## RESUMOS/ABSTRACTS

### WOES DE CONTROLE

**KOPPART, S.N.M., KURUP, A.M., SIVARAM,** M. Problems and coping strategies of families having patients with and without deformities. Indian Leprosy, v.67, n.2, p.133-152, Apr- Jun., 1995.

Deformity in leprosy is a major problem causing serious socio-economic and psychological consequences to the patients and their families, as well as for the programmers. This paper examines the nature and extent of social and economic problems of leprosy-affected families having patients with and without deformities and their strategy to cope with those problems. The data were collected from 500 sampled families in two monotherapy districts in Tamil Nadu in 1989-1990. About 20% of the families reported facing socioeconomic problems. The proportion of families having patients with deformities facing problems was ten time higher (57.3%) than those having patients with no deformities (5.7%). Majority of the problems of the affected families were economic. The major strategy adopted to deal with economic problems was to adjust within the earnings of other family members to make up the loss or reduction in income from the patient. The major social problem faced was denial of participation in the community. While families with deformed patients adopted "acceptance of their existing situation", families with non-deformed patients adopted "avoidance" their coping strategy. Appropriate rehabilition programmes to restore economic security to the patients and their families is called for. There is also the need to educate the community about the disease in order to dispel the myths and fears associated with leprosy.

**PEDRAZANI, E.S.** Levantamento sobre as ações de enfermagem no programa de controle da hansenfase no Estado de Sao Paulo. Rev. Lat. Am. Enfermagem, v.3, n.1, p.109-115, January, 1995.

The present study assesses nursing actions in the Leprosy Control Program in the state of São Paulo. Nursing care, education, epidemiological control and administrative actions are primitive. Revision of practices being developed in the new model of health care are necessary.

**PREMKUMAR, R., DAVE, Si.** Professional freedom of govenment leprosy personnal. Natl. med. j. India, v.8,n.2, p.54-57, Mar- Apr., 1995.

BACKGROUND. Government employment in India is known for its lack of flexibility. We studied whether this also involved professional freedom among health personnel working for the National Leprosy Eradication Programme. METHODS. The sample population consisted of National Leprosy Eradication Programme employees from Tamil Nadu and Andhra Pradesh and 8 health professional groups. A questionnaire was developed for each of them to elicit information on 5 aspects of their autonomy. They were studied individually and as homogeneous groups so that comparisons were possible both within and between groups in different regions who were conducting similar health programmes. RESULTS. National Leprosy Eradication Programme personnel enjoy a high degree of autonomy within the organization. This autonomy was evident in both states investigated, despite different administrations and it was not connected with the professional positions they held. Professional freedom correlated with the training activities, promotional prospects and commitment to the organization. CONCLUSIONS. The National Leprosy Eradication Programme job is not rigid because the organization is small and the intellectual needs of the professionals are met within it.

## CLÍNICA

**AHSAN, N., WHEELER, D.E., PALMER, B.F.** Leprosy-associated renal disease: case report and review of the literature. J. Amer. soc. Nephrol., v.5, n.8, p.1546-1552, February, 1995.

Leprosy is an infectious disease the principal clinical manifestations of which are anesthetic skin lesions and the development of peripheral neuropathy. The most common renal manifestation in leprosy patients is glomerulonephritis. Both immunofluorescent and electron microscopic studies suggest that the varied glomerular lesions found in these patients are immune and 93.9% (19.7 to 1.2/10,000) in Wenshan. The decrease in the detection rate was 99.9% (35.2 to 0.05/10,000) in Weifang and 91.7% (69.9 to 5.8/10,000) in Wenshan. The decrease was more apparente in these two prefectures since the implementation of multidrug therapy (MDT) in 1986. Findings such as specific detection rates by age, sex and type, as well as the multibacillary, child, and deformity rates of patients detected since 1980 were studied. Using the detection and prevalence rates between 1980 and 1993, the number of patients until the year 2000 is extrapolated for these two prefectures.

**AROLKAR, S.K., ANTIA, N.H.** Vascular surgery of the posterior tibial compartmentfor plantar ulceration in leprosy. Leprosy Rev., v.66, n.1, p.48-54, March, 1995.

Traditional surgical decompression of the posterior tibial nerve yields equivocal results. The authors postulate that the posterior tibial artery is the most compromised structure in the neurovascular compartment and that the best surgical results in healing of plantar ulcers are achieved by the rechannelling of the blood flow in the posterior tibial artery during posterior tibial neurovascular compartment surgery.

This procedure has been of benefit to patients with plantar ulcers of greater than 7-10 years' duration in whom all other modes of healing had failed. It has been undertaken procedure under local anaesthesia, supported by postoperative vasodilator drugs. The use of tourniquet, antibiotics and surgical interference with the ulcer per se was eschewed. A report of 156 patientis is presented with follow-up of uo to 6 years for the earlier cases.

**ARUNTHATHI, S., SAMUEL, J., EBENEZER, G.L. et al.** Localized borderline lepromatous leprosy. Indian J. Leprosy, v.67, n.2, p.177- 181, Apr-Jun., 1995.

Multibacillary (MB) leprosy, which includes both lepromatous (LL) and borderline lepromatous (BL) types of leprosy, is a generalized disease with widespread skin infiltration, numerous macules, papules, plaques or nodules and multiple nerve involvement. In untreated patients, the smears are almost always positive in routine sites. Multibacillary leprosy patients presenting with solitary or only a few lesions and a high bacterial count are rare occurrences (Yoder et al 1985, Job et al 1989, Jha et al 1991, Misra et al 1991).

In this paper we describe a patient who presented with two skin lesions localized to the right upper arm and showed histopathological features of borderline lepromatous leprosy, but without any nerve enlargement.

**BANSAL, R., GARG, B.R., ADITAHN, C. et al.** Cortisol status in different types of leprosy. *J. Dermatol.,* v.22, n.2, p.95-97, February, 1995.

Basal plasma cortisol levels in 12 controls and 60 patients with different types of leprosy were within normal limits. They were significantly lower in multibacillary leprosy patients; this abnormality might be due to long standing stress leading to adrenal exhaustion. The plasma cortisol level significantly increased after the ACTH (Synacthen) stimulation test in all of the varieties of leprosy tested, which suggests that the adrenal reserve is maintained in such cases.

**BARRERAS, E.R., CASTELLS, E.G.A., SEGREDO, A.G. et al.** Estudio de un caso sospechoso de infección subcl Mica de lepra. Rev. Leprol Font/los, v.19, n.6, p.625-629, Septiembre-Diciembre, 1994.

In this report a case is described in whom antibodies to theM. lepraespecific antigen phenolic glycolipid I were demonstrated. This case was followed up for 5 years, without specific treatment, until the antibody level declined to a normal value. No clinical signs of leprosy were observed during the surveillance period therefore, it was assumed that the serological reactivity might have expressed the course of a subclinical infection with M. leprae.

**BOOCOCK, P.A., ROBERTS, C.A., MANCHESTER, K.** Prevalence of maxillary sinusitis in leprous individuals from a medieval leprosy hospital. Int. J. Leprosy, v.63, n.2, p.265-268, June, 1995.

The maxillary sinuses of 133 skeletons from the medieval hospital of St. James and St. Mary Magdalene, Chichester, England, were analyzed for evidence of sinusitis. Of the sample, 16 individuals were considered to have suffered from lepromatous leprosy and 13 from tuberculoid leprosy. The most common bone change seen within the sinuses was the presence of new bone formation followed by pitting. Bone change was seen in 56.3% (9 of 16) of the individuals with lepromatous leprosy and 54.8% (57 of 104) of nonleprous individuals. These results are not statistically significant. Clinical evidence suggests that one should see a higher frequency in the lepromatous group. Possible explanations of this include environmental factors promoting the spread of droplet infection in an immunosuppressed community, in addition to which the small sample of leprous skeletons may bias the result.

**CARUS, N.H., RAIZMAN, M.B., WILLIAMS, D.L. et al.** Relapse of Mycobacterium leprae infection with ocular manifestations. Clin. infect. dis., v.20, n.4, p.776-780, April, 1995.

A case of ocular leprosy as the manifestation of persistent or relapsed Mycobacterium leprae infection approximately 20 years following treatment is reported. The clinical and pathological features of this case are described, and the molecular methods needed to arrive at the definitive diagnosis are examined. If blindness is to be averted, clinicians must have a high index of suspicion for the diagnosis of ocular leprosy when anterior segment changes are noted during ophthalmologic examination of a patient from an area in which M. leprae is endemic. The indolent nature of ocular leprosy may require lifelong surveillance and therapy to insure sight preservation.

**DAUMERIE, D., PANNIKAR, V**. Issues in evaluating information on relapses in leprosy. In: SYMPOSIUM ON RELAPSE IN LEPROSY, 1994. Indian J. Leprosy, v.67, n.1, p.27-33, January-March, 1995.

The conclusions of studies on relapses in leprosy, either after monotherapy or after multidrug therapy (MDT), show different results which are not always attributable to the efficacy of treatment. Various methods are used to describe the risk of relapse including the proportion of patients relapsing, relapse rate, cumulative relapse risk and average or median incubation time of relapse. Before the era of MDT, leprosy was usually considered a disease of lifelong duration and the reappearance of lesions were attributed to treatment failure or resistance. With the introduction of MDT, and in particularfixed-duration therapy, it has become possible to clearly define a relapse as 'a patient who successfully completes an adequate course of MDT, but who subsequently develops new signs and symptoms of the disease..." (WHO 1988). Shortly after this definition was proposed, the concept of a cure for leprosy was generally accepted. However, many experts have expressed their concem about the possibility of relapse, especially for multibacillary (MB) patients, long after the completion of treatment. The main difficulty in addressing the problem of relapse after MDT is the absence of specific tools to diagnose them and to differentiate between

treatment failures, reinfection, resistance and reactions. In addition, it is very difficult in the field to collect information on cohorts of patients over decades. The purpose of this article is to discuss some of the difficulties of collecting and interpreting data on relapses and to propose various solutions which could be applied according to the individual situation.

**DESIKAN, K.V.** Relapse, reactivation or reinfection? In: SYMPOSIUM ON RELAPSE IN LEPROSY, 1994. Indian J. Leprosy, v.67, n.1, p.3-11, January-March, 1995.

With the advent of potent anti-leprosy drugs and introduction of multidrug therapy, the cure of leprosy is much quicker and more effective than with the time-old monotherapy with dapsone. While we achieve the cure and elimination of the bacilli, we have to be extremely on guard to see that the cure is complete and there is no relapse of the disease. When lesions do recur after cure, the natural doubts that arise in the minds of the clinicians are.

**FIALLO, P., PESCE, C., LENTI, E. et al.** Short report: erythema nodosum leprosum lymphadenitis.Amer. j. trop. med. hyg., v.52, n.4, p.279-279, April, 1995.

A case of isolated erythema nodosum lymphadenitis involving the paravertebral, intercostal, and cervical lymph nodes without concomitant skin involvement is reported in a 62-year-old male patient under treatment for lepromatous leprosy.

**GIBSON, T.** Bacterial infections: the arthritis of leprosy. Baillieres clin. RehumatoL, v.9, n.1, p.179-191, February, 1995.

Arthritis is a common feature of leprosy and contributes to disability. Direct invasion of joints and bones by mycobacteria may lead to a destructive arthritis in lepromatous disease. The infective process may involve few or many joints. Reactional states may occur spontaneously but usually after the initiation of anti-mycobacterial treatment. In both the type 1 reaction of borderline case and the type 2 reaction of the lepromatous disease, intense inflammation may occur at sites of infection. The immunology of the reactions is different but they share clinical features including a polyarthritis which may resemble rheumatoid disease. The joint disease may be chronic or relapsing, affecting the wrists and small joints of the hands in particular. Radiological erosions may occur. *Mycobacterium leprae* is not found in the synovium in this pattern of arthritis. Further study of this phenomenon might yield useful information above the mechanism of joint inflammation in other rheumatic diseases.

**HUSSAN, R., LUCAS, S.B., KIFAYET, A. et al.** Clinical and histological discrepancies in diagnosis of ENL reactions classified by assessment of acute phase proteins SAA and CRP. *Mt. J. Leprosy,* v.63, n.2, p.222- 230, June, 1995.

Sixteen out of 45 (36%) leprosy patients with clinical features of acute erythema nodosum leprosum (ENL) did not show the characteristic presence of neutrophils (polymorphs) in histology of the ENL lesion. The acute-phase reactants, serum amyloid, A (SM) and C-reactive protein (C R P) which are systemic markers of inflammation, and IgM and IgG antibody toMycobacterium leprae were determined in these patients in order to understand the differences in histological diagnosis. Both SM and CRP were elevated in ENL patients, irrespective of the presence of polyrnorph infiltrates, as compared to nonreactional lepromatous patients, patients with histologically confirmed reversal reactions and endemic controls, indicating that all clinically diagnosed ENL patients had ongoing inflammatory reactions. On the other hand, IgM and IgG antibodies were significantly lower (> 70%) in ENL patients as compared to nonreactional lepromatous patients. When the two ENL groups [ENL-PMN +ve (positive for neutrophils) and ENL-PMN -ve (negative for neutrophils) were compared, there were no significant differences in the mean SM, IgM or

IgG antibody concentrations, but CRP was eightfold lower in ENL-PMN -ve as compared to the ENL-PMN +ve group. This may indicate that the timing or modulation of the reaction was different in the two ENL groups. Thus, measurement of the acute-phase response and the ratio of SAA/CRP in particular are helpful in the clinical diagnosis of ENL reactions in leprosy.

**KOYUNCU, M., CELIK, O., INAN, E. et al.** Doppler sonography of vertebral arteries and audio vestibular system investigation in leprosy. Int. J. Leprosy, v.63, n.1, p.23-27, March, 1995.

Thirty-six patients with leprosy and 12 sex- and age-matched controls were investigated for disorders of the audiovestibular system, and vertebral artery measurements were calculated using a color Doppler ultrasound technique. Sensorineural hearing loss found to be of cochlear origin was detected in 8 of the leprosy patients. Maximal flow velocity and mean flow velocity were measured, and the total vertebral artery flow was calculated by adding flows from the right and left sides. There was a significant reduction in the total maximal peak flow velocity of the vertebral artery of the lepromatous patients compared to the controls. Doppler sonography of the vertebral artery gave useful information about some pathology seen in lepromatous patients.

**KUMARAVEL, S.** Multiple subcutaneous lipomatosis in a case of relapsed lepromatous leprosy masquerading as history leprosy. Indian J. Leprosy, v.67, n.2, p.187-190, Apr-Jun., 1995.

Histoid leprosy is a variant of lepromatous leprosy which was originally described by Wade (Wade 1963) and later by others (Ramanujam & Ramu 1969, Rodrigues 1969, Chaudhury et al 1971). The lesions of histoid leprosy are subcutaneous nodules which tend to remain so indefinitely, but they may also migrate towards the surface and fuse with the dermis. Occasionally, cutaneous nodules and cutaneous plaques are seen in cases with histoid leprosy (Dharmendra 1967).

Lipomas are soft tissue tumours which are very common. They may arise anywhere in the body, but the commonest site is the subcutaneous plane. Multiple lipomata are also not uncommon (Harding-Rains & Mann 1991, Das 1988).

**LEWIS, M.E., ROBERTS, C.A., MANCHESTER, K.** Inflammatory bone changes in leprous skeletons from the medieval hospital of St. James and St. Mary Magdalene, Chichester, England. *Mt. J. Leprosy,* v.63, n.1, p.77-85, March, 1995.

The extent and location of an inflammatory bone lesion, periostitis, were examined in 50 leprous skeletons from the Chichester cemetery of the Hospital of St. James and St. Mary Magdalene in Sussex, England. Although the presence of periostitis is not pathognomonic of leprosy, it predominantly indicates dermal and neuropathic changes that the patient would have presented in life. The spread of inflammation across the knee joint and the ossification of the interosseous membrane due to inflammation are also suggested.

**LIENHARDT, C., CURRIE, H., WHEELER, J.G.** Inter-observer variability in the assessment of nerve function in leprosy patients in Ethiopia. Int. J. *Leprosy,* v.63, n.1, p.62-76, March, 1995.

One of the major problems in leprosy is to detect any change in nerve function early enough so as to increase the chances of recovery and prevent disability. Several tests have been developed to assess nerve function and are used in leprosy control programs worldwide, but they are frequently performed by different workers on different occasions and under variable conditions. In this study we investigated the variability between different groups of observers in the assessment of nerve function in leprosy patients in Ethiopia. Sensory function was assessed by using a set of

nylon monofilaments (NF) and a ball-point pen (BP), and motor function was assessed by using voluntary motor testing (VMT). We also studied the variability between observers in the assessment of the clinical signs of neuritis.

Duplicate measurements were performed in random order on 50 leprosy patients by two physio-technicians and on 50 other patients by two health assistants. The percent agreement between observers was calculated for each single nerve, and weighted kappa statistics were used to assess whether agreement was better than expected due to chance alone. Systematic differences between observers were evaluated using the Wilcoxon signed rank test. On sensory testing, interobserver variability was found to be related to the training and experience of the observer, to the nerve tested, and to the neurological status of the patient.

When tests were performed by physiotechnicians, we observed 32% to 58% agreement with the NF test and 71% to 84% agreement with the BP test, measured on different scales. After weighting for the scale difference, the agreement seemed comparable with these methods but the differences in measurements with the BP test were found to be dependent upon the neurological status of the patient. The variability between observers differed according to the nerve tested, and there was some evidence of systematic differences between observers with both methods.

When performed by the health assistants, agreement was between 34% and 46% with the NF and between 66% and 82% with the BP tests. After weighting for the scale difference, the agreement seemed comparable but the BP was not liable to the systematic differences seen in the NF results. These differences could be attributed to the differences in the experience of the workers with these tests.

With the VMT, small variability between observers was found for all nerves tested, except the facial nerve, when performed by both the physio-technicians and by the health assistants (72% to 98% agreement). Change agreement, however, could not be excluded since the ratings were extremely homogenous. The assessment of neuritis signs was extremely variable between observers (14% to 41% agreement), with evidence of a systematic difference between observers.

Implications of these findings are discussed with the view to improving comparability of the nerve function tests under field conditions for early detection of nerve damage in leprosy patients.

**NAAFS, B.** Features of relapse in paucibacillary leprosy after multidrug therapy. In: SYMPOSIUM ON RELAPSE IN LEPROSY, 1994. *Indian J. Leprosy,* v.67, n.1, p.61-67, January-March, 1995.

The recommendation of multidrug treatment (MDT) by a study group of the WHO in 1982 has undoubtedly been the most important development in the control of leprosy during the past two decades (Becx-Bleumink 1994).

When the recommendations were reviewed and introduced for the leprosy control programmes, many experienced leprologists feared that the shortened course of treatment would result in a great number of relapses (Ellis, Katoch, Waters - personal communications).

For paucibacillary leprosy, the first relapses were soon noticed and reported (Jesudasan & Christian 1985, Pavithran 1988). It seemed that they consisted of two groups. In one group the relapse was diagnosed within a few weeks to months after the discontinuation of MDT, whereas in the other group the relapse occurred after six months. It was noticed that most of these patients must have had a positive BI in the skin or nerve at the start of treatment. Therefore, the WHO changed its definition of paucibacillary leprosy from patients with a BI of less than 2 at any place to no bacteria detectable in smear or biopsy (WHO 1988). After this, the number of relapses decreased markedly.

During dapsone monotherapy, relapse after discontinuing the treatment was a common occurrence for both pauci- and multibacillary leprosy (Touw-Langendijk & Naafs 1979, Becx-Bleumink 1992). For paucibacillary (PB) leprosy, the reported relapse rates ranged from one to 17%, or, from five to 22 per 1000 patients per year (Becx-Bleumink 1994). From a compilation of the data from 17 leprosy control programmes it was

observed that after the WHO-PB leprosy-MDT only 0.5% of the patients had relapsed, or, two to three individuals per 1000 patients per year. This was a marked reduction in the number of relapses. However, the relapses in general were diagnosed under field conditions with different policies with regards to the classification of the patients, duration of treatment and methods of follow-up after release from MDT (Rangaraj & Rangaraj 1986, Reddy & Mohinuddin 1988, Pavithran 1988, Revankar et al 1989, Katoch et al 1989, van Brakel et al 1989, Pattyn et al 1990, Grugni et al 1990, Boerrigter et al 1991, Ekambaram & Rao 1991, Becx-Bleumink 1994).

There is much controversy about the definition of a relapse after MDT, especially since an increase in the clinical symptoms after stopping treatment is frequently seen (Naafs 1984, Katoch et al 1985, Naafs et al 1986, Katoch et al 1986, Ramachandran & Seshadri 1988. WHO 1988, Pannikar et al 1989, Becx-Bleumink 1992). The question is whether the recurrence or increase in the severity of the clinical signs in a patient released from treatment is a real relapse or not. To answer this question the bacteriology and the immunopathology of leprosy have to be taken into account.

**OWEN, B.M., STRATFORD, C.J.** Assessment of the methods available for testing sensation in leprosy patients in a rural setting. *Leprosy Rev.,* v.66, n.1, p.55-62, March, 1995.

The aim of this study was to assess the efficacy, practicality and patient understanding of 5 methods used for testing sensation in leprosy patients, in a rural setting. The tests used were the WHO test, cottonwool, pin-prick, monofilaments and the biothesiometer. We concentrated on testing sensation in the hands, and the various tests were carried out on 75 patients and 32 controls, all taken from villagers living at Kindwitwi Leprosy Village, Tanzania. Our results showed that although the WHO test, cottonwool and pin- prick were all easy to use, cheap and well accepted they were not sensitive enough to be of any practical value. We found that the monofilaments, as well as being cheap and easy to use, had great potential value, as the 2-g monofilament could be used as a threshold value (indicative of leprosy, but not diagnostic) for protective sensation with a combined false-positive and false-negative value of only 4%. Finally, the biothesiometer was found to be a precise test that can accurately identify leprosy patients from controls and identify patients at risk of ulceration. It was, however, associated with its own problems, chiefly those of expense and its need of electricity, although we found this latter problem could be easily and relatively cheaply solved by the use of a solar powered recharger (Appendix).

**RAFI, A., DONOGHUE, HD., STANFORD, J.L.** Application of polymerase chain reaction of *Mycobacterium leprae* DNA in specimens from treated leprosy patients. *Mt. J. Leprosy,* v.63, n.1, p.42-47, March, 1995.

In this study of leprosy patients apparently cured by dapsone monotherapy, the polymerase chain reaction (PCR), one of the most reliable and sensitive DNA-based assays, was used for the specific detection of Mycobacterium leprae DNA. Sputum and slit-skin samples from 44 such patients at Baba Baghi Leprosy Sanatorium in Iran were examined. Primers for a 530-base-pair fragment of the gene encoding the 36-kDa antigen of M. leprae were used for the study. The PCR results were compared with microscopy for acid-fast bacilli. Of the 44 sputum samples, 2 were positive by PCR (4.5%) and of the 44 slit-skin swabs taken from the same patients, 10 were PCR positive (22.7%). Only one patient was PCR positive for both sputum and slit-skin specimens (2.3%). No positive results were found by acid-fast microscopy. In total, 11 of 44(25%) patients in this study were found to be PCR positive forM. leprae, and it was thought probable that this indicated the presence of live organisms. Particularly interesting was the statistically significant association of positive results from slit-skin swabs with paucibacillary rather than multibacillary leprosy. It is suggested that whereas relapse or immu- nological reaction in paucibacillary disease may result from surviving organisms, in multibacillary leprosy this may be due to re-infection.

**RAMU, G.** Clinical features and diagnosis of relapses in leprosy. I: SYMPOSIUM ON RELAPSE IN LEPROSY, 1994. Indian J. Leprosy, v.67, n.1, p.45-59. January-March, 1995.

1. The definition of relapse as occurrence of new signs and symptoms of the disease during the period of surveillance or thereafter in a patient who successfully completes an adequate course of multidrug therapy" accommodates the current policy of releasing patients even when there are clinical and bacteriological signs of activity after fixed duration treatment.

2. The predisposing cause of relapse is the persistence of live M. leprae in various tissues in MB leprosy and in the nerve in PB leprosy.

3. The precipitating causes of relapse include (a) inadequate therapy due to miscategorization of MB cases as PB when there are solitary or few MB lesions since skin smear examinations for AFB are not routinely done in PB cases. (b) Previously sulphone treated LL cases inactive for more than two years are not included for MDT. Relapses commonly seen in NLEP units are in such cases. (c) Multiple skin and nerve lesions in PB leprosy. (d) Pregnancy and lactation. (e) Mental depression which downgrades immunity. (f) HIV infection.

4. There may be a change in type on relapsing, PB cases relapsing as MB and MB cases relapsing as PB.

5. Criteria for diagnosis of relapse are: increase in the extent of lesions, infiltration and erythema, fresh skin and nerve lesions, positive skin smears for AFB in previously negative cases; and in bacteriologically positive cases during surveillance, an increase in BI by two logs at any site over the previous BI in two successive examinations.

6. Relapses are but too often diagnosed as reversal reactions inspite of the absence of symptoms and signs of acute inflammation to the detriment of patients; course of steroid therapy which is administered to these patients on the diagnosis of reversal reaction does not halt the progress of the disease especially in the nerve, resulting in disability.

**RAO, S.P., TAORI, G.M., DESIKAN, K.V. et al.** Clinical and electroneurophysiological assessment of leprosy patients on dapsone monotherapy - a two year follow-up study. Indian J. Leprosy, v.67, n.2, p.167-176, Apr-Jun., 1995.

Fifty-three persons with tuberculoid type of leprosy having a thickened nerve on one side and a clinically normal nerve on the contralateral side were studied before, during and after two years of therapy for electrophysiological abnormalities in apparently normal and in obviously thickened nerves. Twenty-seven patients had received treatment with dapsone 100 mg orally and 26 cases had received rifampicin therapy.

It was found that there was no extension of anesthesia or diminution of motor power over a period of two years. There was no significant difference between the initial and final recordings of motor and sensory nerve conductions if aggregate figures were taken. However, taking individual cases, deterioration in nerve conduction (increased latency and decreased velocity) was found in two patients, of whom one had received dapsone and the other had received rifampicin.

**SALAFIA, A., DE GEIKING, I.** ENL necroticans - report on 5 cases. Rev. Leprol. Fontilles, v.20, n.1, p.645-649, Enero-Abril, 1995.

Between the years 1987-88 we have seen 18 cases of ENL necroticans and in 1993 another 4. In this paper we present 5 of these cases because of some common features and detailed records as they were hospitalized and under direct care. ENL necroticans in one of the many manifestations of type II reaction.

**SALAFIA, A., GEI KING, I.** Neurites and rifampicin. *Rev. Leprol. Fontilles,* v.19, n.6, p.635-638, Septiembre-Diciembre, 1994.

The authors present their observation of neuritis precipitated or aggravated by RFM in 20 patients all hospitalized except three. The authors believe that, as per literature, none of the drugs

used in the MDT programs reach the nerves, however once a nerve is damaged by ischemia, drugs do penetrate and can cause further damage; this explains why many patients asymptomatic before therapy, complain of neural pain after starting the therapy.

**SANTOS, S.N.M. dos, ARAÚJO, M.G., PATRUS, O. et al.** Variação da concentração da hemoglobina em doentes de hansenfase tratados com sulfona.An. *bras. Dorm.,* v.64, n.4, p.281-284, Julho/Agosto, 1994.

BACKGROUND - The hemolysis has been observed, frequently, as one of the sulfone's effects. This seems to happen also in doses applied to the treatment of the leprosy patients.

OBJECTIVE - To know the variation of homoglobin caused by sulfone in the dosage used in leprosy therapy.

METHOD -One hundred and four leprosy patients in use of sulfone were studied and 33 were statistically analysed.

RESULTS - There was no significant statistical correlation with hemoglobin (hb) variation and initial level of hb, interval between laboratorial tests, age and weight in the male sex. In the female sex, there was moderate correlation with the weight. Eighty-four, eighty-four percent of patients (84,84%) had a fall of hemoglobin concentration of 1g/di or more, confirming reports in the literature.

CONCLUSION - It's very important to observe this fact carefully. This may have serious clinical implication, specially in endemic areas, where, owing to nutrition, malaria, and intestinal parasitism, the hemoglobin concentration is already compromised.

Key words: Dapsone; leprosy; hemoglobins; hemolysis; sulfones.

**TERENCIO DE LAS AGUAS, J.** Lepra en la infancia. *Rev. LeproL Fontilles,* v.19, n.6, p.639-648, Septiembre-Diciembre, 1994.

The importance of Leprosy in children, the frequency in endemic countries and it's uncommoness in children under 4 years is reviewd.

The most frequent clinical forms are Tuberculoid incluying the children nodular form and the Indeterminate with the Lepromatous type being exceptional.

The importance of the clinical examen in contacts for detection, together with the therapeutical regimens is described.

**VIJAYAKUMARAN, P., MANIMOZHI, N., JESUDASAN, K.** Incidence of late lepra reaction among multibacillary leprosy patients after MDT. *Int. J. Leprosy,* v.63, n.1, p.18-22, March, 1995.

Multidrug therapy (MDT) recommended by the World Health Organization (WHO) had been administered in 1982 to a cohort of multibacillary (MB) leprosy patients. Treatment was administered for a minimum period of 2 years or until skin-smear negativity for acid-fast bacilli was achieved (whichever was later). Among 980 MB leprosy patients who completed treatment, 11 patients (1.1%) experienced lepra reactions during surveillance. Probable predictive factors are discussed.

The incidence of lepra reaction seemed to be three times more common in borderline (BL) leprosy than in lepromatous (LL) leprosy. The majority of these events occurred during the first 3 years of surveillance. All of these episodes were treated with steroids without antileprosy chemotherapy. None of these patients was confirmed as experiencing a relapse during the subsequent period of surveillance.

**VORA, N.S., MULKHOPADHYAY, A.K., ROY, K. et al.** A case of histoid leprosy responding to ofloxacin along with standard MDT. *Indian J. Leprosy,* v.67, n.2, p.183-186, Apr-Jun., 1995.

Dr Wade was the first to report in 1963, under the name of histoid leproma, a lepromatous lesion characterized histopathologically by the predominance of *spindle-shaped histiocytes. There appears to be some relation between histoid

leproma and dapsone resistance but it has also been reported in cases which were not instances of relapse (Rodriguez 1969). Its significance is not yet clear.

Clinically, the histoid nodules may be cutaneous, subcutaneous or both. The typical lesions are reddish, shiny, domed, round or oval nodules with a tendency to group or fuse with others. 'Soft' histoid nodules are flatter and less well defined. The subcutaneous nodules are non- tender masses, not attached to the overlying skin and are usually found on the elbows or wrists (Canizares et al 1992).

We report here a case of histoid leprosy in which the lesions disappeared completely with ofloxacin therapy for 28 days followed by the standard multidrug therapy (MDT).

**WADDELL, K.M., SAUNDERSON, P.R.** Is leprosy blindness avoidable? The effect of disease type, duration, and treatment on eye damage from leprosy in Uganda. *Brit. J. Ophthalmot,* v.79, n.3, p.250-256, March, 1995.

AIMS - The study was designed to measure the prevalence, range, and severity of eye involvement in leprosy patients; to relate this to disease type, duration, and treatment to identify risk factors; and to provide practical guidelines for programme managers and field staff on the prevention of blindness.

METHODS - The visual outcome was assessed in a population based sample of patients in Kasese District, Uganda followed for up to two decades, and related to disease features and treatment. A total of 678 patients responded to an invitation out of 2715 registered since 1973.

RESULTS - Low vision was present in 4.4% of people and blindness in 1.3%, with 1.5% and 0.6% respectively being due to leprosy. Some 12.4% of patients had iritis, of whom 33% had visual loss in one or both eyes, 3.7% of patients had lagophthalmos, and 11.7% had lens opacity. For multi-bacillary (PB) cases, the adjusted odds ratios were: for iritis 4.6 (95% CI 2.6-8.2), for lagophthalmos 1.4 (0.6-3.2), and for lens opacity 1.7 (1.0-3.0). Potentially sight threatening (PST) lesions were present in 16.8% of patients (95% Cl 14.0-19.6).

CONCLUSION - Levels of eye involvement in this study are low compared with many surveys. Visual loss is uncommon and is more often caused by other diseases; in the present era of multidrug therapy (MDT) it is very unlikely to be caused by leprosy. It is more common with advancing age. PST lesions, especially iritis, may occur in both PB and MB cases, even if the diagnosis of leprosy is made early and MDT started immediately; they may occur also after completion of MDT. But eye complications need not proceed to loss of sight if treated promptly, and blindness can be avoided, Training of front line staff is therefore crucial.

**WORLD HEALTH ORGANIZATION.** Risk of relapse in leprosy. In: SYMPOSIUM ON RELAPSE IN LEPROSY, 1994. *Indian J. Leprosy,* v.67, n.1, p.13-26, January-March, 1995.

Until the introduction by WHO of the standard regimens using multidrug therapy (MDT) for the treatment of leprosy, there was a general unwillingness to release patients from treatment. This was mainly due to the high risk of relapse after dapsone monotherapy. After almost a decade of MDT implementation and after releasing more than 4 million patients, it was necessary for WHO to review the risk of relapse following WHO- recommended MDT. The results of this study, carried out on more than 20,000 MB and 50,000 PB patients, revealed that the risk of relapse is very low, 0.77% for MB and 1.07% for PB, nine years after stopping MDT. In comparison to dapsone monotherapy, the risk is 10-times lower. Thus, over the last decade, MDT implementation has probably prevented close to half-a-million relapses.

## EPIDEMIOLOGIA

HERNANDEZ, G.B.C., TORRES, T.M.F. Incidencia de lepra durante la monoterapia y la multiterapia - Ciudad de CamagOey (Cuba) anos 1984-1993. *Rev. LeproL Fontilles,* v.19, n.6, p.603-612, Septiembre- Diciembre, 1994.

A comparative study of the incidence of leprosy in Camagüey, Cuba, was carried out during the last quinquenia of mono-drug therapy (1984-1988) and the first with multidrug therapy (1989-1993).

The epidemiological indexes analized were the incidence and its rates x 100.000 inh., the percentange of clinic forms, sex and age groups.

The results of the study have demostrated a diminution of the incidence of leprosy (from 121 to 81 cases) and its rates (maximum from 11,5 to minimum of 2,7 x 100.000 inh.); a displacement toward the predominance of multibacillary forms (from 48,7 to 63,0%); from a predominance of the LI in mono-drug therapy stage (27,3%) evolved to the minimum percentage (7,4%) among all clinic forms during the MDT; a slight predominance of female (55,0%); a minimum affectation under 15 years (average 1,5%) and a higher affectation in the group of 35-64 and more than 65 years age group.

**ITO, T.** The 69th annual meeting special lecture. Present situation of leprosy. *Kekkaku,* v.70, n.5, p.361-363, May, 1995.

Many leprosy patients have deformity or disability owing to the characteristics of *Mycobacterium leprae i.e. M. leprae* affects skin and peripheral nerve. Optimum growth temperature of *M. lepraewas* estimated by clinical manifestations and animal experiments, and it was concluded that the optimum temperature is 33 degrees C, and this characteristic of *M. leprae* may be one of the reason why *M. leprae* affects skin tissue. There was no reliable treatment of leprosy before 1943, but effectiveness of promin against leprosy was proven in 1943, and chemotherapy of leprosy was gradually improved especially since 1960 afterthe discovery of mouse footpad inoculation of M. leprae. In vitro cultivation technique of M. leprae is still unestablished, but susceptibility of ninebanded armadillo toM. leprae was discovered in 1970. Supply of M. leprae collected and purified from M. leprae infected armadillo tissue became available, then biochemistry, immunology and molecular biology of M. leprae was improved significantly. Ridley- Joppling's classification of leprosy i.e. two types (tuberculoid and lepromatous) and two groups (indeterminate and borderline) classification is being adopted at present. Rifampicin, DDS (dapsone) and clofazimine (lamprene) are widely used for chemotherapy of leprosy. WHO is recommending Multidrug Therapy (MDT) of leprosy i.e. administration of rifampicin and DDS for paucibacillary group, administration of rifampicin, DDS and clofazimine for multibacillary group. About 2.4 million leprosy patients are registered and under chemotherapy in the world at present, and about five hundred thousand new patients are being registered every year. Target of leprosy elimination by WHO is prevalence rate of leprosy should be less than one per ten thousand in every country. (ABSTRACT TRUNCATED AT 250 WORDS).

**JAKEMAN, P., JAKEMAN, N.R.P., SINGAY, J.** Trends in leprosy in the Kingdom of Bhutan, 1982-1992. *Leprosy Rev.,* v.66, n.1, p.69-75, March, 1995.

An evaluation programme was undertaken 11 years after the introduction of multidrug therapy (MDT) into Bhutan, by examining the case notes of 3239 leprosy patients who had been under treatment at any time during the period. The registered prevalence was found to have fallen markedly, as expected, and this had been accompanied by a clear fall in the case detection rate as well. The lepromatous rate among new patients rose considerably, giving epidemiological hope that the disease may be coming under control. However, no concomitant fall in the proportion of child cases was seen. The

disability rate at detection rose slightly, although numbers were small. New cases were increasingly likely to have more highly positive skin smears, and to be self-reported. Programme planners should give thought to the implications of these findings.

**LI, Huan-Ying, WENG, X.M., LI, T. et al.** Long- term effect of control in two prefectures of China, 1955-1993. *Int. J. Leprosy*, v.63, n.2, p.213-221, June, 1995.

In Weifang Prefecture, Shandong Province, and Wenshan Prefecture, Yunnan Province of China, leprosy was highly prevalent in the 1950s. Due to differences in geographical conditions and socioeconomic development, the decline in leprosy prevalence between 1955 and 1993 was 99.5% (10.1 to 0.05/10,000) in Weifang and 93.9% (19.7 to 1.2/10,000) in Wenshan. The decrease in the detection rate was 99.9% (35.2 to 0.05/10,000) in Weifang and 91.7% (69.9 to 5.8/ 10,000) in Wenshan. The decrease was more apparent in these two prefectures since the implementation of multidrug therapy (MDT) in 1986. Findings such as specific detection rates by age, sex and type, as well as the multibacillary, child, and deformity rates of patients detected since 1980 were studied. Using the detection and prevalence rates between 1980 and 1993, the number of patients until the year 2000 is extrapolated for these two prefectures.

**IVIARTELLI, C.M., MORAES NETO, 0.L., ANDRADE, A.L. et al.** Spatial patterns of leprosy in an urban area of central Brazil. *Bull. World Health Organ.,* v.73, n.3, p.315- 319, 1995.

Reported is the spatial variation of leprosy in an urban area of Brazil and its correlation with socioeconomic indicators. From November 1991 to October 1992 a total of 752 newly diagnosed leprosy patients who were attending all outpatient clinics in Goiania city, central Brazil, were identified. A database of leprosy cases was set up linking patients' addresses to 64 urban districts. Leprosy cases were detected in 86% of the districts and three risk strata were identified. The highest-risk area for leprosy was in the outskirts of the city and detection rates increased on moving from more developed to poorer areas. The risk of detecting leprosy cases was 5.3-fold greater (95% Cl: 3.8- 7.4) in the outskirts of the town than in the central zone. Discussed are the methodological issues related to leprosy case ascertainment, completeness and reliability of information, and the interpretation of the spatial distribution of leprosy per unit area. Highlighted also are the lack of leprosy control activities in primary health care units and the usefulness of geographical analysis in planning health services.

**NOORDEEN, S.K.** Elimination of leprosy as a public health problem: progress and prospects. *Bull. World Health Organ.,* v.73, n.1, p.1-6. 1995.

Leprosy is still an important problem in about 80 countries of Asia, Africa and Latin Ame- rica, some 2.4 million persons being estimated to have the disease in 1994. The WHO-recommen- ded standard multidrug therapy (MDT) was introduced in the 1980s and has been shown to be effective in combating the disease. Experiences based on many thousands of patients treated with MDT over the past decade indicate extremely low relapse rates (cumulative relapse rates around 1%). By the end of 1993, some 5.6 million patients had been cured, and the global cumulative MDT coverage of registered patients had reached 89%. The number of registered cases fell from 5.4 million in 1985 to 1.7 million in 1994. The significant progress made in leprosy control enabled the World Health Assembly in 1991 to set a goal for eliminating leprosy as a public health problem by the year 2000. One important epidemiological factor is that leprosy is very unevenly distributed: 80% of the problem is confined to onlyfive countries and 92% to just 25 countries. The elimination strategy envisages identifying and treating with MDT a total of about 5 million cases from 1994 to the year 2000. The cost of dealing with these cases has been estimated at US$ 420 million, including US$ 150 million for the drugs.

**PONNIGHAUS, J.M., STERNE, J.A.C.** Epidemiological aspects of relapses in leprosy. In: SYMPOSIUM ON RELAPSE IN LEPROSY, 1994. *Indian J. Leprosy,* v.67, n.1, p.35-44, January-March, 1995.

Life table methods in which the cumulative probability of relapse in successive periods is calculated are preferable to the presentation of overall relapse rates. Their use facilitates the comparison of relapse rates and trends from different studies independent of duration of follow-up. Results from various studies including data from Malawi indicate that, (1) unlike after dapsone monotherapy, the cumulative probability of relapse in multibacillary patients is near to zero after WHO/MDT if strict definitions of relapse are used and, (2) the cumulative probability of relapse may approach 5% in paucibacillary patients 10 years after completion of WHO/MDT. On the whole, the epidemiological relevance of relapses is insignificant and future treatment regimens should be evaluated concerning their efficacy in preventing disabilities rather than relapses.

**SIFONTES, M.E.L., HERNANDEZ, G.B.C., HERNANDEZ, S.C.** Indicadores epidemiológicos de la incidencia de lepra en un distrito de salud.*Rev. Leprol Fontilles*, v.20, n.1, p.625-643, Enero-Abril, 1995.

During the years 1989-1993 a descriptive survey of the incidence of leprosy in the District of Joaquin de Agüero, Camagiley, Cuba was performed. The following aspects were analized; incidence of leprosy and it's rates, sex distribution, age groups, clinical forms, detection methodes, source of infection, early or late diagnosis, results of the epidemiological survey, first symptoms of the disease and their localization, disabilities present in the moment of diagnosis and treatment compliance. The incidence of leprosy during the 5 years was 32 cases with rates of 10,7 and 2,7 x 100.000 with a decreasing tendency in both cases. A slight predominance in the female group could be detected (56,2%). The most frequent age group was between 35-44 and over 65 years old. The percentage of multibacillary leprosy was 62,5. The most frequent clinical forms were LL (37,5%) and LT (28,1%). The clinical exam of contacts and risk population were satisfactory in the incidence of detection. The indicators related with determinate of the source of infection, early diagnosis of leprosy and results of the epidemiological survey were insatisfactory. The anesthetic macules are the first and mayor sympton mentioned by patients (56,3%). The first symptons are localized on face and limbs. The percentage of patients with disabilities at the moment of diagnosis was (28,1%), with the highest percentage resulting in the hands. The treatment compliance rate was 100%.

**TORRES, T.M.F., HERNANDEZ, G.B.C.** Incidencia de lepra en la ciudad de Camagüey, Cuba ano 1978-1993. *Rev. LeproL Fontilles,* v.20, n.1, p.603-611, Enero- Abril, 1995.

An study was carried out about the incidence of leprosy in Camagaey city, Cuba, during 1978-1993. The diagnostic was based on five main criterion: immunology, histopathology, bacteriology, clinical examination and epidemiology. It was utilized the classification of Madrid and the sanitary for the classification of the cases. The incidence was of 411 patients. The incidence rates varied between 22,5 and 2,7 x 100.000 inh. The average was about 26 new patients each year. It is a tendence towards to decrease in the indice of detection of new cases. It was not significative difference between the multibacillaryforms (50'6%) and the paucibacillary forms (49,4%). In a decreasing order, the clinical forms percentage were the following ones: LL (28,5%), LT (26,3%), paucibacillary LI (23,1%) and LD (21,9%). A slight predominance of females (54,0%) over males (46,0%). Nine cases under 15 years old were reported (2,2%) and 402 of 15 years and older. In adults the greater number of new cases was presented starting form of 35 years old.

## GENÉTICA

**ABEL, L., VU, D.L., OBERTI, J. et al.** Complex segregation analysis of leprosy in southern Vietnan. *Genet Epidemiol*, v.12, n.1, p.63- 83, 1995.

To investigate the nature of the genetic component controlling susceptibility to leprosy and its subtypes, 402 nuclear families were ascertained through a leprosy patient followed at the Dermatology Hospital in Ho Chi Minh City, Vietnam; 285 families were of Vietnamese origin and 117 were of Chinese origin with a higher proportion of lepromatous forms among Chinese patients. Segregation analysis were conducted using the model developed by Abel and Bonney [(1990) Genet Epidemiol 7:391-4071, which accounted for variable age of onset and time- dependent covariates. Three phenotypes were considered: leprosy per se (all forms of leprosy together), nonlepromatous leprosy, and lepromatous leprosy. For each of this phenotype, analysis were performed on the whole sample and separately on the Vietnamese and the Chinese families. The results showed that a single Mendelian gene could not account for the familial distributions of leprosy per se and its two subtypes in the whole sample. However, these results were different according to the ethnic origin of the families. In the Vietnamese subsample, there was evidence fora codominant major gene with residual familial dependences for the leprosy per se phenotype, and borderline rejection of the Mendelian transmission hypothesis for the nonlepromatous phenotype. In Chinese families, strong rejection of Mendelian transmission was obtained in the analysis of leprosy per se, and no evidence for a familial component in the distribution of the nonlepromatous phenotype was observed. Forthe lepromatous phenotype, the discrimination between models was poor, and no definitive conclusion could be reached. Referring to immunological data, we suggest that these results could be explained by a heterogeneity in the definition of the lepromatous phenotype. It is likely that progress in the understanding of the genetic components involved in the expression of leprosy will come from a better definition of the phenotype under study, and immunological studies are on going in this population to investigate this hypothesis (Au).

**FEITOSA, M.F., BORECKI, I., KRIEGER, H. et al.** the genetic epidemiology of leprosy in a Brazilian population. *Am. j. hum. genet.,* v.56, n.5, p.1179-1185, May, 1995.

Data on leprosy patients have been obtained from the Dispensary of Leprosy of Campinas, São Paulo, where records on practically all cases of leprosy in the Campinas area during the period 1960-70 are filed. The whole sample comprises 10,886 individuals, distributed among 1,568 families. Complex segregation analysis was utilized to determine the nature of the genetic factors that may operate on leprosy and its subtypes. The results suggest the presence of a recessive major gene controlling susceptibility to leprosy per se, with frequency of approximately .05, although there are deviations from the expected Mendelian segregation proportions. Possible etiologic heterogeneity was examined by considering two subtypes separately: for lepromatous leprosy and tuberculoid leprosy there are suggestions for a segregating major effect; however, Mendelian transmission could not be demonstrated in either case. Therefore, there is no evidence to suggest unique genetic determinants for leprosy subtypes.

## HANSENÍASE EXPERIMENTAL

**MISRA, N., RAMESH, V., MISRA, R.S. et al.** Clinical utility of LSR/A15 gene for Mycobacterium leprae detection in leprosy tissues using the polymerase chain reaction. Int. J. Leprosy, v.63, n.1, p.35-41, March, 1995.

Skin biopsy and slit-skin smears from 46 leprosy patients and 4 nonleprosy patients were tested for the presence of *Mycobacterium leprae* by the polymerase chain reaction (PCR) using

primers based on the sequence of the LSR/15 kD gene.The PCR was found to be specific and sensitive, with a detection level of 10 and 100 bacilli. PCR using skin biopsies gave a higher detection rate than did slit-skin smears, probably due to the higher density of bacilli in a 4-mm punch biopsy. Dot blot hybridization with radioactive probes was 10-fold more sensitive than the ethidium bromide staining. Eight patients who did not show acid-fast bacilli in tissues by the conventional methods were shown to have PCR- amplified *M. leprae* DNA. False-negative results were obtained in 3 cases even though formal evidence for tissue inhibitors was absent.

**MUKHERJEE, M., CHAKRABARTI, A., CHAKRABARTI,&N.etal.** A pathogenicity model for the agents of epizootic ulcerative syndrome (EUS) in fish. *Indian J. exp. Biol,* v.33, n.2, p.134-135, February, 1995.

Chemoautotrophic nocardioform (CAN) bacteria had been repeatedly isolated from fish with ulcerative disease syndromes (EUS) from the massive epizootics that had repeatedly occurred since 1988 in eastern India as the major or only pathogenic agent in the background of distinctive environmental and epizootic data. Since these isolates bear significant similarity to the human and rat leprosy bacilli, attempts had been made to demonstrate the pathogenicity of this fish pathogen in the «Swiss» strain of mice as a convenient model. The studies reveal that the fish CAN bacteria could produce pathogenic effects in mice similar to that of the rat leprosy bacillus.

**NAKAMURA, M.** Optimal pH for preserving the activity of *Mycobacterium leprae* during incubation of cell in a cell-free liquid medium. *Int. J. Leprosy,* v.63, n.1, p.28-34, March, 1995.

The effect of the pH of a cell-free liquid medium on the activity of *Mycobacterium leprae* during incubation of the cells was investigated. As a parameter for evaluating the activity, the amount of adenosine triphosphate (ATP) extracted from the incubated cells collected by centrifugation was measured. The results demonstrate that the activity of *M. leprae* cells was maintained at a significant level for approximately 4 weeks at 309C in 0.05 M phosphate buffer containing 10% fetal calf serum at pH 7.0 compared to cells at other pHs tested, but activity was not preserved in phosphate buffer at pH 7.0 without serum and incubated at 379C. The maintenance of the activity under these conditions was prolonged somewhat by the addition of glycerin (2%) to the medium, and was definitely inhibited by rifampicin but not by either penicillin or isoniazid. From the results reported here, it could be postulated that the optimal pH of cell-free media for the study of cultivation of *M. leprae* is 7.0.

**SANTOS-ARGUMEDO,L.,GUERRA-INFANTE, F., PASCUAL-QUESADA, F. et al.** Identification and purification of armadillo (Dasypus novemcinctus) immunoglobulins: preparation of specific antisera to evaluate the immune response in theses animals./nt. *J. Leprosy,* v.63, n.1, p.56-61, March, 1995.

In this work we describe the purification and characterization of armadillo immuno- globulins. The IgM was precipitated using low- strength ionic solution and further purified by filtration through Sephadex G-200. The IgG was obtained in pure form by precipitation of serum with ammonium sulfate and DEAE-cellulose ion exchange chromatography. The purity of these immunoglobulins was evaluated by polyacrylamide gel electrophoresis. The results showed 28-kDa light chains and 55-kDa and 70-kDa heavy chains for IgG and IgM, respectively. The rabbit antibodies against these molecules were used to prepare fluorescein (FITC) and peroxidase conjugates. The FITC conjugate was used to quantify IgM-bearing lymphocytes. An average of 17% of peripheral blood lymphocytes were sIgM + from 14 healthy animals. Additionally, in the same animals we quantified lymphocytes with the capacity to form rosettes with sheep red- blood cells; the average for this marker was 10%. Also, the production of crossreacting antibodies to BCG was evaluated in healthy and

*Mycobacterium l*eprae-inoculated animals using the peroxidase conjugates. All animals with active infection recognized BCG antigens.

## HISTÓRIA

**JOHNSTON, P.** BC's "Island of death" marked a sad chapter in Canada's medical history. Can. Med. Assoc. J., v.152, n.6, p.951-952, March, 1995.

Although the first case of leprosy in Canada was detected in 1815 in New Brunswick, the saddest chapter concerning the disease's history in Canada did not open until the late 1800s when leprosy was discovered among Chinese migrant workers on Canada's West Coast - a chapter that was not closed until 1957. Penelope Johnston relates the story of British Columbia's «Island of Death», where lepers used to be quarantined.

## IMUNOLOGIA

**ARANKALLE, V.A., CHADHA, M.S., JHA, J. et al.** Prevalence of anti-HCV antibodies in western India. *Indian J. med. res.,* v.101, p.91-93, March, 1995.

Nearly 2000 serum samples collected from different risk groups from Pune and Bombay metropolitan areas were tested for antibodies to hepatitis C virus (anti-HCV) by Recombinant Immunoblot Assay-3 (RIBA-3). Patients undergoing haemodialysis showed 24.5 per cent seropositivity whereas 5.7 and 5.3 per cent of multiply transfused patients (>2 units) and chronic liver disease patients respectively were anti-HCV positive. Leprosy patients had almost 0.7 per cent seropositivity. In other risk groups the positivity rate was nil. In normal population only one out of 830 persons had anti-HCV antibodies. It is therefore apparent that the prevalence of hepatitis C virus (HCV) in western India is not high. However, special care needs to be taken for dialysis patients. As none of the 430 pregnant women and 86 children below the age of 5 yr were anti-HCV positive, vertical mode of HCV transmission seems to be negligible.

**ARRUDA, M.S.P., FLEURY, R., BASTAZINI, I. et al.** Estudo da reação de Montenegro na hanseníase. *Med. Cut I.L.A.,* v.22, n.6, p.263-267, 1994.

Os autores investigaram o comportamento da reação de Montenegro em 54 pacientes hansenianos, 10 portadores de leishmaniose e 13 com outras moléstias. A reação foi avaliada clinicamente as 48 e 72 horas e, histologicamente, aos 28 dias. A leitura clinica revelou reações positivas em todos os grupos estudados. Contudo, somente nos pacientes com leishmaniose, a indução persistiu por 4 semanas. 0 quadro histopatológico desta manifestação não diferiu, de modo geral, do observado nas reações de Mitsuda positivos.

A nítida relação entre a reação tardia 6 leishmanina e a presença de leishmaniose recomenda seu uso entre os critérios diagnósticos para esta patologia.

Palavras chaves: Leishmaniose. Hansenfase. Reação de Montenegro.

**BALYBIN, E.S.** Immunomodulating role of endogenous thyroid hormones in mycobacteriosis. *Probt Tuberk.,* n.2, p.37- 39, 1995.

Radionuclide tracing in peripheral blood of patients with mycobacterial infections varying in activity (lepromatous lepra, n = 98; pulmonary tuberculosis, n = 51) provided information on lymphocyte proliferative response to PHA, tuberculin, sensitin from lepra mycobacteria, on thyroid hormones concentrations. Endogenic thyroid hormones are shown to have immunomodulating properties closely related to the disease activity.

**BIGI, F., ALITO, A., FISANOTTI, J.C. et al.** Characterization of *anMycobacterium bovis* secreted antigen containing PGLTS repeats. *Infect. immun.,* v.63, n.7, p.2581-2586, July, 1995.

Serum from naturally infected cattle was used to identify a novel *Mycobacterium bovis* antigen from an expression library. The first recombinant product identified was a fusion protein with lacZ (55 kDa). A clone containing the whole gene was also obtained. This clone expressed a 38-kDa protein. A rabbit serum against the recombinant antigen reacts in *M. bovis* supematants with two proteins of 36 and 34 kDa. The new protein was called P36/P34. The gene cloned has a deduced amino acid sequence with a predicted molecular mass of 28 kDa, showing a characteristic signal sequence for exportation. The protein bears partial homology to a 28-kDa protein from *M. leprae.* An interesting feature of the P36/p34 sequence is that it contains several PGLTS repeats, which are not present in the *M. leprae* protein. Antigenic determinants seem also to be conserved between the two proteins because sera from leprosy patients recognized the recombinant *M. bovis* protein. The discrepancy among the molecular mass deduced from the sequence (28 kDa), that of the recombinant protein in Escherichia coli (38 kDa), and that of the native protein in *M. bovis* (36 and 34 kDa) could be attributed to posttranslational modifications or to the high proline content that may alter the migration properties of the protein. This antigen seems to be immunodominant during bovine tuberculosis, because 8 of 9 serum specimens from diseased cattle are reactive. The homology among the *M. leprae* 28-kDa protein, the protein described in this article, and a recently describedM. *tuberculosis* protein suggests the existence of a new protein family in mycobacteria.

**CHATURVEDI, V., SINGH, N.B., SINHA, S.** Immunoreactive antigens for a candidate leprosy vaccine: *Mycobacterium ha bana. Leprosy Rev.,* v.66, n.1, p.31-38, March, 1995.

Mycobacterium habana (M. simiae serovar-1) is a candidate vaccine for mycobacterlal infections on the basis of the protection shown by this strain. We prepared 3 fractions of M. ha bana, i.e. the cell wall (CW), the cell membrane (CM) and the cytosol (CS). Protein antigens of these fractions were resolved by SDS-PAGE and subsequently probed with the sera of leprosy and tuberculosis patients and also antiBCG antibodies.

We saw 3 major protein bands at.a. 33 kD in the OW, a 38 kD in the CM and a22 kD in the cytosol (CS) after coomassie blue staining of the gels. Pool leprosy patients' serum had identified proteins of a, 26 kD in CW, a 35 anda. 18 kD in CM and a 24 kD in the CS which have not been seen by the TB patient's serum pool. Pool serum of tuberculosis patients has identified 1 protein at 10 kD in the CW and a broad band between 20 and 24 kD and 1 at a 4 kD in the CM which have not been visualized in the pool leprosy patient's serum lane. The proteins of M. habana which are recognized only by leprosy antisera or only by tuberculosis antisera could be exploited for developing diagnostic agents against these infections.

**CONVERSE, P.J., HAINES, V.L.,WONDIMU, A. et al.** Infection of SCID mice with *Mycobacterium leprae* and control with antigen-activated "immune" human peripheral blood mononuclear cells. *Infect. immun.,* v.63, n.3, p.1047-1054. March, 1995.

The SCID (severe combined immunodeficient) mouse lacks both B and T cells and tolerates injected mononuclear cells from humans, the principal hosts of Mycobacterium leprae. A SCID mouse model of leprosy could be useful to investigate potential vaccine strategies using human cells in a context in which the growth of the organism is monitored. Initial experiments determined that SCID mice are more susceptible than normal mice to infection and dissemination d M. leprae. Cells from humans, either BCG vaccinated or from countries where leprosy is endemic, were stimulate in vitro with a number of mycobacterial antigens - whole *M. leprae, M.*

*leprae* cell walls, purified protein derivative of *M, tuberculosis,* and *Mycobacterium bovis* BCG - and tested for proliferation and production of interleukin-6, tumor necrosis factor alpha, and gamma interferon. Cell walls were the most efficient and consistent in inducing all of these activities. In vitro-activated human cells retain function better after injection into SCID mice than nonactivated cells. To test the ability of cells to affect the growth of *M. leprae* in the footpads of SCID mice, cells from a known responderto mycobacterial antigens and from a nonresponder were activated by *M. leprae* cell wall antigens. The cells were harvested and coinjected with fresh *M. leprae* into the right hind footpads of SCID mice. After 3 months, there was no growth of *M. leprae* in the footpads of mice coinjected with cells from the mycobacterial antigen responder, while growth was uninhibited in mice receiving cells from the nonresponder. Future experiments will determine requirements for antigen specificity in inhibiting *M. leprae* multiplication.

**DE LA BARRERA, S., FINK, S., FINIASZ, M. et al.** Lack fo activity against *Mycobacterium leprae* 65-kDa heat shock protein (hsp) in multibacillary leprosy patients. *Clin. exp. Immunol.,* v.99, n.1, p.90-97, January, 1995.

Cytotoxic T cells play an important role in host defence mechanisms, as well as in the immunopathology of leprosy. In this study, we evaluated whether *Mycobacterium leprae* hsp18, *hsp65andMyco.tuberculosishsp71* could induce cytotoxic T cell activity against autologous macrophages pulsed with these hsp. Paucibacillary (PB) patients and normal controls generated more effector cells than multibacillary (MB) patients with all three hsp tested. There was no cross-reactivity between any of the hsp tested. *Mycobacterium leprae* hsp65 induced cytotoxic responses only in those MB patients undergoing an arythema nodosum leprosum (ENL) episode. Although hsp65 and hsp18 induced similar proliferation in MB patients, a high proportion of these patients did not generate cytotoxic effector cells in response to hsp65. Hence, those T cells reacting to hsp65 may play an important role in the control of *Myco. leprae* infection.

**DeKRUYFF, R.H., FANG, Y., WOLF, S.F. et al.** IL-12 inhibitis IL-4 synthesis in keyhole limpet hemocyanin-primed CD4+ T cells through as effect on antigen-presenting cells. *J. immunol.*, v.154, n.6, p.2578-2587, March, 1995.

Although IL-12 is known to enhance IFN-gamma synthesis in unprimed CD4+ T cells, the effect of IL-12 on IL-4 synthesis in primed CD4+ T cells, which are thought to have relatively fixed cytokine profiles, has not been clearly examined. We examined the effects of IL-12 on cytokine production by CD4+ keyhole limpet hemocyanin (KLH) - primed memory lymph node T cells and by already established KLH-specific CD4+ T cell clones. First, we found that the presence of IL-12 greatly reduced the development of IL-4 synthesis in resting but not activated memory CD4+ T cells. Although IL-12 did not inhibit th production of IL-4 in cloned Th2 effector cells, it greatly inhibited the development of IL-4 synthesis in primed CD4+ T cells taken from the lymph nodes of mice previously immunized with KLH. Secondly, we found that IL- 12 inhibited IL-4 synthesis either when directly added to cultures fo T cells or when APC were preincubated in IL-12. Inasmuch as the enhancing effect of IL-12 on IFN-gamma synthesis occurred optimally only when the T cells were cultured directly in IL-12, these studies indicate that IL-12 affects IL-4 synthesis via a mechanism that involves APC, a process that differs from that by which it affects IFN-gamma synthesis. These studies also indicate that the administration of IL- 12 would be clinically useful in treating patients, for example those with allergic disease or lepromatous leprosy, in whom memory T cells inappropriately overproduce IL-4.

**HERMANS, P.W., ABEBE, F., KUTEVI, V.I. et al.** Molecular and immunological characterization of the highly conserved antigen 84 fromMycobacterium tuberculosis and Mycobacterium leprae. Infec. immun., v.63, n.3, p.954-960, March, 1995.

Crossed immunoelectrophoresis (CIE) has been used to develop a reference system for classifying mycobacterial antigens. The subsequent use of specific antibodies allowed further determination of antigens by molecular weight. The monoclonal antibody F126-2, originally raised against a 34-kDa antigen *of Mycobacterium kansasii,* reacted with antigen 84 (Ag84) in the CIE reference system for *Mycobacterium bovis* BCG and *Mycobacterium tuberculosis.* To characterize Ag84, we screened a lambda gt11 gene library from *M. tuberculosis* with antibody F126-2 and identified the encoding gene. The corresponding *Mycobacterium leprae* Ag84 gene was subsequently selected from a cosmid library, using the M. tuberculosis gene as a probe. Both genes were expressed as 34-kDa proteins in Escherichia coli, and the recombinant proteins indeed corresponded to Ag84 in the CIE reference system. The derived amino acid sequences of the *M. tuberculosis* and *M. leprae* proteins showed 85% identity, which indicates that Ag84 constitutes a group of highly conserved mycobacterial antigens. Antibodies of almost 60% of lepromatous leprosy patients responded to Ag84, indicating that the protein is highly immunogenic following infection in multibacillary leprosy (Au).

**HOWE, R.C., WONDIMU, A., DEMISSEE, A. et al.** Functional heterogeneity among CD4+ T cell clones from blood and skin lesions of leprosy patients. Identification of T-cell clones from blood and distinct from ThO, Th1 and Th2. *Immunology,* v.84, n.4, p.585- 594, April, 1995.

In the present study we examined the functional properties of T-cell clones reactive with Mycobacterium leprae and other mycobacterial antigens. Clones isolated from the skin lesions and blood of leprosy patients across the spectrum were exclusively CD4+CD8- and expressed the alpha beta T-cell receptor. Substantial heterogeneity in the production of cytokines, in particular interleukin-4 (IL-4), was observed, although no striking correlation with clinical status was apparent. A variety of patterns of cytokine secretion distinct from those of T-helper type-1 (Th1) Th2 or ThO, as defined in murine studies, was evident. Most noteworthy was a large number of clones from skin which secreted neither IL-2 nor IL-4, but large amounts of tumour necrosis factor (TNF) and interferon-gamma (IFN-gamma). Clones isolated from the blood of leprosy patients had a more restricted cytokine secretion profile, and appeared to resemble more closely previously described patterns, including those of high level production of IL-2 and/or IL-4. Virtually all clones, from either skin or blood, produced high levels of I FN-gamma, and thus many clones were IL-4 and I FN-gamma co-producers. The pattern of cytokine production by skin-derived T-cell clones was significantly affected by the in vitro activation status of the cells. Cells enriched in activated blasts tended to produce more IL-4 than small resting cells. In addition, the production of IFN-gamma by skin T-cell clones after < or 10 weeks of culture was strikingly distinct from that of these clones after 5 months of culture. IL-4 and IFN- gamma co-producing clones shifted to a Th2-like pattern with much less IFN-gamma secretion, whereas non-IL-4-producing clones secreted much higher levels of IFN-gamma after prolonged culture, and became much more Th1-like. However, there was still no correlation between clinical status and pattern of cytokines produced. These results imply that a high fraction of T cells existis in leprosy lesions that is distinct from or that has not yet fully matured into Th1 or Th2 cells.

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**HUSSAIN, R., MENZ, B., DOCKR ELL, H.M. et al.** Recognition of *Mycobacterium leprae* recombinant 18,000 MW epitopes by IgG subclasses in leprosy. *Immunology,* v.84, n.2, p.290-297, February, 1995.

IgG subclasses are known to be differentially regulated by cytokines (elaborated by activated T cells), which act as growth factors

and immunoglobulin switch factors on B cells. In leprosy, we have previously shown that IgG subclass antibodies to a purified recombinant antigen of *Mycobacterium leprae* (18,000 MW) are restricted to I gG1 and IgG3 across the disease spectrum. The only significant difference observed was that lepromatous patients with low to undetectable T-cell responses showed a strong correlation between IgG1 and IgG3 (P <0.0001) antibodies while tuberculoid patients who showed strong T-cell responses did not show such a correlation. To examine if these differences were related to T-cell-mediated class switching in tuberculoid leprosy patients, we have studied epitope recognition by IgG1 and IgG3 using a panel of synthetic peptides spanning the 18,000 MW molecule in an enzyme-linked immunosorbent assay (ELISA). In lepromatous patients there was little similarity in peptide recognition by IgG1 and IgG3, with IgG1 recognition being restricted to a single dominant carboxy-terminal peptide while the IgG3 antibodies recognized a diverse set of peptides in the N-terminal half of the 18,000 MW molecule. In tuberculoid patients both IgG1 and IgG3 antibody showed recognition of similar peptides in the N-terminal half of the 18,000 MW molecule. Our results therefore support the hypothesis that complex mediated. Other renal lesions that have been described include amyloidosis, tubulointerstitial disease, acute renal failure, and functional defects in the absence of identifiable histologic abnormalities. In this report, a patient is described who developed the clinical syndrome of rapidly progressive glomerulonephristis. The renal biopsy showed a diffuse endocapillary proliferative process with electron-dense deposits in the glomerular subendothelial and subepithelial spaces. Organisms consistent with *Mycobacterium leprae* were identified within several of the glomeruli.

**HUSSAIN, R., KIFAVET, A., CHIANG, T.J.** Immunoglobulin G1 (IgG1) and IgG3 antibodies are markers of progressive disease in leprosy. *Infect. immun.,* v.63, n.2, p.410-415, February, 1995.

*Mycobacterium leprae*-specific and polyclonal immunoglobulin G (IgG) subclass and IgE antibodies in leprosy patients across the histopathological spectrum were determined by using a quantitative enzyme-linked immunosorbent assay. Antibody responses to *M. lepraesonicates* were detected only in IgG1, -2, and -3 subclasses. Even at 100-times-lower dilutions, very little IgG4 and IgE antibody activity against *M. leprae* was detected in any group of leprosy patients. Quantitatively, antibody responses were highest at the lepromatous pole and decreased towards the tuberculoid pole. The greatest quantitative difference in antibodies between the lepromatous and tuberculoid poles was observed with IgG1 (140-fold), this was followed by the difference with IgG3 antibodies (32-fold). Polyclonal antibodies, on the other hand, were elevated for all four IgG subclasses as well as IgE in both lepromatous and tuberculoid leprosy patients compared with healthy controls from a leprosy-endemic area. Selective elevation of *M. l*eprae-specific antibody responses in IgG1 and IgG3 subclasses, therefore, could not be attributed to selective polyclonal activation in these particular subclasses. Furthermore, polyclonal activation for IgE was observed in both lepromatous and tuberculoid leprosy patients, with higher levels in the tuberculoid group, which does not support selective TH2 activation in lepromatous leprosy patients. IgG1 and IgG3 antibodies also showed the highest Spearman rank correlation with the bacterial index in these patients (rho = 0.748 and P < 0.001 for IgG1; rho = 0.721 and P <0.001 for IgG3). Thus, disease progression in leprosy showed a significant correlation with selective increases in IgG1 and IgG3 responses.

**IUSHIN, Miu, KALIANINA, O.V.** Protective properties of *M. lufuin* experimental leprosy. *Probl. Tuberk.,* n.2, p.47-48, 1995.

A protective potential of *M. lufu* against experimental lepra was studied in mice infected with *M. leprae* according to Shepard. 5 and 9 months after the inoculation quantitation of the causative agent in the animals' paws indicated a protective action of *M. lufu* which exceeded that of BCG, M. *vaccae* and *M. leprae.* High protective

activity of *M. lufu* is due both to its antigenic composition similarity withM. *leprae* and influence on immune response regulation. It is suggested to use *M. lufu* for design of highly effective antilepra vaccine.

**JAGANNATH, C., REDDY, M.V., KAILASAM, S. et al.** Chemotherapeutic activity of clofazimine and its analogues against Mycobacterium tuberculosis. In vitro, iintracellular, and in vivo studies. Am. J. respir. crit Cre Med., v.151, n.4, p.1083- 1086, April, 1995.

Clofazimine (CFM), a riminophenazine drug, is primarily used in therapy for leprosy and *Mycobacterium avium* infections. With an objective of identifying drugs active against *Mycobacterium tuberculosis,* including those with multi-drug resistance, we investigated CFM and nine of its chemical analogues. Among these, B746 and B4101 had better activity than CFM against six drug-susceptible and nine single/multiple drug-resistantM. *tuberculosisstrains.* B746 also showed slightly better activitythan CFM against intracellular *M. tuberculosis* in J774A.1 macrophages and was comparable to CFM in its in vivo activity against experimental tuberculosis in C57BU6 mice. Interestingly, it caused less pigmentation in internal organs.

**KALEAB, B., WONDIMU, A., LIKASSA, R. eta!.** Sustained T-cell reactive to *Mycobacterium tuberculosis* specific antigens in "Split-anergic" leprosy. *Leprosy Rev.,* v.66, n.1, p.19-25, March, 1995.

Split anergy represented by delayed- type hypersensitivity skin reaction to tuberculin, but not to leprosin, is known to occur in a distinct proportion of leprosy patients. The mechanism was originally attributed to Mycobacterium lepra e- specific suppression of T cells toward common mycobacterial antigens. This study ascertained an alternative explanation, attributing the phenomenon to selective responsiveness to M. tuberculosis-specific epitopes. Indeed, the results of blood T-cell proliferative responses in 11 split- anergic patients showed normal responsiveness to the M. tuberculosis-specific 38 kDa lipoprotein and peptide 71 - 91 of the 16 kDa antigen but diminished responsiveness to 2 common mycobacterial antigens, represented by the 65 kDa heat shock protein and the fibronectinbinding Ag85 complex, as compared with leprosin reponsive patients and healtly contacts. These findings support the hypothesis that split anergy is due to selective recognition of M. tuberculosis- specific epitopes and deletion of T cells reacting to shared mycobacterial antigens.

**KANOLKAR-YOUNG, S., RAYMENT, N., BRICKELL, P.M. et al.** Tumor necrosis factor-alpha (TN F-alpha) synthesis is associated with the skin and peripheral nerve pathology of leprosy reversal reactions. *Clin. exp. Immunol.,* v.99, n.2, p.196-202, February, 1995.

Leprosy may be complicated by episodes of increased cell-mediated immunity towards *Mycobacterium leprae* (reversal reactions) which result in severe local immunopathology in skin lesions and peripheral nerves. Using in situ hybridization and MoAb techniques we have demonstrated TNF-alpha mRNA and TNF-alpha protein in macrophages infiltrating leprosy skin and peripheral nerve. Levels of TNF-alpha mRNA are significantly increased in reactional skin and nerve, particularly in borderline tuberculoid patients. TN F-alpha mRNA and TN F-alpha protein levels are higher in reactional nerves than reactional skin. In both reactional skin and nerve TNF-alpha mRNA is more abundant than TNF- alpha protein; this may reflect the rapid turnover of TN F-alpha protein in an immunologically dynamic situation, such as is seen in reversal reaction. Our findings emphasize the importance of documenting both mRNA and protein production when assessing the role of cytokines in pathology. The leprosy reversal reaction may be regarded as a useful model of tissue immunopathology in which TNF-alpha is generated as part of the host response to infection, but also produces local tissue damage.

**KAROPOULOS, C., ROWLEY, M.J., HANDLEY, C.J. et al.** Antibody reactivity to mycobacterial 65 kDa heat shock protein: relevance to autoimmunity. *J. Autoimmun.,* v.8, n.2, p.235-248, April, 1995.

Reactivity to the mycobacterial 65 kDa heat shock protein (HSP 65) has been implicated in the pathogenesis of adjuvant arthritis in the rat, and may be involved in the pathogenesis of rheumatoid arthritis or other autoimmune diseases in humans. Accordingly this study sought quantitative or qualitative differences in the antibody reactivity to HSP 65 between normal controls, patients with the multisystem autoimmune diseases, rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE) and patients with the mycobacterial infections, tuberculosis (TB) and leprosy. Levels of antibodies to recombinant HSP 65 in serum were measured by ELISA in normal subjects and in patients with RA, SLE, TB or leprosy. Antibody reactivity was examined by Western blotting using polypeptide fragments of HSP 65 derived by recombinant DNA techniques, or by digestion with trypsin or cyanogen bromide (CNBr). Reactivity to a synthetic peptide, the adjuvant arthritis T-cell epitope of HSP 65 (180- 188), was tested by ELISA. High levels of antibodies to full lenght recombinant HSP 65 from *Mycobacterium boviswere* present in all the groups tested. By Western blot analysis, most reactivity with intact HSP 65 was retained in a 32 kDa tryptic fragment, judged by sequencing and size estimations to represent amino acid residues 118-approximately 388. This sequence included a major T-cell epitope for adjuvant arthritis (180- 188), but these nine amino acids were not essential for B-cell reactivity since most sera also reacted with residues 188-540 which lack the T-cell epitope. Moreover, the 180-188 synthetic peptide was unreactive by ELISA, and did not inhibit reactivity with the intact recombinant HSP 65. In conclusion, most individuals had antibodies to mycobacterial HSP 65, presumably resulting from previous bacterial infections. The magnitude of the response was unrelated to the occurrence of systemic autoimmune disease, and the pattern of antibody reactivity with recombinant and proteolytic fragments of HSP 65 suggests that the major B-cell epitope is conformational and consists of discontinuous regions of the molecule.

**KLEIN, J.T., HORN, T.D., FORMAN, J.D. et al.** Selection of oligoclonal V beta-specific T- cell in the intradermal response to Kwein-Siltzbach reagent in individuals with sarcoidosis. *J. immunoL,* v.154, n.3, p.1450- 1460, February, 1995.

Sarcoidosis is a multiorgan granulomatous disorder of unknown etiology characterized by noncaseating granulomas in involved tissues. A positive Kwein-Siltzbach reaction is a granulomatous response to an intradermal injection of a suspension of sarcoid tissue extract in individuals with sarcoidosis. The protracted time course and granulomatous features of this reaction have a striking resem- blance to the Mitsuda reaction in tuberculoid leprosy, which suggests that the Kwein-Siltzbach reaction is a response to an unknown Ag(s). To evaluate whether this reaction is Ag-driven, an analysis of the TCR V beta repertoire in 15 Kwein- Siltzbach reaction sites was performed using a PCR technique and primers specific for 20V beta gene families. Results of this analysis demonstrated a pattern of V beta expression dominated by expression of V beta 2, V beta 3, V beta 6, or V beta 8 to levels >20% of total V beta gene expression in nine of 15 individuals. Analysis of paired biopsy and blood specimens revealed a preferential expression of specific V beta genes, such as V beta 3, V beta 5, and V beta 8, at sites of Kwein-Siltzbach reactions to levels fourto seven times that of the corresponding peripheral blood. Sequence analysis demonstrated that preferential expression of specific V beta genes at Kwein- Siltzbach reaction sites is oligoclonal. Furthermore, the dominant V beta 8 sequence present at one of the reaction sites contained a sequence motif in the variable-diversity-joining junctional region previously identified in sarcoid lung and blood T cell populations. These results suggest that the Kwein-Siltzbach reaction is characterized by a limited TCR beta-chain repertoire consistent with an Ag-driven T cell immune response (Au).

**LAUNOIS, P., N'DIAYE, M.N., CARTEL, J.L. et al.** Fibronectin-blinding antigen 85 and the 10-kilodalton GroES-related heat shock protein are the predominant TH-1 response inducers in leprosy contacts. *Infect. immun.,* v.63, n.1, p.88-93, January, 1995.

Peripheral blood mononuclear cells from 27 healthy leprosy contacts were analyzed for lymphoproliferation and TH-1 cytokine secretion (interleukin-2 and gamma interferon) in response to heat shock proteins with molecular masses of 65, 18, and 10 kDa from Mycobacterium leprae and the 30-32-kDa antigen 85 (Ag 85) from Mycobacterium bovis BCG. Cells from 18 and 19 of 19 lepromin-positive contacts proliferated of produced TH-1 cytokines in response to the M. leprae 10-kDa protein and to Ag 85, respectively. Limiting-dilution analysis for two lepromin-positive contacts indicated that about one-third of M. leprae- reactive T cells displayed specificity to the M. leprae 10-kDa protein and Ag 85. The M. leprae 65- and 18-kDa proteins were less potent TH-1 response inducers: gamma interferon and interleukin-2 could be measured in 14 and 19 lepromin-positive contacts, respectively. In contrast, very low or undetectable proliferative and cytokine responses were found for 8 lepromin- negative contacts. Our data demonstrate that the fibronectin-binding Ag 85 and the 10-kDa GroES homolog are powerful mycobacterial TH-1 response inducers inthe vast majority of lepromin- positive contacts and suggest that they might be valuable candidates for a future subunit vaccine.

**MEHRA, N.K., RAJALINGAM, R., MITRA, D.K. et al.** Variants of HLA-DR2/DR51 group haplotypes and susceptibility to tuberculoid leprosy and pulmonary tuberculosis in Asian Indian. *Mt. J. Leprosy,* v.63, n.2, p.241-248, June, 1995.

This study reports our observations on the correlation between HLA-DR2 subtypes and their DR-DQ haplotypes in patients with tuberculoid (TT) leprosy and pulmonary tuberculosis (PTB). DR B1*1501 was significantly increased in patients with PTB (90%) as compared to controls ($p < 0.05$); whereas the prevalence of DRB1*1502 was significantly increased in patients with TT leprosy ($p < 0.05$), suggesting allele-specific binding of the pathogen to form disease-causing motifs to the T-cell receptor. Among DR2-DQ haplotypes, the deviation was noted in the distribution of unique and common haplotypes in patients with TT leprosy and PTB. A significant decrease of haplotype DRB1*1501-DRB5*0101- DQa1*0102-DQB1*0502 in TT leprosy and a significant increase of DRB1*1501-DRB5*0101- DQA1*0103-DQB1*0601 in PTB patients were observed. The occurrence of specific DR2 subtypes and their haplotypes in the two disease groups suggests their involvement in disease pathogenesis.

**NAUMOV, V.Z., SAROIANTS, L.V., BALYBIN, E.S.** Effects of endogenous cortisol on the function of nonspecific T-suppressores and quantitative characteristcs of main subpopulations of circulating T-lymphocytes in leprosy. *ProbL Tuberck,* n.2, p.49-51, 1995.

Serum hydrocortisone levels, cellular immunity and their correlation were studied in 38 patients with lepromatous lepra in regression. 12 of them had exacerbation of specific polyneuritis. The latter condition is accompanied by a rise in hydrocortisone concentration. Relative number of blood CD8+ lymphocytes correlated positively with hydrocortisone content, whereas the quantity of CD4+ cells correlated negatively. In patients without neurological complications in negative correlation between blood hydrocortisone and lymphocyte glucocorticoid sensitivity there was a positive relationship between nonspecific T- suppressor activity and hydrocortisone levels. The involvement of endogenic hydrocortisone in T-suppressor activity regulation in regressive lepra can help understand the role of endocrine dysfunction and stress in pathogenesis of lepra relapses.

**PANUNTO-CASTELO, A., ROO UE-BARR EIRA, M.G.** Identification of IgM as the leprosy patients serum factor responsible for rapid sedimentation of formolized sheep erythrocytes. *Int. J. Leprosy,* v.63, n.2, p.231- 240, June, 1995.

The serum of some leprosy patients with impaired specific cellular immunity for *Mycobacterium leprae* causes rapid sedimentation of forrnolized sheep erythrocytes, a phenomenon known as the Rubino reaction. The Rubino factor was precipitated from positive sera by 5% (w/v) polyethylene glycol (PEG), bound to a concanavalin A (ConA)-Sepharose column and eluted with D-mannose, and was also eluted from a Mono Q column, pH 8.0, with 0.4 M NaCI. The Rubino factor was eluted in a volume which coincided with that of human serum IgM from a Sepharose 6 column. IgM was present in the preparation obtained by this sequence of chromatographic procedures. The correspondence of IgM with the Rubino factor was demonstrated by the following data: a) the Rubino factor was adsorbed to rabbit IgG antihuman IgM-agarose and the activity was recovered in the acid eluate of the column; b) the Rubino reaction was inhibited in the presence of rabbit antihuman IgM antibodies. This behavior was not observed when the same procedures were carried out using anti-a2-macroglobulin antibodies as a control. The rapid sedimentation of formolized sheep red cells caused by the serum of lepromatous leprosy patients was not inhibited by phenolic glycolipid- I, suggesting that the IgM responsible for the Rubino reaction is not directed to this antigen which is specific for *M. leprae.* There was no correlation between the positivity of the Rubino reaction and the increase in total serum IgM levels observed in 42% of the lepromatous patients evaluated. The demonstration that the Rubino factor is an IgM now permits the identification of the epitope recognized by it, and this may be used as a tool to understand the specific cellular immune unresponsiveness which characterizes lepromatous leprosy.

**PARKASH, 0.M., CHATURVEDI, V., GIRDHAR, K. et al.** A study on perfomance of two serological assays for diagnosis of leprosy patients. *Leprosy Rev.,* v.66, n.1, p.26-30, March, 1995.

We compared 2 serological tests for the diagnosis of leprosy to test their performances. The tests include the serum antibody competition test (SACT) for the detection of antibodies to *Mycobacterium* leprae-specific epitope on 35 kDa protein molecule, and *M. leprae* gelatin particle agglutination assay (MLPA), for the detection of antiphenolic glycolipid-1 (PGL-1) antibodies. In both the assays a higher serological positivity was seen amongst multibacillary (MB) patients than those in paucibacillary (PB) patients. Taking all leprosy patients together, the sensitivity of SACI (59.7%) was observed to be statistically comparable to that of MLPA (66.9%). However, SACT proved to be more specific (97.7%) than MLPA (75.0%). The agreement between these 2 assays was observed to be moderate.

**SAMPAIO, E.P., CANESHI, J.R., NERY, J.A. et al.** Cellular immune response to *Mycobacterium leprae* infection in human immunodeficiency virus-infected individuals. *Infect. immun.,* v.63, n.5, p.1848-1854, May, 1995.

The immune response *toMycobacterium leprae* and other mycobacterial antigens were studied in 11 leprosy patients with concurrent human immunodeficiency virus type 1 (HIV-1) infection. Three patients manifested borderline lepromatous leprosy, and eight patients had borderline tuberculoid (BT) leprosy. Despite the low CD4+ T-cell count in the peripheral blood, no histologic or phenotypic change in the cellular infiltrate in either the lepromatous or tuberculoid lesions was observed when compared with HIV- 1-negative patients. Lepromatous lesions contained heavily parasitized macrophages and few CD8+ T cells. Lesions from the patients with BT leprosy showed extensive CD4+ T-cell infiltration despite a significant reduction in CD4+ T-cell counts in the peripheral blood. No acid-fast

bacilli were detected in the tuberculoid lesions. HIV-1 infection did not alter the lack of response in lepromatous leprosy to *M. leprae* antigens either in vitro or in vivo. In contrast, the skin test response b *M. leprae* antigens as well as the in vitro lymphoproliferative responses to mycobacterial antigens that are usually seen in patients with tuberculoid leprosy were abrogated in the BT HIV- 1+ patients. However, production of gamma interferon in response to the same stimuli was preserved in most of the patients. Analysis of cytokine gene expression showed activation of additional cytokine genes in the unstimulated peripheral blood cells of patients with both leprosy and HIV-1 infections as compared with cells from patients with leprosy alone. These results suggests that granuloma formation in leprosy can be independent of the impaired CD4+ T-cell response of the HIV-1 infection. Furthermore, in HIV-1+ individuals with *M. leprae* infection, activation of cytokine genes is observed even when the circulating CD4+ T-cell count is significantly reduced.

**SHEELA, R., SHANKERNARAYAN, N.P., RAMU, G. et al.** I gG subclass antibodies to mycobacterial sonicate and recombinant antigens in leprosy. *Leprosy Rev.,* v.66, n.1, p.10-18, March, 1995.

In this study the IgG subclass antibodies to sonicated preparations of Mycobacterium leprae (leprosin A) and BCG (BCG-S) as well as to purified recombinant 65 kDa protein of M. leprae (rML65) were analysed in sera from leprosy patients endemic population. In LBI + (lepromatous bacterial index positive) patients, IgG3 was predominant in the responses to sonicated antigens of M. leprae. Following chemotherapy, IgG3 responses were reduced while IgG2 levels were increased. On the other hand, IgG response to rML65 was dominated by IgG1 in all the patient and control groups. Interestingly, the level of antileprosin A IgG antibody in erythema nodosum leprosum (ENL) was similar to that of lepromatous groups, while the level of anti-rML65 IgG antibody was significantly reduced in ENL. IgG4 antibodies to the antigens studied were only at low levels in all groups, including ENL. Significant differences were observed between HNC and HFC in the pattern of IgG subclass antibodies to sonicated antigens, even though their antigen specific IgG levels were similar. While HNC showed equivalent proportion of IgG1 and IgG2 in their responses to leprosin A and BCG-S, HFC showed a specific increase in IgG1 levels, suggesting that both groups are distinctly different. Further studies are required to elucidate the functional significance of IgG subclass pattern in pathogenesis and the mechanism of immunoregulation resulting in the high levels of IgG1 and IgG3 antibodies to M. leprae protein antigens in lepromatous leprosy.

**SIELING, P.A., SAKIMURA, L., UVEMURA, K. et al**. IL-7 in the cell-mediated immune response to a human pathogen.J. Immunol., v.154, n.6, p.2775-2783, March, 1995.

The goal of the present study was to investigate the role of IL-7 in regulating immune responses to infection. Leprosy provides a model for understanding human immune responses to infection; the disease presents as a spectrum in which the clinical manifestations correlate with the levels of cell-mediated immunity to the pathogen, Mycobacterium leprae. To determine whether IL-7 is produced at the site of infection in leprosy, we used the PCR to measure IL-7 and IL- 7R mRNA in skin lesions. IL-7 mRNA was more strongly expressed in the tuberculoid form of the disease, in which the infection il limited (mean cpm = 48 +1-8; n = 11), as compared with the progressive lepromatous form (17 +1- 2; n = 11). IL-7 mRNA, both membrane-bound and soluble forms, were also more strongly expressed in tuberculoid lesions, although these differences were not as striking as those for IL-7. The cellular source of IL-7 included Ag-stimulated monocytes and IFN-gamma-induced keratinocytes.M. lepra e-inducedPBMC responses in tuberculoid patients involved up-regulation of IL-7 and IL-7R mRNA and was IL-7 dependent. In contrast,M. leprae did not induce IL-7 mRNA in lepromatous patients, and their T cell responses were weakly augmented by a-7. These data suggest that IL-7, produced at the site of disease, contributes to the cell-

mediated immune response to human pathogens.

**ULRICH, M., RODRIGUES, V., CENTENO, M. et al.** Differing antibody IgG isotypes in the polar forms of leprosy and cutaneous leishmaniasis characterized by antigen-specific T cell energy. *Clin exp. ImmunoL,* v.100, n.1, p.54-58, April, 1995.

Leprosy and American cutaneous leishmaniasis are tropical diseases which present a spectrum of clinical and immunological manifestations. Lepromatous leprosy and diffuse cutaneous leishmaniasis are the severe, progressive polar forms of disease characterized bypersistent T cell anergy. Relative concentrations of antibodies belonging to the four IgG isotypes have been determined in these forms of disease as well as active visceral leishmaniasis, which presents transitory T cell anergy. Leishmania-specific IgG4 antibodies predominated in 19/20 sera from patients with diffuse cutaneous leishmaniasis, and IgG1 antibodies predominated in 9/10 cases of untreated visceral leishmaniasis. The predominant IgG isotype of Mycobacterium /eprae-specific antibodies in untreated lepromatous leprosy was remarkably variable (IgGl, IgG2, IgG3 and IgG4 in 8, 6, 2 and 1 sera, respectively). Differing IgG antibody isotypes have been associated with distinct CD4+ T cell helper subpopulations and theircharacteristic lymphokine profiles in several pathologies. These results suggest that T cell anergy in chronic intracellular infections may be associated with as yet undefined mechanisms which modulate reported T helper cell-lymphokine isotype relationships.

**WORLD HEALTH ORGANIZATION. STEERING COMMITTEE.** Analysis of vaccine prepared from armadillo-derived *M. leprae;* Results of an Inter-Laboratoty Study Coordinated by the World Health Organization. *Int. J. Leprosy,* v.63, n.1, p.48-55, March, 1995.

Preparations of armadillo-derived *Mycobacterium leprae* used in vaccine trials were analyzed using a combination of morphological, chemical and immunological criteria. When compared to more recent preparations, vaccine lots prepared in 1984 and 1985 were found to contain fewer intact bacilli and lower amounts of *M. leprae* antigens. These differences may be characteristic of the original preparations, or alternatively, may have arisen during prolonged storage. The early vaccine lots were those used in the recently published Venezuela trial.

## MICROBIOLOGIA

**BASAK, P., BANERJEE, P.P.** Culture of nocardioform bacilli from leprosy patients & clinical evaluation of nocardioform bacilli derived antigen. *Indian J. med. res.,* v.101, p.150-153, April, 1995.

Ab: An antigen derived from cultured nocardioform bacilli was compared with Mitsuda lepromin in intradermal skin test reactions. Nocardioform bacilli were cultured in gelatin minimal medium from the tissue fluid of 85 lepromatous patients (56 M, 29 F). Of these, 65 samples showed uncontaminated growth of the organism, which were pooled for the manufacture of the test antigen. This antigen was intradermally tested in 50 untreated leprosy patients irrespective of the type, together with Mitsuda lepromin and sterile gelatin minimal media, which served as a control. No early reaction was observed at 72 h, while the late reaction at 28 days was positive in all patients in the Tuberculoid (Ti) group with both antigens. Eighteen patients (81.8%) in the Borderline tuberculoid (BT) group reacted strongly to Mitsuda lepromin at 28 days, while 21 patients (95.5%) in this group showed a strong late reaction with the test antigen. The lepromatous (LL) group did not show any reaction with the two antigens. It is inferred that nocardioform bacilli are easy to cultivate, and that the test antigen compares well with Mitsuda lepromin (Au).

**BERMUDEZ, LE., KAPLAN, G.** Recombinant cytokines for controlling mycobacterial infections. *Trends microbiol,* v.3, n.1, p.22-27, January, 1995.

Ab: Knowing how mycobacteria exploit host cytokines to survive and which cytoklnes have important roles in host defense against mycobacteria should allow the use of these molecules in the treatment of mycobacterial infections. Both interleukin 2 and interferon gamma have been used to treat patients with leprosy, and granulocyte-macrophage colony-stimulating factor is presently being administered to AIDS patients infected with *Mycobacterium avium* (Au).

**WICHITWECHKARN, J., KARNJAN, S., SHUNTAWUTTISETTEE, S. et al.** Detection of *Mycobacterium leprae* infection by PCR. *J. clin. MicrobioL,* v.33, n.1, p.45-49, January, 1995.

Ab: PCR amplification of the 531-bp fragment of the *Mycobacterium leprae* pra gene in fresh biopsy and slit skin smear samples was evaluated for its usefulness in the detection of leprosy bacilli in patients in Thailand. In multibacillary patients, 87.1% (27 of 31) of biopsy specimens and 41.9% (13 of 31) of slit skin smear specimens were positive by PCR, whereas in paucibacillary patients, 36.4% (8 of 22) of biopsy specimens and 18.2% (4 of 22) of slit skin smear specimens yielded detectable PCR amplification. Compared with other diagnostic procedures, PCR showed a clear advantage over both microscopic examination of slit skin smears and serologic detection of anti-phenolic glycolipid 1 antibody, especially in paucibacillary patients when bacterial indexes were 0 and seropositivity was only 6.25% PCR was also evaluated for its potential to help monitor bacterial clearance in some of these patients during chemotherapeutic treatment. The PCR results on slit skin smear samples at 1, 3 and 6 months of chemotherapy showedthat the number of PCR-positive cases of both multibacillary and paucibacillary types decreased sequentially. The results of this study are encouraging. However, investigation of a larger number of clinical specimens with an improvement in PCR methods, especially on slit skin smears, needs to be done before PCR can be established as a diagnostic procedure for leprosy patients and subclinical cases or as a tool for drug assessment (Au).

## PATOLOGIA

**CREE, I.A., COGHILL, G., SUBEDI, A.M., et al.** Effects of treatment on the histopathology of leprosy. *J. clin PathoL,* v.48, n.4, p.304-307, April, 1995.

Ab: AIMS - To identify the histological changes in leprosy skin lesions over the first few weeks after the start of leprosy treatment and to examine their relationship to reversal reaction.

METHODS - Sequential skin biopsy during treatment with multiple drug therapy. In this study, a series of 28 patients was studied, from whom two or more biopsies were taken at two week intervals. Fourteen patients had paucibacillary leprosy (PBL) and 14 had multibacillary leprosy (MBL).

RESULTS - In most cases, granuloma fraction and bacterial index fell during treatment, the bacterial index being less sensitive than the granuloma fraction. Since the biopsies were fixed in buffered formalin and processed through to paraffin wax, little immunohistochemistry was feasible. However, there was strong evidence of immune activation, with increased expression of HLA-DR in the granulomas of MBL and PBL cases: the epidermis also expressed HLA-DR in several patients. Such changes may reflect gamma IFN production from granuloma lymphocytes. Patients with reversal reaction often showed HLA- DR expression on admission which decreased with corticosteroid treatment.

CONCLUSION - The results suggest that activation of cell mediated immunity in leprosy lesions occurs during treatment with multiple drug therapy and may not be restricted to those with clinical evidence of reversal reaction (Au).

**JAIN, A., MAUKHERJEE, A., CHATTOPADHYA, D. et ai.** Biometals in skin and sera of leprosy patients and their correlation to trace element contents of *M. leprae* and histological types of the diseases; A comparative study with cutaneous tuberculosisint *J. Leprosy,* v.63, n.2, p.249- 256, June, 1995.

The present study has provided information on the biometal contests of killed and dried *Mycobacterium leprae* as well as dermal granulomas induced by the invading mycobacteria in various histological types of leprosy patients. For comparison, the biometal contents of the contralateral leprosy-unaffected skin of the same patients also were measured. The study also reports changes of serum levels of the biometals in these patients which were compared with those in healthy control subjects and patients with skin tuberculosis. These data show that *M. leprae* is rich in zinc. During the course of the evolution of the disease there is gross alteration of the dynamics of the inflammatory cell population that infiltrates into leprosy granulomas, resulting in the alterations of trace element contest of the disease- affected skin lesions. Interestingly, the changes of the biometal contents in the granulomas of the patients with skin tuberculosis are similar to those in leprosy patients. It is postulated that the significant decrease of the contents of copper, zinc, iron, calcium and magnesium in the disease- affected skin in comparison to that of the contralateral healthy skin is a local effect, perhaps due to erosion or influx of biometal-deficient inflammatory cells into the affected skin with eventual loss of connective tissue of skin and mobilization of tissue-bound microelements into the vascular compartment. On the contrary, the changes in biometal levels in the sera of leprosy patients appear to be a general effect perhaps due to the release of interleukin-1, a product of inflammatory cells, causing hypercupremic, hypozincemic and hypoferremic responses in the hosts. Moreover, growth and multiplication of *M. leprae,* especially in polar lepromatous leprosy patients with a high bacillary load, demand essential biometals which may be mobilized into the bacterial bodies from the hosts. This perhaps results in the change in the homeostasis of the essential biometals in the hosts.

**JOB, C.K.** Histopathological features of relapsed leprosy. In: SYMPOSIUM ON RELAPSE IN LEPROSY, 1994. *Indian J. Leprosy,* v.67, n.1, p.69-80, January-March, 1995.

Multidrug therapy has ushered in a new era of hope, achievement and joy in the lives of both leprosy patients and of those engaged in leprosy work. Enslavement to a life time of antileprosy therapy is a thing of the past. Complete cure of leprosy after a short period of treatment has become an established reality.

**OKANO, Y.** Ocular histopathological studies in leprosy in the silent stage-II. Immunohistochemical studies. *Nippon GankaGakkailasshi,* v.99, n.3, p.342-348, March, 1995.

Ah: The distribution of leprosy antigen in 21 eyes from 12 autopsy cases of lepromatous leprosy patients (5 eyes from 3 cases in the silent stage, 16 cases from 9 cases in the active stage) were examined with acid-fast staining and immunohistochemistry. Anti-BCG antibody, anti-phenolic glycolipid-I (PGL-I0 antibody, and anti-lipoarabinomannan-B (LAM-B) antibodywere used as primary antigens. In the active stage, anti-BCG antibody and anti-LAM-B antibody showed almost the same staining pattern. Some cases, which showed negative reaction to acid-fast staining, occasionally showed positive staining pattern with anti-BCG antibody and anti-LAM-B antibody, which had high sensitivity and the advantage of detection of leprosy antigen. Some anti-PGL-I antibody showed a different staining pattern from acid-fast staining, anti-BCG antibody and anti-LAM-B antibody. These findings seemed to be caused by the difference in structure of the epitope. In the silent stage, clinically nonpigmented epithelium of 6 cases from 4 eyes showed positive staining pattern with anti-PGL-I antibody. These findings suggested that leprosy antigen still remained in this stage (Au).

**TRINDADE, M.A.B., FLEURY, R.N.** Reação de Mitsuda em contatos (consanguíneos ou não) de doentes de hansenfase multibacilar - análise histológica. *Med. Cut. I.L.A.,* v.23, n.1, p.22-24, 1995.

A reação de Mitsuda foi realizada em 23 contatos não consanguíneos e 17 consanguíneos de doentes de hansenfase multibacilar. As respostas histológicas negativas foram significativamente mais freqüentes entre consanguíneos (15%) do que entre não consanguíneos (5%). Reações com alguma induragdo clínica sem concordância histológica ocorreram entre os consanguíneos. A baciloscopia foi positiva em 1 não consanguíneo e 5 consanguíneos. Os resultados foram comparados com os de contatos ou não e com os de doentes, sugerindo-se que a reação histológica dos não consanguíneos se assemelharia à dos não contatos, enquanto a reação dos consanguíneos se assemelharia à dos doentes de hansenfase multibacilar. Palavras Chaves: Reação de Mitsuda. Histologia. Contatos.

## REABILITAÇÃO

**ANANDARAJ, H.** Measurement of dehabilitation in patients of leprosy - a scale. *Indian. J. Leprosy,* v.67, n.2, p.153-160, Apr-Jun, 1995.

Leprosy interferes with the psychological and social life of the patients leading to their "dehabilitation". Therefore, it is necessaryto assess the extent and direction of dehabilitation in order to make the treatment plan comprehensive and effective. The objective of this work was to: (a) construct a scale for measuring dehabilitation and, (b) to standardize it. The methodology included preparation of 52 statements (in English) spread over four subareas of life, namely family relations, vocational condition, social interaction and self-esteem. It was administered to 122 randomly selected respondents. Scores were awarded by summing up the weights of each statement, a high score indicating low dehabilitation. Statistical tests were applied for standardizing the scale. To establish reliability, split-half reliability test and item discriminant analysis were used. Factor analysis was used to test the validity. The results show, that the split- half reliability coefficient ranged high (from 0.64 to 0.83) in all four subareas. The item discriminant analysis had a level of significance of 0.001 for 42 statements while the factor analysis explained variance covered over 70 percent. Hence the scale can be an useful intervention strategy for counselling, case work or rehabilitation.

## TERAPÊUTICA

**ARBISER, J.L., MOSCHELLA, S.L.** Clofazimine: a review of its medical uses and mechanisms of action. *J. Amer. Acad. Dermatol.,* v.32, n.2, part 2, p.241-247, 1995.

Ab: Clofazimine has been in clinical use for almost 40 years, but little is known of its mechanism of action. The primary indication for clofazimine is multibacillary leprosy, but it is useful in several infectious and noninfectious diseases, such as typical mycobacterial infections, rhinoscleroma, pyoderma gangrenosum, necrobiosis lipoidica, severe acne, pustular psoriasis, and discoid lupus erythematosus. Postulated mechanisms of action include intercalation of clofazimine with bacterial DNA and increasing levels of cellular phospholipase A2. Clinical experience, possible mechanisms of action, and side effects of clofazimine are summarized (Au).

**CHOUDHRI, S.H., HARRIS, L, BUTANY, J.W. et al.** Clofazimine induced cardiotoxicity - a case report. *Leprosy Rev.,* v.66, n.1, p.63- 68, March, 1995.

A 66-year-old Indian male who had been treated for recurrent erythema nodosum leprosum with 300 mg of clofazimine per day for 11 months presented to hospital with a 4 week history of severe gastrointestinal upset. Soon after admission he developed several short runs of

ventricular tachycardia with a morphology suggestive of torsade de pointe. The patient had a slightly low magnesium level which was corrected within 2 days; however, his rhythm disturbance persisted for 5 days despite management with intravenous lidocaine. His gastrointestinal symptoms abated 2 weeks after clofazimine was discontinued.

Subsequent investigations showed that the patient had a keratopathy and myelin-type figures in his polymorphonuclearwhite cells similar to that seen with the cardiotoxic drugs chloroquine and amiodarone. It is postulated that clofazimine alone or in conjuction with electrolyte disturbance was responsible forthe patient's cardiac arrythmia.

**FAJARDO, T.T., VILLAHERMOSA Jr., L.G., DELLA CRUZ, E.C.** et **al.** Minocycline in lepromatous leprosy. *Int. J. Leprosy,* v.63, n.1, p.8-17, March, 1995.

Twelve patients were treated with three dose levels of minocycline for 30 days, primarily to detect the dose-related effects on *Mycobacterium leprae* viability, followed by another 5 months of daily minocycline for overall efficacy and persistence of clinical and antibacterial effects. Subsequently, the patients were given standard WHO/MDT chemotherapy for multibacillary leprosy.

Clinical improvement was recognizable during the first month, occurring much earlier among those on minocycline 200 mg daily than those who received minocycline 100 mg daily. A similar change also was observed in one patient 11 days after three daily doses of 100 mg of minocycline. At the end of 6 months, all patients were clinically improved with a slight reduction in the average bacterial index (BI) and logarithmic index of bacilli in biopsy (LIB).

The effects of minocycline on viability by mouse foot pad inoculation and palmitic acid oxidation assays were noted beginning at 10 to 14 days of daily dosing and becoming more definite after 30 days of treatment. Both tests correalted fairly well. Doses of 200 mg daily did not appear to be more effecient than minocycline 100 daily. Phenolic glycolipid-I (PGL-I) antigen

determinations done on some patients during the first month remained positive and did not correalte with changes in viability results.

At the end of 6 months, after 5 months of 100 mg of minocycline montherapy, no viable organisms could be demonstrated by mouse foot pad inoculation and palmitic acid oxidation assays; assays for PGL-I antigen were all negative.

No lepra reactions were observed during the 6 months of the therapy. Tolerable side effects, dizziness and abdominal discomfort were noted only during the first week of treatment in 2 of 12 patients. A generalized light-brown pigmentation was observed, which was more intense and blue- gray over the sites of subsided localized lesions.

The results of this study further confirm the early effects of minocycline on clinical lesions and the viability of *M. leprae* with antibacterial and clinical effects becoming definitely more demonstrable after 6 months of treatment. Thus, minocycline is a valuable drug in the treatment of leprosy, and studies to determine its efficacy in combination with other antileprosy drugs, dosage levels and pulsed dosaging, as well as the effects of lepra reaction, should be pursed.

**GELBER, R.H., SW, P., TSANG, M. et al.** Activity of combinations of dapsone, rifampin, minocycline, clarithromycin, and sparfloxacin against *M.* /eprae-infected mice. *Int. J. Leprosy,* v.63, n.2, p.259-264, June, 1995.

In these studies we evaluated the activity of low levels of five antimicrobials against Mycobacterium /eprae-infected mice when administered singly and in all possible two and three-drug combinations. Antibiotics studied were: dapsone (D) 0.0001% in the diet, rifampin (R) 20 mg/kg by gavage once monthly, minocycline (M) 0.004% in the diet, clarithromycin (C) 0.001% in the diet, and sparfloxacin (S) 5 mg/kg by gavage five times weekly. Singly each agent was found bacteriostatic (D + R) or partially bactericidal (M,C and S) but not fully bactericidal. All 10 two-drug regimens were found at least bacteriostatic, 2 being "partially bactericidal" and 4 being "fully bactericidal". Of the 10 three-drug regimens, 9 were found 'fully bactericidal" and the other

"partially bactericidal". We conclude that combinations of antibiotics active againstM. *leprae* are generally additive in combination.

**GIDOH, M., MATSUKI, G., TSUTSUMI, S. et al.** Inhibition of the multiplication of *Mycobacterium leprae* in nude mice by intermitent administration of a new rifamycin derivative, 3'-hydroxy-5'-(4-isoluty1-1-piperazinyl benzoxazinorifampicin (KRM- 1648) combined with sparfloxacin. *Leprosy Rev.,* v.66, n.1, p.39-47, March, 1995.

Inhibition of the multiplication of *Mycobacterium leprae* in the footpads of nude mice by the oral administration of sparfloxacin, a new quinolone, and 3'-hydroxy-5'-(4-isobuty1-1- piperazinyl) benzoxazinorifamycin (KRM-1648), selected from a series of newly synthesized benzoxazinorifamycins, was studied. When the 2 drugs were administered alternately at intervals of 3 or 4 days, (i.e. each drug was administered once weekly), or simultaneously once weekly, between 3 and 5 months after inoculation of nude mice with M. *leprae,* 10 mg sparfloxacin and 0.6 mg KRM- 1648 per kg bodyweight were sufficient to prevent multiplication of the organisms. Only partial inhibition of multiplication was achieved by alternate administration of 5 mg sparfloxacin and 0.3 mg KRM-1648 per kg, as was the case for 20 mg sparfloxacin per kg or 1 mg KRM-1648, each drug administered alone once weekly. The addition to these 2 drugs of dapsone, administered in the diet in a concentration of 0.001 g per 100 g, enhanced their effect.

The potential usefulness of multidrug regimens including these compounds is considered.

**JACOBSON, P.R.** Treatment of relapse leprosy. In: SYMPOSIUM ON RELAPSE IN LEPROSY, 1994. *Indian J. Leprosy,* v.67, n.1, p.99-107, January-March, 1995.

Relapses in leprosy have perhaps become a somewhat less common problem with the widespread use of WHO-MDT, and their treatment is discussed in various sections of the newest WHO Chemotherapy of Leprosy Guidelines (WHO 1994). Basically, to prevent further disability and/ortransmission of the infection such cases should be detected and placed back on chemotherapy as quickly as possible. Several factors need to be considered in choosing a regimen for treatment of such patients.

**JAMET, P., BAOHONG, J.** Relapse after long- term follow up of multibacallary patients treated by WHO multidrug regimen. *Mt. J. Leprosy,* v.63, n.2, p.195-201, June, 1995.

Thirty-five multibacillary (MB) leprosy patients were treated with 2 years of multidrug therapy (MDT) and followed up regularly for relapse. Relapse was defined as: a) an increase of the bacterial index (BI) by 2+ over the previous value from any single site of old lesions and b) the occurrence of definite new skin lesion(s) which demonstrated a higher BI than any pre-existing lesion. After a mean duration of 72.7 17.3 months of follow up per patient, seven relapses were diagnosed; the mean incubation period of relapse was 62.7 ± 18.7 months. The overall relapse rate was 20.0% (or 3.3 per 100 patient- years), very significantly higher than the figures obtained from the same group of patients analyzed 21/2 years earlier, indicating that relapses occurred late (at least 5 ±- 2 years) after stopping MDT. Further analysis indicated that the relapse rate was closely correlated with the bacterial load of the patient, occurring far more frequently among patients with a BI of >= 4.0 before MDT or with a BI of >. 3.0 at the end of MDT. To avoid the alarmingly high relapse rate, it is proposed that the duration of MDT be doubled to 4 years in patients with an average BI of >7:- 4.0 before MDT.

**KATOCH, K., KATOCH, V.M., NATRAJAN, M. et al.** Treatment of bacilliferous BULL cases with combined chemotherapy and immunotherapy. *Int. J. Leprosy*, v.63, n.2, p.202-212, June, 1995.

Thirty-six, untreated borderline lepromatous/lepromatous (BULL) leprosy patients with an initial bacterial index (BI) of 4+ to 6+ were serially allocated to three treatment groups. Group I patients received a slightly modified WHO regimen (rifampin once a month, clofazimine and dapsone daily) and BCG intradermally (i.d.) (0.1 mg/per dose). Group II patients were administered the same MDT and Mycobacterium w (2 x 108) killed bacilli/dose i.d., and Group III received the same MDT with 0.1 ml of distilled water i.d. Vaccination was repeated every 6 months. Biopsies were taken from the local site of vaccination and from a distant site, i.e., the back. The progress was monitored periodically by clinical, histopathological and bacterial (BI, mouse foot pad, ATP) parameters. Twenty-five patients and completed a follow up of more than 2 years. These included: 7 in Group I, 10 in Group II, and 8 in Group Ill. One patient of the MDT + BCG group who was progressing well dropped out after 28 months. In cases on combined chemotherapy and immunotherapy, no viable bacilli were demonstrable by mouse foot pad and ATP measurement after 6 months (at 12 months or afterward). However, in come of the control cases on MDT alone, viable bacilli could be detected even up to 18 months (by mouse foot pad) and 2 years (by ATP estimation). With 36 months of treatment, the mean BI decreased from 4.64+ to 1.66+ in the group on MDT alone (controls), 4.9+ to 0.08+ in the MDT + BCG group, and 4.75+ to 0 in the MDT + *Mycobacterium wgroup.* Compared with the MDT and MDT + BCG groups, the fall in the BI was significantly more in the MDT + *Mycobacterium* wgroup at 12, 18, and 24 months. While all of the cases in the *Mycobacterium* w groups became smear negative by 36 months, it took 42 months for all of the BCG group to achieve negativity. Immunotherapy appears to have a significant effect on the killing and clearance of bacilli and should be considered as an adjunct to chemotherapy, especially in bacilliferous lepromatous cases.

**LAU, G.** A fatal case od drug-induced multi-organ damage in a patient with Hansen's disease: dapsone syndrome or rifampicin toxicity? *Forensic. sci. Int.,* v.73, n.2, p.109-115, May, 1995.

Ab: An elderly patient with borderline tuberculoid Hansen's disease (leprosy) developed the diaminodiphenylsulphone syndrome after approximately 8 weeks of multi-drug therapy comprising dapsone and rifampicin. Postmortem histological examination, following autopsy, demonstrated features consistent with drug-induced hepatitis, tubulo-interstitial nephritis and myocarditis. Although these could have been engendered by dapsone toxicity, it was thought that a concommitant adverse reaction to rifampicin, which is known to be hepatotoxic, nephrotoxic and possibly capable of predisposing to the dapsone syndrome, could not be excluded (Au).

**PINNIGHAUS, J.M., BOERRIGTER, G.** Are 18 doses of WHO/MDT sufficient for multibacillary leprosy; Results of a trial in Malawi. *Int. J. Leprosy,* v.63, n.1, p.1-7, March, 1995.

A trial comparing 18 monthly and 30 monthly doses of the World Health Organization-recommended multidrug therapy (WHO/MOT) in 305 multibacillary leprosy patients in Malawi is described. Patients were randomly allocated to one of the two regimens at the time of taking the 18th supervised dose of WHO/MDT. The mean follow-up period was 3 years (maximum 6 years). No relapse was observed in either group. The cumulative probabilities of remaining slit-skin smear positive were significantly higher among patients receiving only the 18 monthly doses of WHO/MDT, but reached zero at month 60 of follow up. The percentage of patients who developed new disabilities during the trial period was similar in both groups. However, the overall percentage of patients who developed new disabilities (50/ 305, 16.4%) remains disturbingly high. On the

whole, the results of the trial argue in favor of 18 monthly doses of WHO/MDT taken within 24 months as being sufficient for the treatment of multibacillary leprosy.