%, and that this impact would increase with aging the vaccinated cohorts.

A retrospective examination of the detailed records of initial examinations revealed that 62 (13%) of the incidence cases were recorded as having skin hypopigmentation or blemishes, at the site of subsequent confirmed leprosy lesions, several months or years before they were suspected of having leprosy. The nonspecificity of these lesions, some of which were probably attributable to Mycobacterium leprae infection, highlights the difficulty of diagnosing leprosy in its earliest forms.

SUITE, M., EDINBOROUGH, B., LEWIS, M., TOLLEFSON, J. A survey to determine the prevalence of leprosy in a community in East Trinidad. Lepr. Rev., 65, n. 2, p. 122129, June, 1994.

A house-to-house survey was conducted in a community in East Trinidad, where a clustering of cases had been observed. There were 1355 residents, of whom 73.5% had a complete visual skin examination.

No new cases of leprosy were found but a variety of skin disordes were diagnosed. The most common disorder was pityriasis versicolor, which is one of the differential diagnoses of hypopigmented skin lesions. This has serious Implications for the delayed diagnosis of leprosy.

In all, 5 of the 9 old cases residing in the survey area suffered from paucibacillary disease, and had a history of contact with a lepromatous case. They were not listed initially as contacts of this index case. Contact lists should therefore include nonfamilial persons having frequent contact with an index case. The definition of 'frequent' should be determined by each programme.

It may also be necessary to review the duration of surveillance of contacts. The survey was estimated to have cost about US$ 2,500 and was not considered to be cost-effective.

THEUVENET, W.J., SOARES, D., BARAL, J.P. et al. Mass survey of leprosy in Lalitpur District, Nepal. Mt. J. Leprosy, 62, n. 2, p. 256-262, June, 1994.

An intense mass survey of leprosy in Lalitpur District, Nepal, was carried for the period 1986 to 1990. This was the first such large scale survey in Nepal; 85% of the total population was examined. The 5-year case detection rate was 13 per 10,000; the 5-year child detection rate was 4 per 10,000. By the end of the survey the prevalence rate was 6.8 per 10,000; at the end of 1992 this had dropped to 2.2 per 10,000. In 1989, after a 3-year interval, a re-survey was done in three village development committees (VDCs) and 4 new cases were detected, bringing the 3-year case detection rate to 3.3 per 10,000; 36% of the old cases, 20% of the new adult cases, and 3% of the new child cases were classified as multibacillary. Overall, 62.7% of the patients had no disability, 18.8% had disability grade 1, and 12.7% had disability grade 2 while for 5.8% the

data were incomplete. By the end of the survey 91% of the patients needing medical treatment were on multidrug therapy (MDT). At present this has increased to 100%. The regularity rate was 86%; at the end of 1992 this had increased to 96%. The cost for detecting one new patient was US$ 298. Because of the high cost, it is recommended that Intense mass surveys not be performed when the estimated prevalence rate is less than 10 per 10,000 inhabitants. From the data collected conclusions were drawn and recommendations were formulated for developing new strategies for the National Leprosy Control Programme of the Government of Nepal.

Van BEERS, S.M., IZUMI, S., MADJID, B. et al. An epidemiological study of leprosy infection by serology and polymerase chain reaction. *Mt. J. Leprosy, 62,* n.1, p.1-9, March, 1994.

A population-based study has been carried out in two adjacent villages in a highly leprosy-endemic area of South Sulawesi, Indonesia. The prevalence of clinical leprosy was 10.0 per 1000 inhabitants. A total of 1015 serum samples and 1228 nasal swab specimens were collected. IgM antibodies in blood to phenolic glycolipid-I (PGL-I) of Mycobacterium leprae were demonstrated by the gelatin particle agglutination test (MLPA) and by indirect ELISA (19M-PGL). IgG antibodies to PGL-I (IgG-PGL) and lipoarabinomannan-B (IgG-LAM) were measured by indirect ELISA. The presence of M. leprae in nasal swab specimens was established by a polymerase chain reaction (PCR).

The seropositivity rates in the population were 32% for MLPA, 30.8% for IgM-PGL, 6.7% for IgG-PGL, and 11.6% for IgG-LAM. Seropositivity rates for MLPA and IgM-PGL were highest in the younger age groups. There was no difference in seropositivity in any of the tests between household contacts of leprosy patients and noncontacts. The seropositivity rates in the MLPA and IgM-PGL were not randomly distributed among all households. The presence of M. leprae by PCR was demonstrated In 7.8% of the nasal swab specimens. No correlation was found between the results of the PCR and serology. This study indicates that M. leprae is widespread in the population, and that in endemic areas many individuals carry M. leprae in their nasal cavities without having obvious symptoms of leprosy.

IMUNOLOGIA

BALYBIN, E.S., VINNICK, L.A. Autosensitization to connective tissue elements and endogenous adaptation hormones in mycobacteriores. Mt. J. Leprosy, 62. n. 2, p. 225-228, June, 1994.

The contribution of some adaptation hormones to the process regulating production of auto antibodies to collagen (Abc) and elastin (ABE) was studied in leprosy (37 patients) and tuberculosis (31 patients). In both mycobacterioses the Abc and Abe titers were increased and inversely correlated with endogenous cortisol levels. In leprosy the antibody titers directly correlated with the triiodothyronine (T3) levels which were significantly higherthan the values in healthy controls. A new approach to research for remedies and methods of preventing and curing auto sensization to connective tissue is suggested by combining medications according to individual endocrine and immune indices.

DAVIDSON, S.K., GEORGE, G.T. Detection and characterization of a 411 recombinant clone of *M. leprae* that express an antigenic determinant of a 64-kDa protein. *Int. J. Leprosy, 62,* n.2, p. 237-244, June. 1994.

A genomic library of Mycobacterium leprae in the expression vectorygt11 was screened with rabbit polyclonal hyperimune antiserum elicited with a sonicated extract of M. leprae. Numerous reactive clones were isolated by this immunoscreening, indicating a broad antibody response of the rabbit. None of the recombinant

clones was reactive with monoclonal antibodies to the previously well-characterized *M. leprae* recombinant clones. One of the clones isolated, clone A, encoded a large 132-143-kDa pgalactosidade fusion protein expressing an epitope of *M. leprae.* Monospecific antibodies eluted from this fusion protein reacted on Western blots with a 64-kDa *M. leprae* protein. The DNA of this clone was shown to be distinct from the gene encoding the well-characterized immunodominant 65-kDa protein by DNA hybridization. We have identified a new a.gt11 recombinant clone encoding a fusion protein with a 64-kDa protein. This protein is recognized by the humoral immune response of the rabbit in response to a challenge with an *M. leprae* cell extract.

ILANGUMARAN, S., ROBINSON, P., SHANKERNARAYAN, N.P. at al. T lymphocite reactivity of leprosy patients and healthy contacts from a leprosy-endemic population to delipidifield cell components of *Mycobacterium leprae. Leprosy Rev., 65,* n. 1, p. 34-44, March, 1994.

In this study, we measured *in vitro* proliferative responses of peripheral blood mononuclear cells from both leprosy patients across the clinical spectrum and also healthy contacts from a leprosy-endemic population to delipidified cell components of *Micobacterium leprae* (DCC) and Dharmendra lepromin. Dharmendra lepromin was poor in inducing *in vitro*T cell proliferation in all the study groups, even though it elicited marked *in vivo* skin test reaction in tuberculoid leprosy patients and healthy contacts. In contrast, Dharmendra preparation of BCG induced marked T-cell response in tuberculoid as well as bacterial index negative lepromatous patients. DCC induced a significantly higher lymphoproliferative response than Dharmendra lepromin in all study groups. A significant positive correlation was observed between the lymphoproliferative responses to DCC and BCG. The present study, based on a large number of leprosy patients and healthy contacts, clearly demonstrates that DCC, depleted of glycolipids and lipopolysaccharides, is a good antigenic preparation for evaluation T-cell reactivity to *M. leprae.*

LAUNOIS, P., NIANG, M'B. N'D., DROWART, A. at al. IgG response to purified 65- and 70kDa mycobacterial heat shock proteins and to antigen 85 in leprosy. *Int.J.Lepr., 62,* n.1, p. 48-54, March, 1994.

IgG antibody response to mycobacterial heat-shock proteins (hsp) (the 70 kDa antigen from *Mycobacterium tuberculosis* and *M. bovis* BCG; the 65-kDa antigen from *M. leprae* and *M. bovis* BCG) and to the fibronectin-binding antigen 85 from *M. bouts* BCG was analyzed in a dot-blot assay in plasma from leprosy patients and their contacts. Most plasma - whatever the status of the subjects - reacted to the hsp 70; 8 of 9 (89%) of paucibacillary patients recognized the 65 myco-bacterial hsp but only 2 of 9 (22%) recognized the antigen 85. In contrast, 12 of 12 (100%) of multibacillary patients reacted with the antigen 85 and only 4 of 12 (33%) reacted to the hsp 65 from *M. leprae.* On the one hand, 7 of 25 (28%) of the lepromin-positive contacts and 2 of 9 (22%) of the lepromin-negative contacts recognized the antigen 85. On the other hand, 11 of 25 (44%) of the lepromin-positive contacts but only 1 of 9 (11%) of the lepromin-negative contacts reacte to the hsp65 from *M. leprae.* Finally, very few (10%) of the lepromin-positive controls showed a positive reaction to the *M. leprae* 65-kDa antigen, the BCG 65-kDa antigen, and the 85-kDa antigen of BCG. Thus, differences in binding to the hsp65 from *M. leprae* and to antigen 85 could be helpful in distinguishing different forms of the disease.

SANTOS, D.O., SUFFYS, P.N., MOREIRA, Al., BONIFACIO, K., SALGADO, J.L., ESOUENAZI, D., BERTHO, A.L., SARNO, E.N. Evaluation of chemiluminescence, procoagulant activity and antigen presentation by monocytes from lepromatous leprosy patients with or without reactional episodes. *Lepr. Rev., 65,* n. 2, p. 88-99, June, 1994.

In this study, we evaluated the activity of peripheral blood mononuclear cells (PBMC), isolated from treated and untreated lepromatous leprosy patients, from lepromatous leprosy patients during and after reactional episodes (erythema nodosum leprosum (ENL) and reversal reaction (RR), and from normal healthy individuals. We determined reactive oxygen intermediate (ROI) production, procoagulant activity (PCA) and HLA-DR antigen expression of monocytes, besides lymphoproliferation, both in the presence and absence of various stimulatory agents. Phorbol myristate acetate (PMA) stimulated ROI production by monocytes from all the groups studied, with patients during reactional episodes (ENL and RR) showing a significantly higher response ($p < 0.009$ and $p < 0.00001$). Irradiated *Mycobacterium leprae,* although having little effect when added alone, strongly suppressed PMAstimulated ROI production. Muramyl dipeptide (MDP) had no influence on either basal or on PMA-induced ROI production. Basal monocyte PCA, as well as *M. leprae* or concanavalin A (ConA)-induced monocyte PCA, was comparable in monocytes from all the groups studied. ConA was able to induce mitogenic activity in mononuclear cells isolated from all the groups studied. *M. leprae,* although stimulatory for normal individuals, did not induce lymphoproliferation in lepromatous leprosy patients, except for cells from patients during RR, which respondded equally to *M. leprae* and ConA. The absence of *M. leprae*induced lymphoproliferation in lepromatous leprosy patients is not caused by the lack of basal HLA-DR expression, as PBMC from all individuals studied showed the same level of this antigen. Our results suggest an increase of spontaneous or PMA-induced monocyte activity, as detected by ROI production, during the reactional episode; addition of *M. leprae* suppressed this response. The increase in monocyte activity could be correlated with the increase of lymphoproliferation response to *M. leprae* during RR, but not during ENL. The importance of a possible immune suppressive action of *M. leprae* is discussed.

MICROBIOLOGIA

BHATIA, V.N. Repeated isolation of dermatophilus-like organism from leprosy material. *Indian J. Leprosy,* 66, n. 2, p.149156, Apr - June, 1994.

An organism having actinomycetoid type of colonies has been grown repeatedly in pure culture from leprosy material using a solid medium. The isolates obtained from different biopsies, skin scrapes and mouse foot-pad harvests were found to be similar to each other in the routine taxonomical tests and had many characters common with Dermotophilus congolensis. Similar growth could be obtained from a strain of M. leprae from armadillo and also from a DOPA- positive mycobacterium isolated previously from the blood of a leprosy patient.

KATO, L., SZETLI, J., SZENTE, L. Water soluble complexes of C^{74} and C^{18} fatty acids and alcohols in media for cultivation of leprosy- derived psychrophilic mycobacteria. Int. J. Leprosy, 62, n. 1, p. 75-88, March, 1994.

Host-grown *Mycobacterium leprae* cell suspensions oxidized water-soluble complexes of palmitic acid, myristic acid, cetyl alcohol, and myristyl alcohol prepared with randomly methylated fl-cyclodextrin as host molecules. Gas chromatography analysis showed that the water- soluble complexes retained their chemical structure following sterilization in the autoclave. Bioavailability of the two long-chain fatty acids and the corresponding long-chain alcohols was con-

firmed by Warburg manometric techniques with host-grown *M. leprae* cell suspensions. Inoculated with host-grown *M. leprae* cells in chemically well-defined, simple liquid and agar media, acid- fast bacilli were cultivable in primary cultures and subcultures at 10°C with $(NH_4)_2SO_4$ as the N source and watersoluble palmitic acid, myristic acid, cetyl alcohol or myristyl alcohol as the C and potent energy sources.

M. ph/eioxidized the complexed palmitic acid and myristic acid but not cetyl alcohol or myristyl alcohol. On agar media with any of these four carbon sources and $(NH_4)_2SO_4$ but not ammonium thioglycolate as the N source, *M. phlei* grew abundantly at 36°C. In liquid media only myristyl alcohol suported growth of *M. phlei* without any growth with palmitic acid, cetyl alcohol or myristic acid.

The leprosy-derived, cold-loving cultures *("M. psychrophilum")* were not fully testes for classification and identification. The cells are strongly acid-fast facultative psychrophiles, adapted in subcultures to mesophilic growth. They grow in chemically well-defined media with 14 and 16 C long-chain fatty acids or alcohols as the C and energy sources. None of the cultures grow on Lowenstein or 71-19 media. Heat-killed suspensions of the 4th and 6th subcultures provoke Mitsuda-type late skin reactions *in* tuberculoid, borderline and borderline-tuberculoid but not in lepromatous leprosy volunteers. When grown with $(NH_4)_2SO_4$ as the N source (but not with the reducing agent ammonium thioglycolate) the subcultures multiplied abundantly in the foot pads of mice.

It became evident that leprosy-derived, facultative psychrophilic mycobacteria really exist. Mycobacteria of this cluster do not distinguish between 14 or 16 C long chains with COOH or CH_2OH as terminal bindings. Cells are quite aerophilic and grow preferentially on agar slant surfaces. This is probably due to the abundant 0_2 requirement of each palmitic-acid molecule to produce 129 ATP molecules. The reducing agent, ammonium thioglycolate, was toxic in culture media dor *M. phlef. "M. psychrophilunf* lost infectivity with ammonium thioglycolate as the N source in the media.

REDDI, P.P., AMIN, A.G., KHANDEKAR, P.S. et al. Molecular definition of unique species status of *Mycobacterium w,* a candidate leprosy vaccine strain. *Int. J. Leprosy, v. 62,* n. 2, p. 229-236, 1994.

Mycobacterium w, a candidate leprosy vaccine strains, is an atypical cultivable mycobacterium. Based on its growth and metabolic properties, M. w was listed in Runyon Group IV, along with other rapid growers such as *M. fortuitum, M. smegmatis, M. chelonae* and *M. vaccae.* However, M. w was not fully identical to any one of these. In the present study, a molecular biology approach was used to define the species identify of M. w. in a manner that allows reliable comparison to be made with over30 known mycobacterial species. A 383-bp region, present at the amino terminus of the conserved mycobacterial 65-kDa gene, has been polymerase chain reaction (PCR) amplified in M. w and the DNA sequence was determined. A comparison of the M. w DNA sequence with those of *M. tuberculosis, M. avium, M. paratuberculosis* and *M. fortuitum* revealed a species-specific polymorphism, i.e., the presence of nucleotide substitutions unique to M. w. In an alternate approach, a 441-bp region, also a part of the 65-kDa gene, has been PCR amplified in M. w. and a Hae Ill restriction pattern was generated. The 142/127/59-bp Hae Ill pattern of M. w. was found to be unique when compared with *M. tuberculosisH37Rv, M. bovi, M. avium, M. intracellulare, M. scrofulaceum, M. kansasii, M. gastri, M. gordonae, M. shimoidei, M. ma/moense, M. haemophilum, M. terrae, M. nonchromogenicum, M. triviale, M. marinum, M. f/avescens, M. simiae, M. szu/gai, M. xenopi, M. asiaticum, M. aurum, M. smegmatis, M. vaccae, M. fortuitum* subsp. *fortuitum, M. fortuitum* subsp. *peregrinum, M. chelonae* subsp. *chelonae, M. chelonae* subsp. *abscessus* and *M. genavense;* mycobacteria for wich the 441-bp Hae Ill patterns have been documented in the literature. These results established the species identify of M. w. at the nucleotide level.

NEUROLOGIA

de BLAQUIÈRE, G.E., CURTIS, J., PEREIRA, J.H. et. al. Denatured muscle grafts for nerve repair in an experimental of nerve damage in leprosy. 1. A functional and morphometric study. *Mt. J. Leprosy, 62,* n. 1, p. 55-63, March, 1994.

The effectiveness of denatured autologous muscle grafts for nerve repair in an experimental model of leprosy was assessed. Nerve damage resembling that caused by Mycobacterium leprae in humans was induced by the injection of cobalt-irradiated M. leprae into the tibial nerve of guinea pigs. At the time of maximm functional loss, caused by the formation of a granuloma within the nerve, the area of damage was excised and a denatured autologous muscle graft was used to repair the nerve. Assessment of nerve regeneration through the graft was made using clinical, electrophysiological and microscopic morphometric analysis at intervals up to 20 weeks. The results were compared with regeneration after grafting of a normal nerve. Clinically, some motor and sensory recovery occurred in all of the graft recipients in the normal nerve by 8 weeks, and by 11 weeks in the recipients of grafts in the granulomatous nerve. Full sensory recovery occurred in all but one animal by 20 weeks. Motor function recovered to near normal levels at 14 weeks after repair of the normal nerve but, at 20 weeks, there was variation in motor recovery after repair of the granulomatous nerve. Electrophysiology showed increased conduction velocity of the nerve fibers, at each timepoint. The conduction velocity at 8 weeks after grafting of the normal nerve was similar to that at 12 weeks after grafting of the granulomatous nerve. Morphometry showed an increasing number of myelinated fibers repopulating the distal nerve up to 20weeks. Myelin fiber numbers, at this time, were one third of normal after repair of the granulomatous nerve and two thirds after repair of the normal nerve. This study demonstrates that denatured autologous muscle grafts enable the regeneration and functional recovery of nerves despite their being damaged by mycobacteria-induced granulomas, but the damage causes some delay.

MALAVIYA, G.N., HUSAIN, S., GIRDHAR, A. et al. Sensory functions in limbs of normal persons and leprosy patients with peripheral trunk damage. *Indian J. Leprosy,* 66, n. 2, p. 157-164, Apr - June, 1994.

The threshold to touch was tested in hands and feet of normal persons using Semmes- Weinstein graded monofilament nylons. The minimun stimulus to which response could be elicited was nylon number 3.61 in palms and 4.31 in soles. These numbers relate to the logarithm of the force applied, 3.61 corresponding to 0.217 gm force and 4.31 to 2.35 gm force respectively.

The area of pain insensitivity complained by the patient more or less corresponds to that revealed by objective testing. It was interesting to observe that loss of pain sensitivity was confined to a smaler area compared to touch and thermal insensibility in the part innervated by the same nerve trunk.

RIDLEY, M.J., WATERS, M.F.R., RIDLEY, D.S. Effect of *Mycobacterium leprae* in peripheral nerve trunk on the evolution of skin lesions. *Mt. J. Leprosy, 62,* n. 1, p. 99-107, March, 1994.

Comparative histological studies were made of a) 41 peripheral nerve lesions and the skin in the area of supply, and b) 12 peripheral nerve lesions and concurrent but unrelated skin lesions. In the first study, small, relatively early, histologically classifiable skin lesions were found in all cases, even though there were no clinical lesions. In every case the lesion was centered on a dermal nerve. In some cases disruption of the perineurium was associated with emergence of the lesion into the dermis and a small silent local reaction. It was concluded that there was a descending spread of the disease down the neural

pathway to the dermis, although it was not necessarily associated with transport of bacilli.

Although the first study showed a discrepancy in the classification between skin and nerve lesions in nearly 50% of the cases (as previously reported), the second study showed no discrepancies. It is suggested that discrepancies are relatively uncommon, and that those in the first study are exceptional. The probable explanation is that microreactions in the nerve trunks had caused a shift In classification, which was not yet reflected in the immature skin lesions. In the second study, the mature skin lesions had reached immunological equilibrium. Discrepancies in classification between skin and nerve lesions, as between concurrent skin lesions, are the result of reaction. Attention is drawn to the probable role of subliminal reactions in the evolution of Infections.

SANTAMARIA, L., TERENGHI, G., CUTIS, J. et al. Denature muscle grafts for nerve repair in art experimental model of nerve damage in leprosy. 2. Recovery of peripheral peptide-containing nerves assessed by quantitative immunohistochemical study. *Mt. J. Leprosy, 62, n.* 1, p. 64-74, March, 1994.

A marked depletion of neuropeptide-immunoreactive nerves, a consequence of the nerve damage which is commonly found in leprosy, has been reported in peripheral tissues of leprosy patients and of a leprosy animal model. The aim of this study was to investigate peripheral reinnervation following a denatured autologous muscle graft In an animal model of leprosy nerve damage. Possible reinnervation of the foot-pad skin was studied by immunohistochemistry using antisera to the neuronal marker protein gene product 9.5 (PGP), the neuropeptides calcitonin gene-related peptide (CGRP), substance P (SP), vasoactive intestinal peptide (VIP), and the C- flanking peptide of neuropeptide Y (CPON). The extent of the reinnervation process was assessed by image analysis quantification at different time points. At 8 weeks after muscle grafting, there were small numbers of immunoreactive nerves ($p < 0.05$). At 12, 16, and 20 weeks postoperatively there was a gradual increase in all immunostaining. At 20 weeks, no significant difference was found for PGP-, CGRP-, and SP-immunoreactive nerves in the epidermal and subepidemial layers compared to control (contralateral) tissue. In experimental tissue the recovery of immunoreactive nerves around sweat glands took longer (up to 12 weeks) than in other skin compartments, but after that time the recovery was rapid and at 20 weeks no difference was measured for VIP-immunoreactive nerves in comparison with controls. Around blood vessels, the recovery of CGRP - and CPON - immunoreactive fibers was slow, and at 20 weeks a difference with controls samples ($p < 0.01$) was noted. In the same area, there was no significant difference for PGP immunoreactivity between controls and tissues at 20 weeks. In contrast, the immunoreactive nerve bundles in the dermis showed a faster recovery than nerves in other skin areas, with amounts similar to controls at 20 weeks. The significant recovery of immunoreactive nerves, in particular of those containing sensory neuropeptide, is consistent with the described funcional recovery.

OUTROS

HIRATA, T., HARADA, N. Electron microscopic observations of the relationship between peripheral nerve tissue proper and an endoneurial capillary in a dermal lesion of a relapsed lepromatous patients. *Mt. J. Leprosy, 62,* n. 1, p. 89-98, March, 1994.

The origin of relapse in clinically cured leprosy patients and the dissemination of *Mycobacterium leprae* in such patients are hitherto litle understood phenomena. A detailed electron microscopical examination of a small dermal nerve in a lepromatous lesions of a presently relapsed patient was carried out. Our observations showed the presence of *M. leprae* in Schwann cells, perineurial cells, vacuolar spaces located in axoplasm and elsewhere. The course of a capillary, entering the endoneurium from the epineurium

via the perineurium, suggested the possibility of hematogeneous spread of *M. leprae* which had been tucked away in the dermal peripheral nerve. At the time of relapse, bacilli may multiply in the nerve, may enter the bloodstream, and thus disseminate from the nerve into other nerves and other tissues via hematogenous spread.

REABILITAÇÃO

KAUR, S., DHAR, S. Some observations on patients from two leprosy colonies in North India attending a city clinic. *Indian J. Leprosy, 66,* n. 2, p. 173-178, Apr - June, 1994.

Fifty-eight patients (26 males - mean age 52.5 years, 32 females - mean age 58.5 years) from two different leprosy colonies (Ambala and Jagadhari) were studied. Maximum number of the patients (48.4%) belonged to Uttar Pradesh. The clinical diagnosis was LLp:41 (70.7%), LLs: 14 (24.2%), LL-bumt-out, BB-BL and BT: one each (1.7%). Mean duration of disabilities/deformities in these patients was 21.5 years. A peculiar myokymic movement of periorbital muscles was observed in 20 patients (34.5%). While dapsone monotherapy was continued in 55 patients, MDT (WHO-multibacillary regimen) was started in three patients. Vocational advice was given to 23 patients; and 35 (60,4%) patients were declared as "destitutes".

STRATFORD, C. J., OWEN, B.M. The effect of footwear on sensory testing in leprosy. *Leprosy Rev., 65,* n. 1, p. 58-65, March, 1994.

The aim of this study was to identify the effect of footwear on sensory testing in leprosy. This was achieved by using 3 methods of sensory testing within 1 district of East Africa. We included 72 leprosy patients and 36 controls (nonleprosy patients) in the study and these were subdivided into 2 groups, depending on whether they normally wore shoes or went barefoot. The methods used were the WHO sensory test, graded monofilaments and the biothesiometer. The results showed significant differences in the threshold levels between both groups of patients with the biothesiometer and monofilaments, demonstrating the importance of having separate values when screening for leprosy and assessing which patients are the most risk of developing ulcers. The importance of having quantitative methods of testing was also demonstrated, as only then can the results be sufficiently standardized to identify the at-risk groups and also be sufficiently sensitive to differentiate between shoe wearing and nonshoe wearing patients.

TERAPÊUTICA

CARTEL, J.L., NAUDIN, J.C.. Rate of ralapse in multibacillary patients after cassation of long- course dapsone monotherapy supplemented by a final supervised single dose of 1500 mg of rifampin. *Int. J. Leprosy, 62,* n.2, p. 215-219, June, 1994.

When multidrug therapy was implemented in Senegal, 406 multibacillary (MB) patients who had been treated for more than 10 years by dapsone alone, and who had become clinically inactive and skin-smear negative, were relesead from treatment. Of these 406 patients, 298 were given a supervised single dose of 1500 mg of rifampin. Subsequently, 302 of them (229 who had been given rifampin and 73 who had not) were followed up by means of annual clinical and bacteriological examination. Of the former 229 follwed up for a mean period of 4.9 years, 34 patients relapsed (22 males and 122 females) giving a crude relapse rate of 15% and an overall risk of relapse of 3.1 per 100 patient-years. Of the latter 73 followed up for a mean period of 2.4 years, 5 relapsed (4 males and 1 female), giving a crude relapse rate of 6.8% and an overall risk of relapse of 2.9 per 100 patient-years. Such results, which are in agreement with those of a similar study conducted recently in Mali, indicate that the intake of a single dose of 1500 mg of rifampin by MB patients when they are released from long-

course dapsone monotherapy does not result in a decrease of the relapse rate. Therefore, MB patients who have been treated with dapsone alone, even for long periods, should be put under multidrug therapy prior to their release from control.

HEBERT, D. , PARAMASIVAN, C.N., PRABHAKAR, R. et al. In vitro experiements with Centella asiatica: investigation to elucidate the effect of an indigenously prepared powder of this plant on the acid - fastness and viability of M. tuberculosis. Indian J. Leprosy, 66, n. 1, p. 65-68, Jan - Mar, 1994.

The herb Centella asiatica (Linn), found throughout India, is acclaimed to have medicinal properties and has been used in leprosy patients from very early times. It is considered that the active compound of this herb, called asiaticoside, probably acts on the waxy covering of M. leprae. The in vitro effect of an indigenously produced dry power of Centella asiatica (CA) on the acid-fastness and viability of M. tuberculosis was investigated in the present study. The results indicate that CA may not have any direct action on the acid- fastness or viability of M. tuberculosis H37Rv in vitro. Further studies using purified asiaticoside of the plant or in vivo studies are required.

JAMET, P., BLANC, L., FAYNE, O.C. et al. Relapses after a single dose of rifampin in skin- smear negative multibacillary patients after dapsone monotherapy. Int. J. Leprosy, 62, n. 2, p. 209-214, June, 1994.

Between 1982 and 1985, a single 1500 mg dose of rifampin (RMP) was given to 136 multibacillary leprosy patients who had become clinically inactive and skin-smear negative after various durations of dapsone monotherapy, and then antileprosy chemotherapy was totally stopped. By the end of June 1992, 15 relapses were detected among these patients. The overall relapse rate was 11% the relapse rate per 100 patient-years was 2.1% which was the highest among those publishied to date; the cumulative risk of relapse at year 7 of follow up was 8.8%. All of these figures indicate that the relapse rate among this group was at least the same as in other studies where patients received dapsone monotherapy only. Therefore, the administration of a single large doses of RMP could neither prevent relapse nor reduce its rate among multibacillary patients who had already become clinically and skin-smear negative after dapsone monotherapy.

MAHAJAN, P.M.,JADHAV, V.H., PATKI, A. et al. Oral zinc therapy in recurrent erythema nodosum leprosum: a clinical study. Indian Leprosy, 66, n. 1, p. 51-57, Jan - Mar, 1994.

Effect of oral zinc as immunomodulator was studied clinically in patients with recurrent ENL over a period of one year. In this study, 40 leprosy patients with chronic ENL, requiring more than 30-40 mg of prednisolone/day for the control of their reactions, were given oral zync sulphate for a period of four months, and, marked improvement in the frequency, duration and severity of reactions was observed after zinc therapy. Also evident was marked reduction in the steroid requirement after oral zinc therapy. It appears that zinc maybe a good substitute for the presente day anti-reaction treatment which is not free from disadvantages. Further investigations to know the precise action of zinc on immune-system may help to understand the role of zinc therapy and its optimum duration.

OOMMEN, S.T., NATU, M.V., MAHAJAN, M.K. et al. Lymphangiographic evaluation of patients with clinical lepromatous leprosy on clofazimine. Int. J. Leprosy, 62, n. 1, p. 3236, March, 1994.

Pedal edema as a possible adverse effect of clofazimine therapy in leprosy was first reported in 1990. Raasch, et al. reported their

lymphangiographic findings on ten patients who had clinical lepromatous leprosy in 1969. None of these patients had been on clofazimine therapy. Our study, therefore, was designed to assess the changes that might be seen in the lymphatic system of patients treated with clofazimine for the management of leprosy. Our findings are compared with those of Raasch and his colleagues.

PATTYN, S.R., GHYS, P., JANSSENS, L.et al. A randomized clinical trial to two single-dose treatments for paucibacillary leprosy. Leprosy Rev., 65, n. 1, p. 45-57, March, 1994.

We compared 2 single-dose regiments for the treatment of paucibacillary leprosy in a randomized clinical trial in Zaire. The regimen were: C2 (rifampicin 40 mg/kg and 1200 mg clofazimine once) and C4 (rifampicin 40 mg/kg, clofazimine 100 mg, DDS 100 mg andethionamide 500 mg once). An analysis of the results of patients enrolled between May 1987 and December 1988, with a maximum follow-up of 4 years, is presented. A total of 622 patients were enrolled and 14 paucibacillary and 1 multibacillary relapses occurred. The overall paucibacillary relapse rate was 2.4 per 100 person years. This relapse rate was higher for older patients as well as for patients with 3 or more lesions. The probability of cure at 3 years is 0.816 for C2 and 0.823 for C4, the difference not being statistically significant. The probability of cure at 3 years with either regimen is higher for patients with 1 or 2 lesions (0.872) than for patients with 3 or more lesions (0.787), and it is higher for patients with a bacterial index of 0 (0.831) than for patients with a bacterial index of 1 (0.699). These results are compared to other studies. we also discuss the potential of single-dose treatment regimens for paucibacillary leprosy.

REGE, V.L., SHUKLA, P., MASCARENHAS, M.F. Dapsone syndrome in Goa. Indian J. Leprosy, 66, n. 1, p. 59-64, Jan - Mar, 1994.

Dapsone syndrome was noted within six weeks of starting treatment in 1.3% of about 700 leprosy patients on MDT reporting to the skin department of Goa Medical College. Skin rash, photosensivity, fever, lymphadenopathy, sore throat, hepatoplenomegaly, abnormal liver function tests and raised reticulocyte count were consistent features in all the patients. Other drugs, infectious monocleosis and viral exanthemata were considered in differential diagnosis. Withdrawal of dapsone and administration of prednisolone controlled the condition within three to four weeks in majority of the patients. One patient died of ischemic heart disease unrelated to dapsone syndrome.

SAITO, H., TAMIOKA H., SATO, K. et al. Therapeutic efficacy of benzoxazinorifamycin, KRM-1648, in combination with other antimicrobials against Mycobacterium leprae infection induced in nude mice. lnt. J. Leprosy, 62, n. 1, p. 43-47, March, 1994.

In this study, the in vitro and in vivo anti-Mycobacterium leprae activity of the newly developed benzoxazinorifamycin, KRM-1648, in combination with clofazimine (CFZ) or dapsone (DDS) was evaluated. In vitro anti-M. leprae activities of KRM-1648, CFZ, and DDS along with their combinations were measured by the BACTEC 460 TB System. KRM-1648 (0.01 p.g/ml), CFZ (0.5 rg/ml), and DDS (2.0 µg/ml) exhibited a significant antiM. leprae activity, reducing growth index (GI) values by 78%, 30%, and 35% by day 18, respectively. Combinations of KRM-1648 with either CFZ or DDS, or both caused only a slight increase in the efficacy. BALB/c nude mice infected subcutaneously with 1 x 106 of M. leprae Thai-53 strain and test drugs were given to mice by gavage once daily six times perweekfor up to 50 days, from day 31 to day 80. Animals were obseved forthe growth of organisms in the hindfoot pad during the 12 months following infection. KRM-1648 given at the dose of 0.001 mg/mouse exhibited potent antileprosy activity. KRM-1648 exhibited significant combined effect with either CFZ or DDS, or

both against M. leprae infection, except that there was no significant difference In efficacy between KRM-1648 + CFZ and CFZ alone. Furthermore, the efficacy was most increased In the three-drug regimen KRM-1648 + CFZ + DDS.

XIONG, J.H., JI, B., PERANI, E.G. et al. Further study of the effectiveness of single doses of clarithromycin and minocycline against Mycobacterium leprae in mice. Mt. J. Leprosy, 62, n. 1, p. 37-42, March, 1994.

The anti-Mycobacterium leprae activities of single doses of rifampin (RMP), clarithromycln (CLARI), or minocycline (MINO) alone, and various combinations of CLARI + MINO were determined in immunocompetent mice by the kinetic method. A single dose of RMP 10 mg/ kg, CLARI 100 mg/kg or 200 mg/kg, MINO 25 mg/ kg or 50 mg/kg alone, or various combinations of CLARI + MINO were active. RMP was more active than the other treatments; the activity of CLARI 100 mg/kg was greater than that of 50 mg/kg, but did not differ significantly from that of 200 mg/kg; MINO 50 mg/kg was more active than 25 mg/kg; and none of the combinations of CLARI + MINO was more active than any of the stronger components administered alone. Therefore, both CLARI and MINO may be applied, either alone or in combination, as components of monthly administered, fully supervised, multidrug regimen for the treatment of multibacillary leprosy. Taking into account the effectiveness of the drugs and the comparative pharmacokinetic data, we propose that the optimal dosage in human trials is CLARI 1000 mg per month or MINO 200 mg per month.