

# LITERATURA CORRENTE

## CURRENT LITERATURE

### ASPECTOS PSICOSOCIAIS

Van BRAKEL, W.H. Measuring leprosy stigma—a preliminary review of the leprosy literature. *Int J Lepr.*, v.71, n.3, p.190-7, Sep. 2003. Comment In: *Int J Lepr.*, v.71, n.3, p.246-7 Sep. 2003.

A literature review was conducted to review work done to date on measuring stigma related to leprosy. References were obtained through a PubMed (Medline) search and through examining relevant bibliographies. Twelve papers were selected that addressed the issue of measurement of stigma and that contained a sample of the instrument used. Three unpublished studies were also included in the review. Studies that attempt to measure stigma can be broadly categorized in two groups, a) studies that assess the effects of stigma on the person affected, and b) surveys that assess community attitudes and/or practices. The study and questionnaire characteristics of the studies in both categories are described and compared. The studies reviewed indicate that leprosy stigma is still a global phenomenon, occurring in both endemic and non-endemic countries. The consequences of stigma affect individuals as well as the effectiveness of leprosy control activities. Despite enormous cultural diversity, the areas of life affected are remarkably similar. They included mobility, interpersonal relationships, marriage, employment, leisure activities, and attendance at social and religious functions. This suggests that development of a standard stigma scale for leprosy may be possible. Data obtained with such an instrument would be useful in situational analysis, advocacy work, monitoring and evaluation of interventions against stigma, and research to better understand stigma and its determinants.

BRIDEN, A.; MAGUIRE, E. An assessment of knowledge and attitudes towards amongst leprosy/Hansen's disease workers in Guyana. *Lepr Rev.*, v.74, n.2, p.154-62, Jun. 2003.

Background leprosy is still prevalent in certain parts of the world, particularly India and South America. In order to reduce the associated stigma, it was renamed Hansen's disease, although the associated prejudice and social stigma are thought to remain obstacles to its eradication. This study, set in Guyana, aims to assess attitudes, ideas and knowledge of the disease amongst healthcare workers. A self-completing questionnaire was designed and distributed amongst healthcare workers in both Georgetown Central Hospital and Suddi Hospital over a 4-

week period in September 2000. The information was then collated and analysed using STATA 6.0. A total of 185 questionnaires were completed and returned. They showed that knowledge of the disease was relatively good, but that certain facts were not widely known. For example, half the respondents did not know that leprosy is now curable, many thought it could be transmitted through touch. Although most respondents did not display prejudice in their own responses, many implied that prejudice was still present in the wider community. A significant minority believed that patients should be kept apart from other people. It is evident from the study that some prejudices and misconceptions still exist. In order to reduce this, an emphasis needs to be placed on education regarding transmission and the low rate of infectivity of leprosy; that it is not spread by touch and is now curable, also that, if treated in the early stages, it has a very good prognosis. It is these areas which health education should focus upon.

NICHOLLS, P.G.; WIENS, C.; SMITH, W.C. Delay in presentation in the context of local knowledge and attitude towards leprosy—the results of qualitative fieldwork in Paraguay. *Int J Lepr.*, v. 71, n.3, p.198-209, Sep. 2003. Comment In: *Int. J. Lepr.*, v.71, n.3, p.246-7 Sep. 2003.

**OBJECTIVE:** The primary objective of our research was to explore help-seeking behavior in the context of knowledge, attitude, and practice as factors contributing to delay in presentation in leprosy. The secondary objective was to demonstrate the value of basic qualitative research methods in this context. **METHODOLOGY:** Fieldwork was based at the Hospital Mennonita Km 81, the referral center for leprosy services in Paraguay. We adopted exclusively qualitative methods for fieldwork, effectively carrying out a rapid assessment of factors contributing to delay. We relied on multiple sources of information and the use of multiple methods to ensure the validity of our findings. **RESULTS:** Our findings linked delay in presentation to traditional beliefs, lack of awareness of the early symptoms of leprosy, stigma, seeking help from natural healers, and to interactions with the health services. Traditional beliefs diminish the importance of the early symptoms of leprosy. Stigma has an impact on decisions to seek help. Natural healers have maintained their traditional status in society; their preferred treatments for leprosy are ineffective. Only rarely do natural healers refer to the health services. Once presented to the health services, some individuals affected by leprosy experienced lengthy delays in diagnosis and start of

treatment. DISCUSSION: To address the traditional values of a society and provide effective public health initiatives is a clearly a major challenge for program organizers and for health education. Increased awareness of leprosy and sensitivity to its social consequences among health service practitioners is a further priority.

SATO, H.; NARITA, M. Politics of leprosy segregation in Japan: the emergence, transformation and abolition of the patient segregation policy. *Soc Sci Med.*, v.56, n.12, p.2529-39, Jun. 2003.

The segregation of leprosy patients, a practice introduced early in the 20th century, was maintained in Japan after World War II. It locked in the viability of subsequent policy choices, and patients' isolation was sustained long after it was proven to be scientifically unnecessary. For leprologists and leprosarium directors, there was little opportunity to conceptualize and test the epidemiological validity and effectiveness of outpatient services as alternatives to the existing policy, since most of the patients were already hospitalized. Since leprosy was no longer a threat to the general public, bureaucratic officials, as well as legislators, lacked strong incentives to reformulate the overall policy. Within the Ministry of Health and Welfare, daily tasks were largely transferred to the section for leprosarium management, and the search for other options lost importance. For patients, long institutionalization elevated their dependency on life in leprosaria. These conditions must be emphasized as policy legacies, the results of past policies, since they posed obstacles to effective policy innovation in accordance with changing scientific knowledge. To make policies reflective of scientific knowledge, it is essential to understand and foresee the effect of policy legacy, when introducing and appraising public health policies.

WITHINGTON, S.G.; JOHA, S.; BAIRD, D.; BRINK, M.; BRINK, J. Assessing socio-economic factors in relation to stigmatization, impairment status, and selection for socio-economic rehabilitation: a 1-year cohort of new leprosy cases in north Bangladesh. *Lepr Rev.*, v.74, n.2, p.120-32, Jun. 2003.

The current leprosy elimination strategy focuses almost exclusively on delivery of leprosy diagnostic services and multi-drug treatment (MDT). However, the specific problems of people newly diagnosed with leprosy or cured with MDT primarily relate to impairment of nerve function and social and economic consequences of the diagnosis of leprosy. This study was carried out to investigate the relation between socio-economic factors and the development of nerve impairments and stigma. In addition the relation between socio-economic factors and selection for socio-economic assistance was studied. The study population was a cohort of 2364 newly diagnosed people with leprosy in rural Bangladesh in 1996, including

42.5% women, with an overall mean age of 31.4 years. Three hundred and sixty people (15.2%) had WHO grade 1 or 2 disability identified at diagnosis, and 50 (2.1%) had stigma identified on interview at home visit conducted within one month of diagnosis. One hundred and eighty-eight people (8%) were selected for specific assistance for rehabilitation, primarily interest-free loans for income generating activities or vocational training. Factors independently associated with WHO grade 1 or 2 disability at diagnosis were multibacillary (MB) classification, adult status, and manual occupations. Smear positivity, female sex, and the presence of dependents were associated with an increase in the experience of stigma. The presence of nerve impairments and stigma, as well as several indices of poverty were clearly associated with selection for inclusion in an integrated program for socio-economic assistance. An increased focus by leprosy services on the socio-economic factors associated with poorer physical and social outcomes is recommended. Where adequate finances and trained staff are available, efforts could be made to identify those at higher risk of poor outcomes, and to provide or to mobilize appropriately targeted socio-economic interventions.

## BIOLOGIA MOLECULAR

BEYENE, D.; ASEFFA, A.; HARBOE, M.; KIDANE, D.; MACDONALD, M.; KLATSER, P.R.; BJUNE, G.A.; SMITH, W.C. Nasal carriage of *Mycobacterium leprae* DNA in healthy individuals in Lega Robi village, Ethiopia. *Epidemiol Infect.*, v.131, n.2, p.841-8, Oct., 2003.

The number of registered leprosy patients world-wide has decreased dramatically after extensive application of WHO recommended Multiple Drug Therapy (MDT). The annual number of new cases has, however, been almost unchanged in several populations, indicating that the infection is still present at community level. Nasal carriage of *Mycobacterium leprae* DNA was studied in Lega Robi village in Ethiopia. MDT had been applied for more than ten years, and 718 residents over 5 years old were eligible for the study. During the first survey nasal swab samples were collected from 664 (92.5%) individuals. The results of a Peptide Nucleic Acid-ELISA test for *M. leprae* DNA interpreted by stringent statistical criteria were available for 589 (88.7%) subjects. Thirty-five (5.9%) individuals without clinical signs of leprosy were positive for *M. leprae* DNA. Seven PCR positive individuals lived in a household where one or two other members were also positive for *M. leprae* DNA. During a second survey 8 (46%) of 175 interpretable PNA-ELISA tests were positive. Of 137 individuals tested twice, only two were positive on both occasions whereas 10 were PCR positive only once. The study confirms the widespread distribution of *M. leprae* DNA in healthy individuals. The feasibility of curbing possible transmission of subclinical infection needs further consideration.

GASPAR, P.K. Neuropeptídeos na pele / Neuropeptides in the skin. *An. bras. dermatol*; v.78, n.4, p.1483-498, jul.-ago.2003.

Há evidências crescentes de que a inervação cutânea é capaz de modular uma variedade de fenômenos cutâneos agudos e crônicos, interagindo com as células da pele e seus componentes imunes. Essa forma de sinalização local entre tecido nervoso e tecido cutâneo ocorre especialmente por meio dos neuropeptídeos, uma numerosa família de neurotransmissores de natureza química comum e nomenclatura heterogênea presentes em todo o sistema nervoso e secretados pelas fibras nervosas cutâneas. São alvo desta revisão os neuropeptídeos substância P (SP), o peptídeo relacionado ao gene da calcitonina (CGRP), o peptídeo vasoativo intestinal (VIP), o peptídeo ativador da adenilato-ciclase pituitária (PACAP), o neuropeptídeo Y (NPY) e a somatostatina (SOM). Serão discutidas suas ações sobre as células da pele e sistema imune, bem como estudos recentes que sugerem a participação dos neuropeptídeos nas respostas inflamatórias cutâneas, nas reações de hipersensibilidade e em dermatoses humanas, notadamente na psoríase, dermatite atópica, hanseníase e alopecia.

KANG, T.J.; KIM, S.K.; LEE, S.B.; CHAE, G.T.; KIM, J.P. Comparison of two different PCR amplification products (the 18-kDa protein gene vs. RLEP repetitive sequence) in the diagnosis of *Mycobacterium leprae*. *Clin Exp Dermatol.*, v.28, n.4, p.420-4, Jul. 2003.

To determine the best molecular method for diagnosing leprosy, two sets of *Mycobacterium leprae*-specific primers were compared. Fresh biopsies and slit skin smear samples were obtained from 67 leprosy patients and examined by touchdown (TD) PCR using primers amplifying either a 129-bp fragment of the RLEP repetitive sequence or a 360-bp fragment of the 18-kDa protein gene of *M. leprae*. Seventeen of 30 (56.7%) biopsy specimens and four of 37 (10.8%) slit skin smear specimens were positive using the primer for the 18-kDa protein gene, whereas 24 of 30 (80%) biopsy and 27 of 37 (73%) slit skin smear samples showed detectable PCR products in the RLEP repetitive sequence. Twenty-one of 31 cases (67.7%) with a bacterial index of zero were PCR positive for the primer RLEP repetitive sequence. These results demonstrate that detection of *M. leprae* using PCR with primers to a RLEP sequence is more sensitive and specific than PCR with the 18-kDa protein gene primers and also slit smears with acid fast staining. PCR of RLEP repetitive sequences is therefore a useful means of detecting *M. leprae* DNA even when it is present at very low levels.

RAJESH, M.; SULOCHANA, K.N.; SUNDARAM, A.L.; KRISHNAKUMAR, S.; BISWAS, J.; RAMAKRISHNAN, S. Presence of a 88 kDa Eales protein in uveitis, tuberculosis, leprosy and rheumatoid arthritis. *Med Sci Monit*; v.9, n.2, p.95-9, Feb. 2003

BACKGROUND: Eales disease (ED) is an idiopathic retinal vasculitis affecting young adult males. We have earlier reported the identification, purification and partial characterization of a novel 88 kDa protein found in the serum of patients with ED. The aim of the present study was to look for the 88 kDa protein in serum samples obtained from cases of retinal vasculitis mimicking ED and in other systemic inflammatory diseases. MATERIAL/METHODS: Serum samples from healthy volunteers and from patients with ED, uveitis, parsplanitis ocular sarcoidosis, toxoplasmosis, leprosy, diabetic retinopathy, viral hepatitis, and rheumatoid arthritis were analyzed for the presence of the 88 kDa protein by polyacrylamide gel electrophoresis (PAGE). The immunological identity of the 88 kDa protein found in ED and in other diseases was investigated by Western blot. Immunohistochemistry was performed on epiretinal membranes (ERM) obtained from ED patients to localize the 88 kDa protein. RESULTS: 88 kDa protein were detected in serum samples obtained from patients with posterior uveitis, tuberculosis, leprosy and rheumatoid arthritis. The 88 kDa protein found in serum from patients with ED is immunologically identical to that found in other systemic inflammatory conditions. 88 kDa protein was localized in inflammatory cells and in nonvascular endothelium in ERMs obtained from patients with ED. CONCLUSIONS: We have identified a novel acute phase reactant, which is elaborated in ocular and systemic inflammatory conditions other than Eales disease. Further work is necessary to decipher the precise role of the 88 kDa protein in the pathophysiology of these inflammatory diseases.

TORRES, P.; CAMARENA, J.J.; GOMEZ, J.R.; NOGUEIRA, J.M.; GIMENO, V.; NAVARRO, J.C.; OLMOS, A. Comparison of PCR mediated amplification of DNA and the classical methods for detection of *Mycobacterium leprae* in different types of clinical samples in leprosy patients and contacts. *Lepr Rev*; v.74, n.1, p.18-30, Mar. 2003.

Traditional staining and microscopic examination techniques for the detection of *Mycobacterium leprae*, DNA amplification by polymerase chain reaction (PCR) of a 531-bp fragment of the *M. leprae* specific gene encoding the 36-kDa antigen, and serodiagnosis with *M. leprae* specific antigens (PGL-1 and D-BSA) were compared on different clinical specimens (serum samples, slit-skin smears, biopsies and swabs) from 60 leprosy patients attending the Sanatorium of Fontilles. Patients were divided into groups; (i) 20 multibacillary patients (MB) with positive bacteriological index (BI) by conventional methods and on WHO multidrug therapy (MDT); (ii) 30 MB patients with negative BI and completed minimum 2 years treatment MDT; (iii) 10 paucibacillary (PB) patients who had completed 6 months MDT at least 8 years ago. Control groups included four non-leprosy patients for PCR methods and 40 health control patients and 10 tuberculosis patients for serological methods.

In the multibacillary BI positive group, there was a good correlation between all methods. All tests were negative in the paucibacillary group, although only a few patients were tested and all had been treated many years ago. One must be cautious concerning the diagnostic potential of these techniques in this type of leprosy. We also studied different combinations of leprosy diagnosis methods to determine the potential risk in a leprosy contact individuals group. The prevalence of antibodies to *M. leprae* antigens in serum was measured, together with the presence of *M. leprae* DNA in the nose and lepromin status in a group of 43 contacts of leprosy patients (12 household and 31 occupational) to evaluate the maintenance of infection reservoirs and transmission of the disease. Only two individuals were found to form a potential high risk group.

VIDAL PESSOLANI, M.C.; MARQUES, M.A.; REDDY, V.M.; LOCHT, C.; MENOZZI, F.D. Systemic dissemination in tuberculosis and leprosy: do mycobacterial adhesins play a role? *Microbes Infect.*, v.5, n.7, p.677-84, Jun. 2003.

More than one century after the discovery of their etiological agents, tuberculosis and leprosy remain as major health threats for humans, and the molecular mechanisms that lead to the development of both diseases are poorly understood. The elucidation of these mechanisms, and especially those allowing for the mycobacteria to systemically disseminate, should facilitate the development of new prophylactic and/or therapeutic strategies. This review is focused on the routes that *Mycobacterium tuberculosis* and *Mycobacterium leprae* may use to disseminate within the human body, and the potential roles played by recently characterized adhesins in this process.

## BIOLOGIA MOLECULAR E IMUNOLOGIA

HATTA, M. Epidemiology of leprosy. Molecular, biological, and immunological approach. *Adv Exp Med Biol*; v.531, p.269-78, 2003.

Leprosy is an infectious disease for which humans are considered the only source of infection. The major hindrance in leprosy control and thus in reaching the elimination goal is that numerous leprosy cases remain undetected for a long time. Many of these patients are a continuous source of infection and, hence perpetuate transmission. The goal of the World Health Organization (WHO) is to eliminate leprosy as a public problem by the year 2000; that is, to reach as a global prevalence of <1 per 10,000 people. The epidemiological data generated routinely by health services are greatly influenced by their policies and activities. The data do not, however necessarily reflect the true situation in the field. Information on the magnitude of the leprosy problem in any one area is

important for the health services with regard to their planning, monitoring and evaluation of leprosy control activities. Our studies have suggested that the high prevalence of antibodies in children may be indicative of the active transmission of *M. leprae* in their surroundings. The prevalence of these antibodies may also be important for leprosy control programs in order to detect new patients as early as possible and in an effective and sustainable manner. Based on PCR data, it seems that the environment also plays an important role in the transmission of leprosy in endemic areas. The results of our study show that contact with a leprosy patient is the major determinant in the incidence of leprosy and that this concept shows similarities with the "stone-in-the-pond" principle of tuberculosis transmission in concentric circle around patients.

## CITOLOGIA

SINGH, N.; MALIK, A.; ARORA, V.K.; BHATIA, A. Fine needle aspiration cytology of leprosy neuritis. *Acta Cytol.*, v.47, n.3, p.368-72, May-Jun. 2003.

OBJECTIVE: To document the cytomorphologic features of leprosy neuritis and their correlation with bacterial density. STUDY DESIGN: A partly retrospective, partly prospective study of the fine needle aspiration cytology of enlarged nerves in leprosy. Cytomorphologic features of nerve aspirates from 28 patients were studied. May-Grünwald-Geimsa and Ziehl-Neelsen staining methods were employed. RESULTS: Five cytomorphologic patterns were observed in smears of nerve aspirates in 19 group I patients with concurrent skin and nerve lesions: (1) inflammation composed of epithelioid cell granulomas (5), bacillary index (BI) = 0; (2) epithelioid cell granulomas with necrosis (5), BI = 0-1+; (3) acellular necrosis (5), BI = 0-4+; (4) macrophage granuloma (3), BI = 5-6+; and (5) granulation tissue (1), BI = 1+. In 9 group II patients with pure neuritic leprosy, 3 patterns were seen: (1) epithelioid cell granulomas (5), BI 0-6+; (2) epithelioid granulomas with necrosis (1), BI = 0; and (3) acellular necrosis (3), BI = 0-6+. CONCLUSION: The entire spectrum of leprosy is seen in nerve aspirates. Necrosis is often a prominent feature. Recognition of the range of cytomorphologic patterns and their correlation with BI contribute to accurate calibration of the disease in nerves, resulting in appropriate choice of treatment.

## CLÍNICA

ANG, P.; TAY, Y.K.; NG, S.K.; SEOW, C.S. Fatal Lucio's phenomenon in 2 patients with previously undiagnosed leprosy. *J Am Acad Dermatol.*, v.48, n.6, p.958-61, Jun. 2003.

We report 2 cases of Lucio's phenomenon, a rare, aggressive, occasionally fatal type 2 reaction occurring in the diffuse nonnodular type of lepromatous leprosy. The clinical

diagnosis of Lucio's phenomenon is difficult, and there are no known predictive or prognostic factors. Despite institution of aggressive treatment after diagnosis, our 2 cases had fatal outcomes.

BAKER, B.; EVANS, M.; DECASTRO, F.; SCHOSSER, R. Leprosy in a Mexican immigrant. *J Ky Med Assoc.*, v.101, n.7, p.289-94, Jul. 2003.

A new diagnosis of borderline lepromatous leprosy was established in a man who had immigrated to Kentucky from Mexico. He was placed on a World Health Organization treatment regimen consisting of dapson, clofazimine, and rifampin. The biology of leprosy, its diagnosis, treatment, and worldwide impact are reviewed. Because of the potential for highly mobile populations to export endemic diseases, Kentucky physicians must expand their lists of differential diagnoses.

BHAT, R.M.; RADHAKRISHNAN, K. A case report of fatal dapson-induced agranulocytosis in an Indian mid-borderline leprosy patient. *Lepr Rev.*, v.74, n.2, p.167-70, Jun. 2003.

Fatal agranulocytosis in an Indian male receiving 100mg of dapson daily, hospitalized for mid-borderline leprosy in type I reaction with triple nerve paralysis is reported. Various case reports concerning dapson-induced agranulocytosis are reviewed.

DELOBEL, P.; LAUNOIS, P.; DJOSSOU, F.; SAINTE-MARIE, D.; PRADINAUD, R. American cutaneous leishmaniasis, lepromatous leprosy, and pulmonary tuberculosis coinfection with downregulation of the T-helper 1 cell response. *Clin Infect Dis*; v.37, n.5, p.628-33, Sep 1. 2003.

Cutaneous leishmaniasis, leprosy, and tuberculosis are caused by intracellular pathogens whose development depends on impaired cell-mediated immunity. We report an exceptional triple association of American cutaneous leishmaniasis, lepromatous leprosy, and pulmonary tuberculosis in a man with no recognized immunodeficiency. Normal immunological assessment of the interferon-gamma pathway does not support the hypothesis of a genetic defect in any of the genes involved in the T helper (Th)-1 cytokine cascade in this patient. Unresponsiveness to interleukin (IL)-12 of his T cells after stimulation with *Leishmania guyanensis*, *Mycobacterium bovis* bacille Calmette-Guérin, and *Mycobacterium leprae* antigens suggested the inability to mount an appropriate Th cell response to upregulate the IL-12 receptor expression.

GREENSTEIN, R.J. Is Crohn's disease caused by a mycobacterium? Comparisons with leprosy, tuberculosis, and Johne's disease. *Lancet Infect Dis.*, v.3, n.8, p.507-14, Aug. 2003.

Although Crohn's disease is considered to be autoimmune in origin, there is increasing evidence that it may have an infectious cause. The most plausible candidate is *Mycobacterium avium* subspecies paratuberculosis (MAP). Intriguingly, Koch's postulates may have been fulfilled for MAP and Crohn's disease, even though they still have not been met for *Mycobacterium leprae* and leprosy. In animals MAP causes Johne's disease, a chronic wasting intestinal diarrheal disease evocative of Crohn's disease. Johne's disease occurs in wild and domesticated animals, including dairy herds. Viable MAP is found in human and cow milk, and is not reliably killed by standard pasteurisation. MAP is ubiquitous in the environment including in potable water. Since cell-wall-deficient MAP usually cannot be identified by Ziehl-Neelsen staining, identification of MAP in human beings requires culture or detection of MAP DNA or RNA. If infectious in origin, Crohn's disease should be curable with appropriate antibiotics. Many studies that argue against a causative role for MAP in Crohn's disease have used antibiotics that are inactive against MAP. However, trials that include macrolide antibiotics indicate that a cure for Crohn's disease is possible. The necessary length of therapy remains to be determined. Mycobacterial diseases have protean clinical manifestations, as does Crohn's disease. The necessity of stratifying Crohn's disease into two clinical manifestations (perforating and non-perforating) when interpreting the results of antibiotic therapy is discussed. Rational studies to evaluate appropriate therapies to cure Crohn's disease are proposed.

GOPALAKRISHNAN, K.; DANIEL, E.; JACOB R; EBENEZER G; MATHEWS M. Bilateral Bipolaris keratomycosis in a borderline lepromatous patient. *Int. J. Lepr.*, v.71, n.1, p.14-7, Mar. 2003.

This is a report of an unusual case of *Bipolaris* mycotic keratitis infecting the corneas of both eyes in a cured, immunocompetent patient with previous borderline lepromatous disease. *Bipolaris* keratomycosis is probably more common than is generally appreciated, and is probably often overlooked in patients with Hansen's Disease.

HANDA, S.; SARASWAT, A.; RADOTRA, B.D.; KUMAR, B. Chronic macrocheilia: a clinico-pathological study of 28 patients. *Clin Exp Dermatol.*, v.28, n.3, p.245-50, May 2003

Chronic macrocheilia has a multifactorial aetiology and is often a diagnostic and therapeutic challenge. Epidemiological information on this condition is scarce, most of the data reported relating only to granulomatous cheilitis. We have performed a detailed clinico-pathological analysis of all patients with chronic macrocheilia presenting to us during the last 6.5 years. Of the 28 patients identified, 13 (46.4%) had granulomatous cheilitis (GC), six (21.4%) had tuberculosis of the lip, three (10.7%) had leprosy macrocheilia, two (7.1%) had multiple endocrine neoplasia type IIb, and one each had Ascher's syndrome and non-Hodgkin's

lymphoma. Two patients were diagnosed as 'nonspecific cheilitis'. Histopathological differentiation between tuberculosis and GC was often not possible; but PCR for *Mycobacterium tuberculosis* was positive in all patients with tuberculosis and negative in four patients with GC in whom *M. tuberculosis* was sought. In spite of detailed clinical examination and investigations, a therapeutic trial was required to confirm the diagnosis in five (17.9%) patients. We have reviewed the available literature on this subject, and to our knowledge this study is the first of its kind. More such studies from other centres will help physicians to make an accurate aetiological diagnosis and treat this uncommon but disfiguring condition with confidence.

INAMADAR, A.C.; PALIT, A.; ATHANIKAR, S.B.; SAMPAGAVI, V.V.; DESHMUKH, N.S. Generalized anetoderma in a patient with HIV and dual mycobacterial infection. *Lepr Rev.*, v.74, n.3, p.275-8, Sep. 2003.

A middle-aged HIV infected man receiving treatment for pulmonary tuberculosis, presented with a febrile illness along with evanescent, erythematous nodular lesions all over the body. On examination, he had features suggestive of lepromatous leprosy with lesions of erythema nodosum leprosum. In addition, there were multiple small, circumscribed areas of slack skin, clinically and histopathologically suggestive of anetoderma. Both leprosy and HIV infection are known to give rise to lesions of anetoderma. Pathogenesis of anetoderma in these infectious conditions is discussed.

KEITA, S.; FAYE, O.; KONARE, H.D.; SOW, S.O.; NDIAYE, H.T.; TRAORE, I. Evaluation de la classification clinique des nouveaux cas de lèpre. Etude réalisée à l'Institut Marchoux (Bamako, Mali). [Evaluation of the clinical classification of new cases of leprosy. Study conducted at the Marchoux Institute in Bamako, Mali]. *Ann Dermatol Venereol.*, v.130, n.2, Pt 1, p.184-6, Feb. 2003.

**INTRODUCTION:** The difficulties related to the bacilloscopic diagnosis of leprosy, providing a more reliable classification of cases, in 1995 led the WHO to recommend the use of a new classification, in endemic countries, based on clinical criteria alone, in order to simplify the poly-chemotherapeutic regimens. According to our experience in the Marchoux Institute, this classification may lead to errors in diagnosis through overzealous or mis-interpretation of the two forms of leprosy. The aim of our study was to evaluate the concordance between this clinical classification and that based on a bacilloscopic examination. **PATIENTS AND METHODS:** We conducted a descriptive study of new cases of leprosy seen at the Marchoux Institute, without distinction in gender or age, from January to December 2000. All the patients included underwent clinical examination and a bacilloscopic exploration to provide a double

classification. The concordance between the two classifications was assessed using the Kappa test. **RESULTS:** Two hundred new cases of leprosy were included. Out of 126 clinically multi-bacillary cases, 61 were confirmed bacteriologically, and 65 were false positives. Out of 74 clinical cases with few bacilli, 2 were bacteriologically multi-bacilli. The concordance between the two classifications was average (Kappa=0.40). There was a significant difference between the percentages of multi-bacilli observed in both classifications ( $p < 10^{-8}$ ). **DISCUSSION:** The clinical classification may well overestimate the multi-bacillary form. In the absence of a reliable bacilloscopic apparatus, a more detailed clinical classification of leprosy forms must be developed.

KIRIYAMA, I.; OHGAKI, K.; OHBA, S.; EGAWA, K.; NISHIMURA, T. Prostate cancer in patients with Hansen's disease. *Int J Urol*; v.10, n.3, p.177-9, Mar. 2003.

Hansen's disease causes testicular failure secondarily, and because of this, it has been considered that prostate cancer would not be found in association. Three of 14 patients with chronic leprosy in Suruga National Sanatorium Hansen's Disease Hospital were found to have prostate cancer. A 72-year-old with lepromatous leprosy was diagnosed with stage T3a prostate cancer and treated with radical prostatectomy after hormonal therapy, plus irradiation. An 80-year-old with lepromatous leprosy was diagnosed with stage T2 prostate cancer and treated with irradiation and follow up only without hormone therapy and surgery because of his low testosterone level and old age. An 82-year-old with borderline leprosy was diagnosed with stage T1c prostate cancer and because of the pathological finding of low Gleason score and his old age, he was treated with hormonal therapy only. Two of the three cases had elevated concentrations of follicle-stimulating hormone and luteinizing hormone, which suggests that their prostatic cancers might have been equivalent to be under the influence of hormone therapy. Therefore, in aged male patients with Hansen's disease, the follicle-stimulating hormone, luteinizing hormone and testosterone concentrations should be measured, as well as that of prostate-specific antigen, and a prostate biopsy should be also considered if the prostate-specific antigen concentration is increased, even with hypogonadism.

LAWN, S.D.; WOOD, C.; LOCKWOOD, D.N. Borderline tuberculoid leprosy: an immune reconstitution phenomenon in a human immunodeficiency virus-infected person. *Clin Infect Dis*; v.36, n.1, p.5-6, Jan. 1 2003.

Two months after starting highly active antiretroviral treatment (HAART), an individual with human immunodeficiency virus type 1 (HIV-1) infection and profound CD4+ T lymphocytopenia developed several erythematous plaques on his face, which were due to borderline tuberculoid leprosy with reversal reaction. The temporal association between

the development of these lesions and changes in blood CD4+ lymphocyte count and plasma HIV-1 load observed during HAART strongly suggests that the presentation of leprosy resulted from immune reconstitution.

LEE, H.N.; EMBI, C.S.; VIGELAND, K.M.; WHITE, C.R. Concomitant pulmonary tuberculosis and leprosy. *J Am Acad Dermatol*, v.49, n.4, p.755-7, Oct. 2003.

Concomitant tuberculosis and leprosy is uncommon, even in endemic countries. We report a patient with borderline lepromatous leprosy and type 1 reversal reaction initially diagnosed while the patient was undergoing treatment for pulmonary tuberculosis. The diagnosis was on the basis of characteristic histopathology and Fite-Faraco stain.

MISRA, U.K.; KALITA, J.; MAHADEVAN, A.; SHANKAR, S.K. Pseudoathetosis in a patient with leprosy. *Mov Disord.*, v.18, n.5, p.598-601, May 2003.

A 35-year-old man with borderline tuberculoid leprosy developed Type I lepra reaction 12 days after anti-leprosy treatment. There was acute worsening of neuropathic symptoms and skin lesions. He developed severe sensory ataxia and pseudoathetosis resulting in marked disability. His symptoms significantly improved on corticosteroid therapy.

MOSES, A.E.; ADELOWO, K.A.; AJAYI, B.B. Prevalence of HIV-1 infection among patients with leprosy and pulmonary tuberculosis in a semi-arid region, Nigeria. *J R Soc Health*, v.123, n.2, p.117-9, Jun. 2003.

Much evidence exists on pulmonary tuberculosis (PTB) as a presenting feature of HIV infection or AIDS-related complex, while few reports exist of a direct association between HIV infection and leprosy. This study was carried out to see whether or not an association between leprosy and HIV infection existed, similar to that of PTB in the region of Maiduguri, Nigeria. Of 105 patients with leprosy, 11(10.5%) were positive for HIV antibody. Of 58 patients with suspected PTB, 11(19%) were positive for HIV antibody. Twenty-seven (47%) of the 58 had active PTB, with results of sputum smear and culture positive for mycobacterium, and six of these (22.2%) were also positive for HIV antibody. Odds ratios (OR) obtained by conditional logistic regression (matched) analysis were 3.52 (95%, CI 1.03-12.07) and 2.53 (95%, CI 1.04-6.15) for association between HIV-1 and PTB and leprosy, respectively. HIV infection was more prevalent among leprosy patients aged under 30 years, OR = 4.25 (95%, CI 1.25-14.42). The prevalence of HIV-1 infection was at borderline significance, higher in PTB and leprosy patients than in blood donors, Fisher's exact test (two-tailed)  $p = 0.07$  and  $p = 0.05$ , respectively.

NAKAYAMA, S.; UESAKA, Y.; KUNIMOTO, M.; MIKATA, T.; SHIMIZU, J.; ISHII, N. [The painful multiple mononeuropathy of acute onset in the left arm which was diagnosed as leprosy neuropathy]. *Rinsho Shinkeigaku*; v.43, n.5, p.265-9, May, 2003.

A 31-year-old man from Myanmar with leprosy neuropathy was reported. The progress of the disease was subacute but the painful symptom at the time of the onset was acute. Multiple mononeuropathy was diagnosed by the biopsy findings of the left superficial radial nerve. He was admitted to our hospital with the complaint of the weakness of his left hand and fingers which were very painful and got worse in several weeks. Motor palsy was observed in his left ulnar, median, and radial nerves, and there was the hypesthesia or anesthesia in his left hand, forearm and the medial side of his left upper arm. On nerve conduction studies, the amplitudes of CMAP and SNAP severely diminished or not detected. The pattern was compatible with multiple mononeuropathy. The biopsy of the left superficial radial nerve was performed. The pathological findings were the destruction of nerve fascicles, replacement of nerve fibers with inflammatory cells, and *Mycobacterium leprae* was found with the specific stain. These findings confirmed the diagnosis of the leprosy neuropathy. Leprosy neuropathy is one of the commonest causes of infectious neuropathy in the world, especially in Southeast Asia. These days many foreign workers from that area are staying in Japan, and the chances to see the disease are increasing. We have to recognize leprosy neuropathy as a candidate for the multiple mononeuropathy of acute onset with painful dysesthesia similar to vascular neuropathy.

THOMPSON, A.M.; LYNN, A.A.; ROBSON, K.; JOYCE, M.P.; FIVENSON, D.P.; SCOLLARD, D. Lepromatous phlebitis of the external jugular vein. *J Am Acad Dermatol*; v.49, n.6, p.1180-2, Dec. 2003.

*Mycobacterium leprae* (*M leprae*), the causative agent of Hansen's disease, is endemic in many areas of Asia, sub-Saharan Africa, South and Central America, the Pacific Islands, and the Philippines. The spectrum of clinical disease is dependent on the patient's cell-mediated immunity and might range from localized anesthetic patches or plaques to disseminated disease. If undiagnosed, progression with damage to the involved sensory and motor nerves might occur. Lepromatous vasculitis occurs most commonly in patients with severe disseminated disease. Vascular disease, as the initial presenting sign of tuberculoid leprosy, is, however, rare. We present one patient in whom the development of Hansen's disease was associated with involvement of the external jugular vein and was initially seen as external jugular vein fibrosis.

## CLÍNICA E EPIDEMIOLOGIA

ARAÚJO, M.G. Hanseníase no Brasil [Leprosy in Brazil] *Rev Soc Bras Med Trop*; 36(3):373-82, May-Jun. 2003.

Leprosy or Hansen's disease is a chronic infectious disease caused by the *Mycobacterium leprae*. The skin and nervous manifestations of the disease present a singular clinical picture that is easily recognized. After India, Brazil still is the second country with the greatest number of cases in the world. Around 94% of the known cases and 94% of the new cases reported in America, come from Brazil. The disease presents itself in two well-defined stable and opposite poles (lepromatous and tuberculoid and two unstable groups (indeterminate and dimorphic). The spectrum of presentation of the disease may also be classified as: tuberculoid tuberculoid (TT), borderline tuberculoid (BT), borderline borderline (BB), borderline lepromatous (BL) and lepromatous lepromatous (LL). The finding of acid fast bacillus in tissue is the most useful method of diagnosis. The effective treatment of leprosy includes the use of specific therapy, suppression of lepra reactions, prevention of physical incapacity, and physical and psychosocial rehabilitation. Chemotherapy with rifampin, dapsone and clofazimine have produced very good results and the control of the disease in Brazil in the foreseeable future is likely.

## CLÍNICA E PATOLOGIA

KAUR, I.; INDIRA, D.; DOGRA, S.; SHARMA, V.K.; DAS, A.; KUMAR, B. "Relatively spared zones" in leprosy: a clinicopathological study of 500 patients. *Int. J. Lepr*; v.71, n.3, p.227-30, Sep. 2003.

In this study, clinically all forms of lesions like macules, plaques, and nodules were found in all the "relatively spared zones," except groins. Histopathology confirmed that the disease process was established and the acid-fast bacilli were not present as a part of bacteremic settlement. Hence, it appears that practically no area on the surface of skin is immune to invasion by *M. leprae*. However, as the incidence of lesions and AFB in these regions is relatively less, especially over axilla and groin, these areas can be considered as relatively spared zones but not completely resistant to development of lesions of leprosy.

## CONTROLE

GALLO, M.E.N.; RAMOS JÚNIOR, L.A.N.; ALBUQUERQUE, E.C.A.; NERI, J.A.C.; SALES, A.M. Alocação do paciente hanseniano na poliquimioterapia: correlação da classificação baseada no número de lesões com exames baciloscópicos / Allocation of leprosy patients for multidrugtherapy: correlation between the classification according to number of lesions and the skin smears examination. *An. bras. dermatol*; v.78, n.4, p.415-424, jul.-ago. 2003.

Fundamentos: A integração das artes de controle da hanseníase, as estratégias dos Programas de Saúde da Família e Agentes Comunitários de Saúde, na conformidade do processo de reorganização da atenção básica, fundamentou a atualização das normas da legislação sobre o controle da doença no Brasil. A classificação operacional adotada, para alocação do paciente na poliquimioterapia, foi adaptada da sugerida pela Organização Mundial da Saúde, essencialmente clínica, baseada no número de lesões cutâneas.

SHUMIN, C.; DIANGCHANG, L.; BING, L.; LIN, Z.; XIOULU, Y. Role of leprosy villages and leprosaria in Shandong Province, People's Republic of China: past, present and future. *Lepr Rev*, v.74, n.3, p.222-8, Sep., 2003.

In the late phase of the leprosy control programme in Shandong Province, People's Republic of China, there are a few old and disabled ex-patients living in 54 leprosy villages/leprosaria. The small, and declining number of patients makes the running of these leprosy villages/leprosaria uneconomic. In this paper, we review the history and the role of leprosy villages/leprosaria in the care of leprosy patients and the control program in Shandong province. We then analyse the present situation of the 643 people still living in these leprosy villages/leprosaria, using information collected from a questionnaire-based survey. Finally, we offer some suggestions and recommendations for policy makers and leprosy control managers, in order to improve the present situation and make better use of existing resources.

TAYLOR, R.; KING, K.; VODICKA, P.; HALL, J.; EVANS, D. Screening for leprosy in immigrants—a decision analysis model. *Lepr Rev*, v.74, n.3, p.240-8, Sep. 2003.

Almost all leprosy cases reported in industrialized countries occur amongst immigrants or refugees from developing countries where leprosy continues to be an important health issue. Screening for leprosy is an important question for governments in countries with immigration and refugee programmes. A decision analysis framework is used to evaluate leprosy screening. The analysis uses a set of criteria and parameters regarding leprosy screening, and available data to estimate the number of cases which would be detected by a leprosy screening programme of immigrants from countries with different leprosy prevalences, compared with a policy of waiting for immigrants who develop symptomatic clinical diseases to present for health care. In a cohort of 100,000 immigrants from high leprosy prevalence regions (3.6/10,000), screening would detect 32 of the 42 cases which would arise in the destination country over the 14 years after migration; from medium prevalence areas (0.7/10,000) 6.3 of the total 8.1 cases would be detected, and from low prevalence regions (0.2/10,000) 1.8 of 2.3 cases. Using Australian data, the migrant mix would



produce 74 leprosy cases from 10 years intake; screening would detect 54, and 19 would be diagnosed subsequently after migration. Screening would only produce significant case-yield amongst immigrants from regions or social groups with high leprosy prevalence. Since the number of immigrants to Australia from countries of higher endemicity is not large routine leprosy screening would have a small impact on case incidence.

## DIAGNÓSTICO

JARDIM, M.R.; ANTUNES, S.L.; SANTOS, A.R.; NASCIMENTO, O.J.; NERY, J.A.; SALES, A.M.; ILLARRAMENDI, X.; DUPPRE, N.; CHIMELLI, L.; SAMPAIO, E.P.; SARNO, E.P. Criteria for diagnosis of pure neural leprosy. *J Neurol.*, v.250, n.7, p.806-9, Jul. 2003.

The clinical diagnosis of pure neural leprosy (PNL) remains a public health care problem mainly because skin lesions—the cardinal features of leprosy—are always absent. Moreover, the identification of the leprosy bacillus is not easily achieved even when a nerve biopsy can be performed. In an attempt to reach a reliable PNL diagnosis in patients referred to our Leprosy Outpatient Clinic, this study employed a variety of criteria. The nerve biopsies performed on the 67 individuals whose clinical, neurological, and electrophysiological examination findings strongly suggested peripheral neuropathy were submitted to *M. leprae* identification via a polymerase chain reaction (PCR). Mononeuropathy multiplex was the most frequent clinical and electrophysiological pattern of nerve dysfunction, while sensory impairment occurred in 89% of all cases and motor dysfunction in 81%. Axonal neuropathy was the predominant electrophysiological finding, while the histopathological nerve study showed epithelioid granuloma in 14% of the patients, acid fast bacilli in 16%, and nonspecific inflammatory infiltrate and/or fibrosis in 39%. PCR for *M. leprae* was positive in 47% of the nerve biopsy samples (n=23). PCR, in conjunction with clinical and neurological examination results, can be a powerful tool in attempting to identify and confirm a PNL diagnosis.

## DIAGNÓSTICO E CONTROLE

Da SILVA SOUZA, C.; BACHA, J.T. Delayed diagnosis of leprosy and the potential role of educational activities in Brazil. *Lepr Rev.*, v.74, n.3, p.249-58, Sep. 2003.

This study identifies possible obstacles to the early diagnosis of leprosy. Semi-structured interviews were held with 40 patients at a secondary health service in upstate São Paulo, Brazil. The data concerning the sample were: 75% males, age range 13-76 years, 85% with elementary school education, 85% multibacillary. Skin lesions associated with sensory alterations had been noticed by 55% of the patients; 32.5% of

the patients had been misdiagnosed as having conditions other than leprosy. The diagnosis was made 1 year after the awareness of signs/symptoms in 55% of the patients. In this group, 54% had impairment grade 1, while 23% had no disabilities. Forty-five percent of all patients interviewed had some information about the disease prior to diagnosis. Eleven patients (27.5%) had previous contact with leprosy patients, but this did not prevent late diagnosis in 64%. After the disease was confirmed, about half of the interviewed patients (47.5%) showed mainly positive feelings due to the prospect of treatment and cure. Our results suggest that misdiagnoses and unawareness of the disease were the main factors that influenced the delayed diagnosis. We consider the effective involvement of various segments of society, particularly the integration and partnership of the public health services and health education centres to be valuable tools for the planning and execution of educational activities directed at risk groups and the community.

## EPIDEMIOLOGIA

AQUINO, D.M.; CALDAS ADE, J.; DA SILVA, A.A.; COSTA, J.M. Perfil dos pacientes com hanseníase em área hiperendêmica da Amazônia do Maranhão, Brasil. [Profile of leprosy patients in a hiperendemic area of Amazonian Maranhão, Brazil]. *Rev Soc Bras Med Trop.*, v.36, n.1, p.57-64, Jan-Feb. 2003.

An epidemiological cross-sectional study of 207 patients with leprosy disease, was undertaken between August 1998 to november 2000, aiming at evaluating the socioeconomic, demographic and ambiental profiles of the patients as well as physical incapacity due to the disease. The study was performed in the municipality of Buriticupu-Maranhão state, a hiperendemic leprosy area in the Amazonian Maranhão. The level of incapacity was assessed from parameters established by the Brazilian Health Minister. The clinical evaluation and the results of the physical tests were registered in a standardized form. It was observed a predominance of married people (45,9%), with low level of education (56%), being farm workers (40,1%), with familiar income to the minimum wage (76,3%), aged from 14 to 44 years (63,3%), males (60,9%) and brown (67,6%); 44% living in mud huts, 82,6% deposited their excrements in cesspits and 63,8% do not treat the drinking water, 58% utilized well-water and 51,7% do not use treated water for ingestion. The most affected segments of the body were the feet (62,3%), eyes (51,2%) and hands (7,2%), being the higher percentage of physical incapacities found among the patients bearing the borderline form of the disease (93%) mainly hands and feet, and in the lepromatous form greatest frequency of eyes incapacities. It is concluded that the hyperendemicity associated with the precarious socioeconomic conditions and with a high level of physical incapacities may be involved with the living quality of the patients.

FIGUEIREDO, I.A.; DA SILVA, A.A. Aumento na detecção de casos de hanseníase em São Luís, Maranhão, Brasil, de 1993 a 1998: a endemia está em expansão?. [Increase in leprosy detection rates in São Luís, Maranhão, Brazil, from 1993 to 1998: is the endemic expanding?] *Cad Saude Publica.*, v.19, n.2, p.439-45, Mar-Apr. 2003

A descriptive epidemiologic study on the detection of new leprosy cases was conducted in São Luís, Maranhão, Brazil, from 1993 to 1998. A database was created for the purpose, covering 2,796 reported cases. General detection rates were calculated, as well as specific rates by gender, clinical type, and age group. Linear, exponential, geometric, and log adjustment models were performed to analyze time trends in the disease. An increase in detection was observed, involving mostly female and paucibacillary cases, mainly of tuberculoid leprosy. The increase in detection was most evident in the 15 to 19 year-old population. The percentage of detection under 15 indicated the need for active case search in this group.

GOTO, M.; KITAJIMA, S.; NOMOTO, M.; TAKI, C.; YONEZAWA, S.; IMAIZUMI, M. Cured tuberculoid patients have a greater life expectancy than cured lepromatous patients in Japan. *Int. J. Lepr.*, v.71, n.2, p.106-12, Jun. 2003.

Leprosy patients lack specific cellular immunity against *Mycobacterium leprae*, but other immunological functions are thought to be preserved. However, in a leprosy sanatorium in South Japan between 1982 and 2000, we found that the average age at death of cured lepromatous leprosy patients was about 5 yrs younger than that of cured tuberculoid patients; [male/lepromatous, 76.0 +/- 10.0 yrs old vs. male/tuberculoid, 79.7 +/- 9.4 yrs old,  $p = 0.026$ ], and [female/lepromatous, 78.0 +/- 10.5 vs. female/tuberculoid, 85.3 +/- 9.8,  $p = 0.0001$ ]. This trend was also observed in autopsy records of two other leprosy sanatoria in Japan. In a prospective study based on their age in 1982, among females in the age group between 60 and 69, lepromatous patients (75.3 +/- 6.0 yrs) died earlier than tuberculoid patients (81.0 +/- 5.1 yrs) ( $p < 0.01$ ). These findings suggest that lepromatous patients have higher risk of death even in a post-chemotherapy era.

## EPIDEMIOLOGIA / GENÉTICA

WALLACE, C.; CLAYTON, D.; FINE, P. Estimating the relative recurrence risk ratio for leprosy in Karonga District, Malawi. *Lepr Rev.*, v.74, n.2, p.133-40, Jun. 2003

Leprosy is a chronic disease caused by infection with *Mycobacterium leprae*. Susceptibility to leprosy is influenced by both genetic and non-genetic factors and the disease is known to cluster in families. One measure of genetic effect is the relative recurrence risk ratio, lambdaR. Estimates of this parameter can be inflated if environmental risk factors which

also cluster in families, such as household contact, are not properly accounted for. We present the results of fitting a cross ratio model that allows estimation of the odds ratio of disease conditional on disease or no disease in a given relative, given measured covariates. From this model we can predict fitted values for lambdaR that represent the familial risk not accounted for by other covariates including observed household contact. If all covariates could be measured, this would be the 'genetic relative risk ratio'. We find lambdaR > 1 for all relative pairs except grandparent-grandchild, and lambdaR > 2 for siblings. Though not in itself evidence for a strong genetic susceptibility to leprosy, this result is consistent with much other evidence which suggests susceptibility to leprosy is under the control of many factors, the strongest of which may be non-genetic, with host genetics playing a small but significant role.

## EPIDEMIOLOGIA E CONTROLE

BYAMUNGU, D.C.; OGBEIWI, O.I. Integrating leprosy control into general health service in a war situation: the level after 5 years in eastern Congo. *Lepr Rev.*, v.74, n.1, p.68-78, 2003

South Kivu Province of the Democratic Republic of Congo, plagued by a turbulent civil war, started a process of integrating leprosy into general health services in 1995. A questionnaire survey was carried out in September 2000 to assess the level of structural and functional integration, after 5 years of the integration process, in nine of its 14 health districts. The survey revealed that a total of 76 clinic nurses remained of those trained in leprosy since 1993. In all, 33-6% of the total 226 health facilities had a trained nurse, but according to the district supervisors who filled the questionnaires, nurses in only 28.3% of health facilities could diagnose leprosy. Less than 40% of the total 226 health facilities were structurally integrated with MDT and other leprosy services. Functionally, the clinic nurses were involved in dispensing MDT drugs and keeping leprosy records in 90.8 and 81.6%, respectively, of the integrated facilities, and diagnostic activities in 43.7%. The degree of involvement put health facilities into four grades of functional integration: 1) fully-functional integrated, 2) semi-functional integrated, 3) semi-integrated (structural but not functional), 4) not integrated (vertical). On this scale, 80% of 107 health facilities reported by the supervisors had some form of integration and 20% were not integrated. Treatment activities were significantly more functionally integrated than the diagnostic and POD activities, which require more skills. The presence of a trained nurse in a health facility made no significant difference to the involvement of clinic nurses in dispensing MDT drugs and performing POD activities, but significantly affected their performance of diagnostic activities and records keeping. The endemic districts had higher levels of structural integration, were not more likely to be functionally

integrated. The levels of structural integration after 5 years are considered low in South Kivu Province, and reflect the significant negative effect of civil conflicts on integration of leprosy programmes in Africa.

CHEN, S.; ZHANG, L.; LIU, D.; LIU, B. Should household contact examination in a low endemic situation of leprosy continue? *Int. J. Lepr.*, v.71, n.2, p.95-100, Jun. 2003.

After more than 40 yrs of effort, leprosy is finally under control in Shandong province with only 50 to 70 new cases detected each year in the past 10 yrs. Contact examination is still compulsory and household contacts will be followed for 5 to 10 yrs, as directed by the guidelines of the national leprosy control program. In order to assess the value of contact examination in terms of case finding in a low endemic situation of leprosy in Shandong, we analyzed the data regarding all newly diagnosed leprosy cases in the past 11 yrs using the data abstracted from the national leprosy recording and reporting system, and a questionnaire-based survey to see how many incident leprosy cases would be detected if we followed the policy for contact examination of leprosy in Shandong. The results showed that 252 out of 547 leprosy cases diagnosed from 1990 to 2001 reported they had contact with different categories of primary leprosy cases. Among them, 90 cases had household primary leprosy cases. The mean incubation of the 252 index cases was 23 yrs. If we followed the national policy for contact tracing for 5 or 10 yrs, then only 12 (13.3%) and 10 (11.1%) of the 90 cases whose source of infection was household contacts would have been detected, respectively. Therefore, other approaches should be sought, in order to detect the few incident leprosy cases as early as possible in such a low endemic situation of leprosy in Shandong.

de AQUINO, D.M.; SANTOS, J.S.; COSTA, J.M. Avaliação do programa de controle da hanseníase em um município hiperendêmico do Estado do Maranhão, Brasil, 1991-1995.. [Assessment of a leprosy control program in a hyperendemic county in the State of Maranhão, Brazil, 1991-1995. *Cad Saude Publica*, v.19, n.1, p.119-25, 2003.

This is a descriptive study to assess the leprosy control program in the municipality of Buriticupu in Maranhão State, Brazil. The records of 214 patients with different forms of leprosy were studied. Patients were treated at a health center of the Federal University in Maranhão located in the above-mentioned municipality. The study population was comprised of 110 cases with paucibacillary leprosy (PB) and 104 with multibacillary leprosy (MB). The patients were registered between January 1991 and December 1995. Data on the form of the disease, number of contacts registered, examined, and assessed, degree of disability at the beginning and end of treatment, and the register's status were collected on a form

designed specifically for this purpose. Analysis of results was based on operational guidelines developed by the Ministry of Health. There was a slight predominance of the PB form. Observation of patients with physical disabilities at the beginning and end of treatment was low, as were levels of successful treatment and examined contacts. There was a high dropout level. The program was considered "low-level performance" for all indicators used in the study.

PHAFF, C.; VAN DEN BROEK, J.; MACARTHUR, A.; NDEVE, A.; STUIP, Y. Characteristics and treatment outcomes of leprosy patients detected during a leprosy elimination campaign in Mozambique compared with routinely detected patients. *Lepr Rev.*, v.74, n.3, p.229-39, Sep. 2003 .

The objective of this study is to assess whether the case-finding method is a determinant for diagnostic characteristics and treatment outcome of newly diagnosed leprosy patients in Northern Mozambique. This is a retrospective cohort study of 3202 patients on the differences between entrance characteristics and treatment outcome in self-reporting patients and patients detected during a leprosy elimination campaign (LEC) in 1999 in Northern Mozambique. As a consequence of LEC activities, 3 times more patients were found compared with the same period 1 year earlier. After the LEC, case detection remained higher in the years 2000-2002 compared with the years preceding the LEC. More young (<15 years) paucibacillary (PB) cases were diagnosed during LEC activities with, surprisingly, equal percentage of disability grades. No gender imbalance was found in diagnosed LEC patients contrary to self-reporting patient groups. Comparing patients detected during a LEC in 1999 with the passive group of 1998 and 1999 showed a slight but statistically significant better treatment result for the passive group. The classification of leprosy (in favour of PB) and age (in favour of older age groups) were also determinants for favourable treatment outcomes. Volunteers had a significantly better result of treatment compared with trained nurses and regardless of detection method. LEC proved to be a useful addition to the National Leprosy and Tuberculosis Programme in Northern Mozambique. As a result, many new cases were diagnosed and put on treatment and their treatment results were very satisfactory. LEC had a lasting impact on case finding. Volunteers make a valuable contribution to leprosy control in Mozambique because they have consistently better treatment results compared with nurses.

VAN DIJK, M.; VISSCHEDIJK, J.; VAN DER KWAAK, A. 'Client satisfaction'—guidelines for assessing the quality of leprosy services from the clients' perspective. *Lepr Rev.*, v.74, n.2, p.112-9, Jun. 2003.

In order to ensure that leprosy patients are detected and

treated adequately, it is essential that they are satisfied with the services provided. Their satisfaction can be analysed by assessing the quality of the services from a client perspective. This will give crucial information for the identification of strengths and weaknesses of leprosy services, e.g. in areas such as health seeking behaviour and regularity of treatment. It necessitates, however, that special attention is given to clients' opinions and ideas, both of which are rarely included in reviews and evaluations of leprosy programmes. Hence, an initiative was taken to formulate guidelines for the conducting of a study on client satisfaction. These guidelines were pre-tested in two countries, Nepal and Brazil. The development and contents of these guidelines are highlighted and discussed in this paper.

## GENÉTICA

BUSCHMAN, E.; SKAMENE, E. Leprosy susceptibility revealed. *Int. J. Lepr.*, v.71, n.2, p 115-8, Jun. 2003.

In order for these findings to have practical significance in terms of leprosy control and prevention, it will be necessary to extend the linkage of chromosome 6q25 to another region endemic for leprosy. Replicative findings would likely mean that the chromosome 6q25 susceptibility gene is a variant of a common gene that promotes susceptibility to infection per se. Identification of the gene variant will hopefully reveal insight about transmission and disease incidence—the longstanding enigmas of leprosy. Whether a more effective, universal MDT treatment or another type of prevention (either vaccine or environmental) could be based on this knowledge, is an exciting prospect to contemplate.

KIM, S.K.; LEE, S.B.; KANG, T.J.; CHAE, G.T. Detection of gene mutations related with drug resistance in *Mycobacterium leprae* from leprosy patients using Touch-Down (TD) PCR. *FEMS Immunol Med Microbiol.*, v.36, n.1-2, p.27-32, May 15, 2003.

The lack of methods to identify *Mycobacterium leprae* with the resistance against multi-drugs quickly and specifically has hindered effective chemotherapy against *M. leprae* infection. To screen *M. leprae* with resistance against multi-drugs, the Touch-Down (TD)-PCR has been used in this study. Sequences of the *folP*, *rpoA*, *B*, and *gyrA*, *B* genes were analyzed for isolates of *M. leprae* from leprosy patients in Korea. We amplified designated region of several genes in *M. leprae* involved in drug resistance and could obtain the PCR products of each gene. The mutations in the particular region of *folP*, *rpoB*, and *gyrB* gene were certified by TD-PCR single-stranded conformational polymorphism and DNA sequencing, respectively.

LEE, S.B.; KIM, B.C.; JIN, S.H.; PARK, Y.G.; KIM, S.K.; KANG, T.J.; CHAE, G.T. Missense mutations of the interleukin-12 receptor beta 1(IL12RB1) and interferon-gamma receptor 1

(IFNGR1) genes are not associated with susceptibility to lepromatous leprosy in Korea. *Immunogenetics.*, v.55, n.3, p.177-81, Jun. 2003.

Interleukin-12 receptor beta 1 (IL12RB1), interleukin-12 receptor beta 2 (IL12RB2), and interferon gamma receptor 1 (IFNGR1) perform important roles in the host defense against intracellular pathogens such as Mycobacteria. Several mutations within their genes have been confirmed as associated with increased susceptibility to mycobacterial infection. However, the association between mutations of the IL12RB1, IL12RB2, and IFNGR1 encoding genes and lepromatous leprosy has not been studied. This study screened for polymorphisms within IL12RB1, IL12RB2, and IFNGR1 encoding genes in the Korean populations using polymerase chain reaction (PCR)/single-strand conformation polymorphism (SSCP) DNA sequencing assay, and an association study was performed using the missense mutations of 705 A/G (Q214R), 1196 G/C (G378R), 1637 G/A (A525T), and 1664 C/T (P534S) of the IL12RB1, 83 G/A (V14M), and 1443 T/C (L467P) for the IFNGR1 encoding genes. There were no differences in the genotype and allele frequencies of IL12RB1 and IFNGR1 genes between 93 lepromatous leprosy patients and 94 control subjects. In conclusion, missense mutations of 705 A/G (Q214R), 1196 G/C (G378R), 1637 G/A (A525T), 1664 C/T (P534S) of the IL12RB1, 83 G/A (V14 M), and 1443 T/C (L467P) of the IFNGR1 encoding genes have no association with the susceptibility to lepromatous leprosy in the Korean population.

MIRA, M.T.; ALCAÏS, A.; VAN THUC, N.; THAI, V.H.; HUONG, N.T.; BA, N.N.; VERNER, A.; HUDSON, T.J.; ABEL, L.; SCHURR, E. Chromosome 6q25 is linked to susceptibility to leprosy in a Vietnamese population. *Nat Genet*; v.33, n.3, p.412-5, Mar. 2003.

Leprosy, a chronic infectious disease caused by *Mycobacterium leprae*, affects an estimated 700,000 persons each year. Clinically, leprosy can be categorized as paucibacillary or multibacillary disease. These clinical forms develop in persons that are intrinsically susceptible to leprosy per se, that is, leprosy independent of its specific clinical manifestation. We report here on a genome-wide search for loci controlling susceptibility to leprosy per se in a panel of 86 families including 205 siblings affected with leprosy from Southern Vietnam. Using model-free linkage analysis, we found significant evidence for a susceptibility gene on chromosome region 6q25 (maximum likelihood binomial (MLB) lod score 4.31;  $P = 5 \times 10^{-6}$ ). We confirmed this by family-based association analysis in an independent panel of 208 Vietnamese leprosy simplex families. Of seven microsatellite markers underlying the linkage peak, alleles of two markers (D6S1035 and D6S305) showed strong evidence for association with leprosy ( $P = 6.7 \times 10^{-4}$  and  $P = 5.9 \times 10^{-5}$ , respectively).

REYNARD, M.P.; TURNER, D.; JUNQUEIRA-KIPNIS, A.P.; RAMOS DE SOUZA, M.; MORENO, C.; NAVARRETE, C.V. Allele frequencies for an interferon-gamma microsatellite in a population of Brazilian leprosy patients. *Eur J Immunogenet*; v.30, n.2, p.149-51, Apr. 2003.

A group of Brazilian leprosy patients and controls were genotyped for a CA-repeat microsatellite polymorphism within the interferon (IFN)-gamma gene. A significantly higher frequency of alleles 5-7 was observed in this patient population, indicating that IFN-gamma gene polymorphism may contribute to the course of leprosy post-infection.

## HISTÓRIA

BENCHIMOL, J.L.; SÁ, M.R.; CRUZ, M.S.A.; ANDRADE, M.M. Fight for survival: the life of a Hansen's disease sufferer through his correspondence with Adolpho Lutz. *Hist. ciênc. saúde-Manguinhos*; v.10, supl.1, p. 361-396, 2003.

Apresenta a série completa da correspondência da família de um portador do mal de Hansen residente no Maranhão, Nordeste do Brasil, com o médico e bacteriologista Adolpho Lutz. Fabrício Caldas de Oliveira e Numa Pires de Oliveira, pai e filho, mantiveram durante mais de vinte anos intensa troca de cartas com o cientista na busca da cura da doença que vitimava Numa desde criança. As 24 cartas aqui reunidas retratam, de maneira única, o drama médico-social enfrentado por esta família, os resultados do uso do chalmugra e outros medicamentos, a busca de tratamentos alternativos.

BENCHIMOL, J.L.; SÁ, M.R. Adolpho Lutz and controversies over the transmission of leprosy by mosquitoes. *Hist. ciênc. saúde-Manguinhos*; v.10, supl.1, p.49-93, 2003.

Quando estudava na Suíça e Alemanha, Adolpho Lutz publicou os primeiros trabalhos sobre zoologia, clínica e terapêutica. Em Limeira, São Paulo, iniciou estudos sobre doenças humanas e animais causadas por germes e parasitas. Em 1885-86, viajou para Hamburgo para estudar microrganismos relacionados a doenças de pele sob a orientação de Paul Gerson Unna, um dos mais renomados dermatologistas alemães. Propôs a inclusão dos bacilos de Hansen e Koch num novo gênero. Em 1889, Unna indicou seu discípulo como chefe dos serviços médicos dos Leprosário Molokai, no Havaí. Lutz passou a defender a transmissão da doença por mosquitos. Realizou pesquisas para provar esta teoria depois que assumiu a chefia do Instituto Bacteriológico de São Paulo (1893-1908) e, sobretudo, após a transferência para o Instituto Oswaldo Cruz (1908-1940).

CUETO, M.; DE LA PUENTE, J.C. Vida de leprosa: the testimony of a woman living with Hansen's disease in the Peruvian Amazon, 1947. *Hist. ciênc. saúde-Manguinhos*; v.10, supl.1, p.:337-360, 2003.

Este es un testimonio de una paciente antes, durante y después de su internamiento en una colonia agrícola de la Amazonía peruana. Narra de una manera vívida el deterioro del cuerpo, el estigma y la segregación compulsiva, así como la esperanza de una vida mejor. Es la perspectiva de un paciente, algo que no es fácil de encontrar en el trabajo histórico sobre la salud.

FONTOURA, A.A.; BARCELOS, A.H.F.; BORGES, V.T. Revealing a history of exclusion: the experience at Hospital Colonia Itapuã. Data and Research Center. *Hist. ciênc. saúde-Manguinhos*; v.10, supl.1, p.397-414, 2003.

Fundado em maio de 1940, no município de Viamão, Rio Grande do Sul, o Hospital Colônia Itapuã foi criado para abrigar os portadores do mal de Hansen. Construído para funcionar como uma microcidade, o hospital foi palco de inúmeras histórias de vida e trabalho. Os fragmentos destas trajetórias coletivas e individuais estão sendo resgatados desde 1999, quando foi implementado o Centro de Documentação e Pesquisa (Cedope/HCI). É através das atividades desse centro que propõe apresentar uma aproximação com a história do hospital e daqueles que viveram e ainda vivem nesta instituição.

JOSEPH, G.D. "Essentially christian eminently philanthropic": The mission to lepers in British India. *Hist. ciênc. saúde-Manguinhos* v.10, supl.1, p.247-275, 2003.

A história antiga da Missão para Leprosos na Índia é a história das relações entre a política, a religião e a medicina, dentro do contexto do imperialismo britânico. A Missão perseguia o par de objetivos inseparáveis da evangelização e da civilização, desenvolvendo não só um programa religioso, como também um político e cultural. Tais atividades e suas conseqüências eram multifacetadas, porque enquanto os missionários seguiam sua vocação religiosa, eles também forneciam cuidados médicos a pessoas e lugares que o governo colonial não podia ou queria atender. Dentro do contexto do programa imperial britânico, o trabalho dos missionários passava ideais sociais e culturais ocidentais para as populações a que serviam, inculcando nos pacientes as crenças cristãs e oferecendo cuidados médicos a indivíduos que haviam sido expulsos de suas comunidades. A cura do físico estava intimamente ligada à salvação da alma, à cura espiritual e ao processo civilizatório.

LEVISON, J.H. Beyond quarantine: a history of leprosy in Puerto Rico, 1898-1930s. *Hist. ciênc. saúde-Manguinhos*; v.10, supl.1, p.:225-245, 2003.

Usa fontes primárias, escritas em espanhol, para reconstruir a história social da lepra em Porto Rico a partir de 1898, quando os Estados Unidos anexaram a ilha a seu território. As políticas de saúde pública desenvolvidas em Porto Rico até a década de 1930 foram específicas, devido a uma combinação de fatores políticos, científicos e sociais. O país sofreu a influência das prioridades sanitárias dos Estados Unidos e desenvolveu suas políticas de controle da lepra sobre os vestígios do sistema de saúde da Espanha colonial. No início da ocupação norte-americana, extrema segregação agrediu a liberdade e os direitos individuais dos pacientes, em nome da proteção à sociedade. Como resultado, as vidas desses hansenianos foram irrevogavelmente transformadas.

LU, H.M. [A study on the measures against Hansen's disease during the Colonial Korea]. *Nippon Ishigaku Zasshi*; v.49, n.2, p.223-61, Jul., 2003.

In order to evaluate the measures taken against Hansen's diseases during the colonial era in Korea, from 1910-1945, I analyzed both Korean and Japanese materials and carried out field research. The Korean government-general established a hospital in 1916 and executed measures against Hansen's disease. These efforts can be divided into three periods. At first they started as a part of colonial policy. Then, in the middle period, with the change of Japanese policy on Hansen's disease, a Korean association was established and the Hansen's Disease Prevention Act was issued in Korea, aiming at the compulsory isolation of lepers. In the later period, during the war, the inmates were forced into an extremely severe environment and deprived of their human rights. My study shows that their policies changed greatly with the passage of time. Though they started them to relieve the suffering of the lepers in the beginning, they turned to be compulsory isolation of the patients in the later period and to the violation of their human rights.

MACIEL, L.R.; OLIVEIRA, OLIVEIRA, M.L.W.D.R.; GALLO, M.E.N.; DAMASCO, M.S. Memories and history of Hansen's disease in Brazil told by witnesses (1960-2000). *Hist. ciênc. saúde-Manguinhos*;10(supl.1):308-336, 2003.

Resultado preliminar de pesquisa sobre memória e história da hanseníase, desenvolvida pela Fundação Oswaldo Cruz (Fiocruz) e Universidade Federal do Rio de Janeiro (UFRJ), através de depoimentos de quem padeceu da doença ou atuou contra ela. Apresenta as opções metodológicas adotadas pelos autores, um sucinto histórico da hanseníase no Brasil e dados a

respeito do estágio em que se encontra a pesquisa, com extratos de depoimentos que constituem o acervo gerado.

MANTON, J. Global and local contexts: the northern Ogoja leprosy scheme, Nigeria, 1945-1960. *Hist. ciênc. saúde-Manguinhos*; v.10, supl.1, p.209-223, 2003.

A missão católica Ogoja Leprosy Scheme aplicou, em nível local, os conhecimentos internacionais de ponta em lepra, com sucesso e resultados abrangentes, graças ao apoio financeiro de instituições missionárias da Irlanda, da Grã-Bretanha e dos Estados Unidos, assim como de organizações internacionais como o British Empire Leprosy Relief Association (BELRA). Tirou proveito também de avanços ocorridos no domínio da saúde pública internacional sob os auspícios da OMS e Unicef, na década 1950. O presente artigo combina a apresentação de um bem sucedido programa de controle da lepra, por obra de missionários, com a análise sobre como as políticas médicas internacionais modelaram os parâmetros de sucesso e desenvolvimento de conhecimentos terapêuticos na Nigéria, no final do período colonial.

MONTEIRO, Y.N. Prophylaxis and exclusion: compulsory isolation of Hansen's disease patients in São Paulo. *Hist. ciênc. saúde-Manguinhos*; v.10, supl.1, p.:95-121, 2003.

Busca resgatar a história da hanseníase no Brasil, analisando o pensamento médico e o direcionamento das políticas de saúde que possibilitaram a implantação, em São Paulo, de uma política profilática centrada na exclusão compulsória de todos os portadores de hanseníase. Analisa ainda como a estruturação e implantação dessa política resultou no 'modelo paulista', que exerceu forte influência no país. Estuda a formação da rede asilar, as suas características e o surgimento de um verdadeiro 'Estado paralelo', que subsistiu até 1967, à revelia das descobertas terapêuticas e das modificações havidas no direcionamento das formas de tratamento e prevenção nacional e internacional.

OBREGÓN, D. The anti-leprosy campaign in Colombia: the rhetoric of hygiene and science, 1920-1940. *Hist. ciênc. saúde-Manguinhos*; v.10, (supl.1), p.179-207, 2003.

Desde a década de 1920, a comunidade médica percebeu que o controle da hanseníase baseada na segregação dos pacientes era ineficaz e dispendiosa. Na década de 1930, o novo governo, mais liberal, incorporou a hanseníase às instituições sanitárias gerais, ao fundir o Serviço de Leprosários ao Departamento Nacional de Higiene. O isolamento começou a ser substituído por uma estratégia geral de saúde pública, que envolvia outras doenças.

PANDYA, S.S. The first international Leprosy Conference, Berlin, 1897: the politics of segregation. *Hist. ciênc. saúde-Manguinhos*; v.10, supl.1, p.161-177, 2003.

Esse artigo analisa as primeiras tentativas de internacinalização do problema da lepra. A última década do século XIX viu muitas pessoas no Ocidente imperialista viverem o medo de uma invasão de lepra via imigrantes. Tais alarmistas clamavam pela adoção de uma forte política segregacionista para os leprosos em suas colônias. A convocação em Berlim do primeiro encontro internacional sobre lepra revelou a existência de visões diferentes e algumas vezes incompatíveis em relação ao combate à lepra através da segregação. O papel das instituições oficiais de diversos países e, principalmente os diferentes papéis de cinco protagonistas da Conferência de Berlim são aqui examinados.

ROBERTSON, J.O. Leprosy and the elusive *M. Leprae*: colonial and imperial medical exchanges in the nineteenth century. *Hist. ciênc. saúde-Manguinhos*; v.10, supl.1, p.13-40, 2003.

No século XIX, abordagens humorais da lepra deram origem a sucessivos modelos da doença baseados na anatomia patológica, na fisiopatologia e na bacteriologia. As relações entre esses modelos da doença foram reforçadas pela onipresente metáfora 'da semente e do solo', difundida tanto antes quanto depois da identificação do *M. Leprae*. A época em que a metáfora fornecia um elo de ligação contínuo entre as várias descrições médicas da doença, Henry Vandyke Carter publicava *On leprosy* (1874), estabelecendo uma convergência de seus diferentes modelos. Simultaneamente, a metáfora se fazia presente nos debates médicos e populares de fins do século XIX, juntamente com o medo do surgimento da lepra na Europa. Mais recentemente, o mapeamento do genoma humano determinou a formulação de um novo modelo para a doença. Mas, ironicamente, enquanto as pesquisas concernentes a ela se apóiam numa visão de mundo em que a metáfora da semente e do solo ainda expressa diferentes aspectos da ação da doença, o próprio bacilo permanece refratário a todos os esforços visando seu cultivo.

SANTOS, V.S.M. Researching documents on the history of Hansen's disease in Brazil. *Hist. ciênc. saúde-Manguinhos*, v.10, supl.1, p.415-426, 2003.

Apresenta resultados parciais de uma pesquisa sobre fontes relativas à lepra, realizada em diversas instituições da cidade do Rio de Janeiro. No Real Gabinete Português de Leitura, no Arquivo Nacional e na Biblioteca Nacional foram pesquisados livros, índices, ofícios e fotografias sobre administração de leprosários e artigos sobre o tratamento da doença. No Centro de Pesquisa e Documentação de História Contemporânea do Brasil (CPDOC-FGV) foram consultados

diversos arquivos, destacando-se as informações referentes à política de saúde adotada durante o primeiro governo Vargas (1930-45). A pesquisa integra o acervo da International Leprosy Association Global Project on the History of Leprosy, e os resultados podem ser consultados no site <http://www.leprosyhistory.org>.

SMITH III, T.H. A monument to Lazarus: the leprosy hospital of Rio de Janeiro. *Hist. ciênc. saúde-Manguinhos*; v.10, supl.1, p.143-160, 2003.

A história desse hospital é uma fonte de conhecimento sobre as relações complexas existentes entre os cidadãos, a Igreja e o Estado. O hospital atualmente chamado Frei Antônio teve importante papel na evolução de profissões ligadas à saúde, no progresso das ciências médicas e na gênese do movimento higienista no Brasil. Esse estudo também contribui para a história de uma doença que persiste no Brasil de 2003 como questão sanitária.

WHITE, C. Carville and Curupaiti: experiences of confinement and community. *Hist. ciênc. saúde-Manguinhos*; v.10, supl.1, p.123-141, 2003.

Apresenta uma breve história da política do isolamento e do desenvolvimento de estruturas comunitárias em duas instituições, Carville e Curupaiti, nos Estados Unidos e no Brasil, respectivamente. Os dilemas modernos frente à administração, às equipes e aos residentes destas instituições também serão discutidos.

## HISTÓRIA/ANTROPOLOGIA

BUCKLEY, H.R; TAYLES, N. Skeletal pathology in a prehistoric Pacific Island sample: issues in lesion recording, quantification, and interpretation. *Am J Phys Anthropol*; v.122, n.4, p.303-24, Dec. 2003.

This paper presents a profile of evidence of disease in a skeletal sample from Taumako Island, Southeast Solomon Islands, Melanesia, and aims to increase awareness of the prehistoric Pacific Island disease environment. It also addresses issues of lesion recording, quantification, and interpretation. Two methodologies for the determination of lesion prevalence were applied, one based on prevalence in observable individuals and one in skeletal elements. The aim of these methodologies was to provide objective data on skeletal lesions in this sample, with transparency in methods for application in comparative studies. The types of lesions observed were predominantly osteoblastic and affecting multiple bones, particularly in the lower limbs. The individual analysis yielded a prevalence of lesions affecting 56.4% of the postcranial sample from birth to old age. As expected, the skeletal element analysis

yielded a lower prevalence, with 15.0% of skeletal elements affected. The skeletal element analysis also revealed a pattern of greater lower limb involvement, with a predilection for the tibia. The pattern of skeletal involvement was similar in both analyses, suggesting the validity of employing either method in paleopathological studies. A differential diagnosis of the lesions included osteomyelitis, treponemal disease, and leprosy. Metabolic disease was also considered for subadult lesions. Based on lesion type, skeletal distribution, and epidemiology of lesions in the sample, an etiology of yaws (*Treponema pertenuis*) was suggested as responsible for nearly half the adult lesions, while multiple causes, including yaws, were suggested for the lesions in subadults.

## IMUNOGENÉTICA

KRUTZIK, S.R.; OCHOA, M.T.; SIELING, P.A.; UEMATSU, S.; NG Y.W.; LEGASPI, A.; LIU, P.T.; COLE, S.T.; GODOWSKI, P.J.; MAEDA, Y.; SARNO, E.N.; NORGARD, M.V.; BRENNAN, P.J.; AKIRA, S.; REA, T.H.; MODLIN, R.L. Activation and regulation of Toll-like receptors 2 and 1 in human leprosy. *Nat Med.*, v.9, n.5, p.525-32, May 2003.

The expression and activation of Toll-like receptors (TLRs) was investigated in leprosy, a spectral disease in which clinical manifestations correlate with the type of immune response mounted toward *Mycobacterium leprae*. TLR2-TLR1 heterodimers mediated cell activation by killed *M. leprae*, indicating the presence of triacylated lipoproteins. A genome-wide scan of *M. leprae* detected 31 putative lipoproteins. Synthetic lipopeptides representing the 19-kD and 33-kD lipoproteins activated both monocytes and dendritic cells. Activation was enhanced by type-1 cytokines and inhibited by type-2 cytokines. In addition, interferon (IFN)-gamma and granulocyte-macrophage colony-stimulating factor (GM-CSF) enhanced TLR1 expression in monocytes and dendritic cells, respectively, whereas IL-4 downregulated TLR2 expression. TLR2 and TLR1 were more strongly expressed in lesions from the localized tuberculoid form (T-lep) as compared with the disseminated lepromatous form (L-lep) of the disease. These data provide evidence that regulated expression and activation of TLRs at the site of disease contribute to the host defense against microbial pathogens.

## IMUNOLOGIA

BÜHRER-SÉKULA, S.; SMITS, H.L.; GUSSENHOVEN, G.C.; VAN LEEUWEN, J.; AMADOR, S.; FUJIWARA, T.; KLATSER, P.R.; OSKAM, L. Simple and fast lateral flow test for classification of leprosy patients and identification of contacts with high risk of developing leprosy. *J Clin Microbiol.*, v.41, n.5, p.1991-5, May 2003.

The interruption of leprosy transmission is one of the main challenges for leprosy control programs since no consistent evidence exists that transmission has been reduced after the introduction of multidrug therapy. Sources of infection are primarily people with high loads of bacteria with or without clinical signs of leprosy. The availability of a simple test system for the detection of antibodies to phenolic glycolipid-I (PGL-I) of *Mycobacterium leprae* to identify these individuals may be important in the prevention of transmission. We have developed a lateral flow assay, the ML Flow test, for the detection of antibodies to PGL-I which takes only 10 min to perform. An agreement of 91% was observed between enzyme-linked immunosorbent assay and our test; the agreement beyond chance (kappa value) was 0.77. We evaluated the use of whole blood by comparing 539 blood and serum samples from an area of high endemicity. The observed agreement was 85.9% (kappa = 0.70). Storage of the lateral flow test and the running buffer at 28 degrees C for up to 1 year did not influence the results of the assay. The sensitivity of the ML Flow test in correctly classifying MB patients was 97.4%. The specificity of the ML Flow test, based on the results of the control group, was 90.2%. The ML Flow test is a fast and easy-to-perform method for the detection of immunoglobulin M antibodies to PGL-I of *M. leprae*. It does not require any special equipment, and the highly stable reagents make the test robust and suitable for use in tropical countries.

HERNANDEZ, M.O.; NEVES, I.; SALES, J.S.; CARVALHO, D.S.; SARNO, E.N.; SAMPAIO, E.P. Induction of apoptosis in monocytes by *Mycobacterium leprae* in vitro: a possible role for tumour necrosis factor-alpha. *Immunology*, v.109, n.(, p.156-64, May 2003.

A diverse range of infectious organisms, including mycobacteria, have been reported to induce cell death in vivo and in vitro. Although morphological features of apoptosis have been identified in leprosy lesions, it has not yet been determined whether *Mycobacterium leprae* modulates programmed cell death. For that purpose, peripheral blood mononuclear cells obtained from leprosy patients were stimulated with different concentrations of this pathogen. Following analysis by flow cytometry on 7AAD/CD14+ cells, it was observed that *M. leprae* induced apoptosis of monocyte-derived macrophages in a dose-dependent manner in both leprosy patients and healthy individuals, but still with lower efficiency as compared to *M. tuberculosis*. Expression of tumour necrosis factor-alpha (TNF-alpha), Bax-alpha, Bak mRNA and TNF-alpha protein was also detected in these cultures; in addition, an enhancement in the rate of apoptotic cells (and of TNF-alpha release) was noted when interferon-gamma was added to the wells. On the other hand, incubation of the cells with pentoxifylline impaired mycobacterium-induced cell death, the secretion of TNF-alpha, and gene expression in vitro.



In addition, diminished bacterial entry decreased both TNF-alpha levels and the death of CD14+ cells, albeit to a different extent. When investigating leprosy reactions, an enhanced rate of spontaneous apoptosis was detected as compared to the unreactive lepromatous patients. The results demonstrated that *M. leprae* can lead to apoptosis of macrophages through a mechanism that could be at least partially related to the expression of pro-apoptotic members of the Bcl-2 protein family and of TNF-alpha. Moreover, while phagocytosis may be necessary, it seems not to be crucial to the induction of cell death by the mycobacteria.

KISZEWSKI, C.A.; BECERRIL, E.; BAQUERA, J.; AGUILAR, L.D.; HERNÁNDEZ-PANDO, R. Expression of transforming growth factor-beta isoforms and their receptors in lepromatous and tuberculoid leprosy. *Scand J Immunol*; v.57,n.3, p.279-85, Mar. 2003.

Leprosy is an infectious disease with two polar forms, tuberculoid leprosy (TT) and lepromatous leprosy (LL), that are characterized by strong cell-mediated immunity (CMI) and CMI anergy, respectively. Transforming growth factor-beta (TGF-beta) belongs to a family of pleiotropic cytokines (TGF-beta1, TGF-beta2 and TGF-beta3) that participate in the control of cell differentiation and proliferation, as well as tissue repair. This cytokine family is unique because it suppresses CMI. In this study, we compared the expression of the three TGF-beta isoforms and their receptors in skin biopsies from LL and TT patients (LL = 20; TT = 20) using immunohistochemistry and automated morphometry. The percentage of cells immunostained for the three TGF-beta isoforms and cells positive for the three TGF-beta receptors in the inflammatory infiltrate located in the papillary dermis, reticular dermis and periadnexal tissue were significantly higher in LL than that in TT, with macrophages being the most common and strongest immunoreactive cells. Some lymphocytes, fibroblasts, keratinocytes and epithelial cells from sweat glands and hair roots were also positive. In situ reverse-transcription polymerase chain reaction corroborated the capacity of these cells to synthesize TGF-beta1 and TGF-beta receptor 2. This high expression of TGF-beta isoforms and their receptors could contribute to CMI anergy and other clinical characteristic features of leprosy, like skin atrophy.

LOIZOU, S.; SINGH, S.; WYPKEMA, E.; ASHERSON, R.A. Anticardiolipin, anti-beta(2)-glycoprotein I and antiprothrombin antibodies in black South African patients with infectious disease. *Ann Rheum Dis.*, v.62, n.11, p.1106-11, Nov. 2003.

OBJECTIVES: To investigate IgG, IgM, and IgA, antiphospholipid antibodies (aPL), against cardiolipin (aCL), beta(2)-glycoprotein I (anti-beta(2)GPI), and prothrombin (anti-PT), in black South African patients with infectious disease. Unlike

patients with systemic lupus erythematosus (SLE) and the antiphospholipid syndrome (APS), raised levels of aPL in infectious diseases are not usually associated with thrombotic complications. PATIENTS AND METHODS: Serum samples from 272 patients with a variety of infectious diseases (100 HIV positive, 112 leprosy, 25 syphilis, 25 malaria, and 10 HCV patients) were studied and compared with autoantibody levels in 100 normal controls. All three aPL were measured using commercial enzyme linked immunosorbent assay (ELISA) kits. RESULTS: Raised levels of all three aPL were found in all patient groups studied: aCL in 7%, anti-beta(2)GPI in 6%, and aPT in 43% of 100 HIV patients, in 29%, 89%, and 21% of 112 patients with leprosy, in 8%, 8%, and 28% of 25 patients with syphilis, in 12%, 8%, and 28% of 25 patients with malaria, and in 20%, 30%, and 30% of 10 HCV patients studied, respectively. CONCLUSIONS: The prevalence of aCL and anti-beta(2)GPI in black South African HIV positive patients, or those with syphilis, malaria, or hepatitis C virus is lower than reported for mixed race or white populations. aPT were the most prevalent aPL detected in these patient groups, except in patients with leprosy, for whom anti-beta(2)GPI was the most prevalent, and where the spectrum of aPL was similar to that seen in patients with SLE and APS.

NGAMYING, M.; SAWANPANYALERT, P.; BUTRAPORN, R.; NIKASRI, J.; CHO, S.N.; LEVY, L.; BRENNAN, P.J. Effect of vaccination with refined components of the organism on infection of mice with *Mycobacterium leprae*. *Infect Immun*; v.71,n.3,p.1596-8, Mar. 2003.

Only native products of *Mycobacterium leprae*, whether cell wall, cytosol, or membrane derived, can confer protective immunity against challenge in the mouse footpad. Previously, recombinant proteins were shown to be ineffective. The cell wall skeleton-the mycolyl-arabinogalactan-peptidoglycan complex-devoid of proteins is not protective.

OLIVEIRA, R.B.; OCHOA, M.T.; SIELING, P.A.; REA, T.H.; RAMBUKANA, A.; SARNO, E.N.; MODLIN, R.L. Expression of Toll-like receptor 2 on human Schwann cells: a mechanism of nerve damage in leprosy. *Infect Immun*; v. 71, n.3, p.1427-33, Mar 2003.

Nerve damage is a clinical hallmark of leprosy and a major source of patient morbidity. We investigated the possibility that human Schwann cells are susceptible to cell death through the activation of Toll-like receptor 2 (TLR2), a pattern recognition receptor of the innate immune system. TLR2 was detected on the surface of human Schwann cell line ST88-14 and on cultured primary human Schwann cells. Activation of the human Schwann cell line and primary human Schwann cell cultures with a TLR2 agonist, a synthetic lipopeptide comprising the N-terminal portion of the putative *Mycobacterium leprae* 19-kDa lipoprotein, triggered an

increase in the number of apoptotic cells. The lipopeptide-induced apoptosis of Schwann cells could be blocked by an anti-TLR2 monoclonal antibody. Schwann cells in skin lesions from leprosy patients were found to express TLR2. It was possible to identify in the lesions Schwann cells that had undergone apoptosis in vivo. The ability of *M. leprae* ligands to induce the apoptosis of Schwann cells through TLR2 provides a mechanism by which activation of the innate immune response contributes to nerve injury in leprosy.

OSKAM, L.; SLIM, E.; BÜHRER-SÉKULA, S. Serology: recent developments, strengths, limitations and prospects: a state of the art overview. *Lepr Rev.*, v.74, n.3, p.196-205, Sep., 2003.

Specific antibodies can be used as a surrogate marker for bacterial load in leprosy. Tests to detect antibodies can be used for (i) the classification of patients for treatment purposes [most multibacillary (MB) patients are seropositive, most paucibacillary (PB) patients are not], (ii) the prediction of an increased risk of relapse and (iii) the identification of contacts having an increased risk of developing leprosy. With the advent of fast, robust and easy to perform serological tests such as lateral flow, agglutination and card tests, the application of serology in the field for these purposes becomes a feasible prospect. We hereby present an overview of the current knowledge and new developments in this area and discuss the strengths, limitations and possible applications of antibody detection in leprosy research and control.

## IMUNOLOGIA E GENÉTICA

BOCHUD, P.Y.; HAWN, T.R.; ADEREM, A. Cutting edge: a Toll-like receptor 2 polymorphism that is associated with lepromatous leprosy is unable to mediate mycobacterial signaling. *J Immunol*; v.170, n.7, p.3451-4, Apr. 2003.

Toll-like receptors (TLRs) are key mediators of the innate immune response to microbial pathogens. We investigated the role of TLRs in the recognition of *Mycobacterium leprae* and the significance of TLR2Arg(677)Trp, a recently discovered human polymorphism that is associated with lepromatous leprosy. In mice, TNF-alpha production in response to *M. leprae* was essentially absent in TLR2-deficient macrophages. Similarly, human TLR2 mediated *M. leprae*-dependent activation of NF-kappaB in transfected Chinese hamster ovary and human embryonic kidney 293 cells, with enhancement of this signaling in the presence of CD14. In contrast, activation of NF-kappaB by human TLR2Arg(677)Trp was abolished in response to *M. leprae* and *Mycobacterium tuberculosis*. The impaired function of this TLR2 variant provides a molecular mechanism for the poor cellular immune response associated with lepromatous leprosy and may have important implications for understanding the pathogenesis of other mycobacterial infections.

MIRA, M.T.; ALCAIS, A.; DI PIETRANTONIO, T.; THUC, N.V.; PHUONG, M.C.; ABEL, L.; SCHURR, E. Segregation of HLA/TNF region is linked to leprosy clinical spectrum in families displaying mixed leprosy subtypes. *Genes Immun*; v.4, n.1, p.67-73, Jan. 2003

Each year an estimated 600000 new leprosy cases are diagnosed worldwide. The spectrum of the disease varies widely from limited tuberculoid forms to extensive lepromatous forms. A measure of the risk to develop lepromatous forms of leprosy is provided by the extent of skin reactivity to lepromin (Mitsuda reaction). To address a postulated oligogenic control of leprosy pathogenesis, we investigated in the present study linkage of leprosy susceptibility, leprosy clinical subtypes, and extent of the Mitsuda reaction to six chromosomal regions carrying known or suspected leprosy susceptibility loci. The only significant result obtained was linkage of leprosy clinical subtype to the HLA/TNF region on human chromosome 6p21 ( $P(\text{corrected})=0.00126$ ). In addition, we established that within the same family different HLA/TNF haplotypes segregate into patients with different leprosy subtypes directly demonstrating the importance of this genome region for the control of clinical leprosy presentation.

## IMUNOPATOLOGIA

AMAKO, K.; TAKADE, A.; UMEDA, A.; MATSUOKA, M.; YOSHIDA, S.; NAKAMURA, M. Degradation process of *Mycobacterium leprae* cells in infected tissue examined by the freeze-substitution method in electron microscopy. *Microbiol Immunol*; v.47, n.6, p.387-94, 2003.

*Mycobacterium leprae* cells (strain Thai-53) harvested from infected mouse foot pads were examined by electron microscopy using the freeze-substitution technique. The population of *M. leprae* cells from the infected tissue consisted of a large number of degraded cells and a few normal cells. These thin sectioned cell profiles could be categorized into four groups depending on the alteration of the membrane structures, and the degradation process is considered to occur in stages, namely from stages 1 to 3. These are the normal cells with an asymmetrical membrane, a seemingly normal cell but with a symmetrical membrane (stage 1), a cell possessing contracted and highly concentrated cytoplasm with a membrane (stage 2), and a cell that has lost its membrane (stage 3). The peptidoglycan layer was found to remain intact in these cell groups.

ANTUNES, S.L.; LIANG, Y.; NERI, J.A.; SARNO, E.N.; HAAK-FRENDSCHO, M.; JOHANSSON, O. Mast cell subsets and neuropeptides in leprosy reactions. *Arq Neuropsiquiatr*; 61(2A):208-19, 2003.

The immunohistochemical identification of neuropeptides (calcitonin gene-related peptide, vasoactive intestinal

polypeptide, substance P, alpha-melanocyte stimulating hormone and gamma-melanocyte stimulating hormone) quantification of mast cells and their subsets (tryptase/chymase-immunoreactive mast cells = TCMC and tryptase-immunoreactive mast cells = TMC) were determined in biopsies of six patients with leprosy reactions (three patients with type I reaction and three with type II). Biopsies were compared with those taken from the same body site in the remission stage of the same patient. We found a relative increase of TMC in the inflammatory infiltrate of the reactional biopsies compared to the post-reactional biopsy. Also, the total number of mast cells and the TMC/TCMC ratio in the inflammatory infiltrate was significantly higher than in the intervening dermis of the biopsies of both periods. No significant difference was found regarding neuropeptide expression in the reactional and post-reactional biopsies. The relative increase of TMC in the reactional infiltrates could implicate this mast cell subset in the reported increase of the immune response in leprosy reactions.

ANTUNES, S.L.; LIANG, Y; NERI, J.A.; HAAK-FRENDSCHO, M.; JOHANSSON, O. The expression of NGFr and PGP 9.5 in leprosy reactional cutaneous lesions: an assessment of the nerve fiber status using immunostaining. *Arq Neuropsiquiatr.*, v.61, n.2B, p.346-52, Jun. 2003.

The effects of reactional episodes on the cutaneous nerve fibers of leprosy patients was assessed in six patients (three with reversal reactions and three with erythema nodosum leprosum). Cryosections of cutaneous biopsy of reactional lesions taken during the episode and of another sample during the remission period were immunostained with anti-NGFr and anti-PGP 9.5 (indirect immunofluorescence). We found no significant statistical difference in the number of NGFr- and PGP 9.5-positive fibers between the reactional and post-reactional groups. A significant difference was detected between the number of NGFr and PGP 9.5-stained fibers inside of the reactional group of biopsy cryosections but this difference was ascribed to the distinct aspects of the nerve fibers displayed whether stained with anti-NGFr or with anti-PGP 9.5; NGFr-positive branches looked larger and so interpreted as containing more fibers. In addition, a substantial number NGFr-positive fibers were PGP 9.5-negative. No differences in the number of stained fibers among the distinct cutaneous regions examined (epidermis + upper dermis, mid and deep dermis) was detected. In conclusion, the number of PGP- and NGFr-positive fibers were not significantly different in the reactional and post-reactional biopsies in the present study. NGFr-staining of the nerve fibers is different from their PGP-immunoreactivity and the evaluation of the nerve fiber status on an innervated target organ should be carried out choosing markers for both components of nerve fibers (Schwann cells and axons).

CAMARGO, L.H.; CALDAS, M.L.; NEIRA, M.; SARMIENTO, L. Utilización de análisis de imágenes para cuantificar células dendríticas S100 positivas en piel con lepra.. [Image analysis to quantify S100-positive dendritic cells in leprosy-affected skin]. *Biomedica*, v.23, n.2, p.131-3, Jun. 2003.

A morphometric analysis of skin dendritic cells was done on biopsies of patients with different forms of leprosy. An anti S100 antibody was used to determine dendritic cell quantity and extension. Patients with a better immune response to the bacillus showed a greater number of dendritic cells in the cases of dimorphic tuberculoid leprosy and tuberculoid leprosy. This result contrasted with that from patients with dimorphic lepromatous leprosy and lepromatous leprosy.

FAKHOURI, R.; SOTTO, M.N.; MANINI, M.I.; MARGARIDO, L.C. Nodular leprosy of childhood and tuberculoid leprosy: a comparative, morphologic, immunopathologic and quantitative study of skin tissue reaction. *Int. J. Lepr.*; v.71, 3, p.218-26, Sep. 2003.

Nodular leprosy of childhood (NL) is a benign clinical variant of tuberculoid leprosy that affects breast-feeding infants and children that remained in a highly infected environment. The lesions resolve with complete healing and NL has been considered a manifestation of allergy and congenital immunity to *Mycobacteria leprae*. We studied the tissue reaction, Mycobacterial antigen frequency, and the lymphocyte subsets (CD45RO+, CD4+, CD8+, B, NK), dendritic cells (epidermal CD1a+ cells and S100+ dermal dendrocytes), and macrophages in skin lesions of a clinically well characterized NL group (N = 11). Results were compared to children (N = 23) and adults (N = 24) with classical tuberculoid leprosy. NL lesion histopathology was characterized by dense granulomatous inflammatory reaction, with a greater number of confluent tubercles when compared to the other groups. Neural compromise was seen in all biopsies. The frequency of Mycobacterium antigen was similar in all groups. The population of CD45RO+, CD4+ and CD8+ T lymphocytes, natural killer cells, B lymphocytes, CD1a+ epidermal cells, and macrophages of NL lesions did not differ from the other groups. The number of S100+ dermal dendritic cells of the NL group was smaller than that of the adult group, although it did not differ from the other group of children. Except for the confluent tubercles, our data could not disclose any other difference in the tissue reaction of NL, in spite of its peculiar clinical features and evolution when compared with the classical tuberculoid leprosy. The localization of NL lesions may be the result of the intimate skin contact with lepromatous parents or relatives, in areas such as cheeks, arms, buttocks, and limbs, and the inoculation of *M. leprae* into skin may strongly stimulate cell mediated immunity (CMI) against the bacilli. These circumstances might explain the good CMI response leading to high resistance, stability.

KISZEWSKI, A.E.; BECERRIL, E.; BAQUERA, J.; RUIZ-MALDONADO, R.; HERNÁNDEZ PANDO, R. Expression of cyclooxygenase type 2 in lepromatous and tuberculoid leprosy lesions. *Br J Dermatol.*, v.148, n.4, p.795-8, Apr. 2003

**BACKGROUND:** Leprosy is an infectious disease with two polar forms, tuberculoid leprosy (TL) and lepromatous leprosy (LL), which are dominated by T-helper (Th) 1 and Th2 cells, respectively. High concentrations of prostaglandin E2 produced by the inducible enzyme cyclooxygenase type 2 (COX-2) in LL could inhibit Th1 cytokine production, contributing to T-cell anergy. **OBJECTIVES:** To compare the COX-2 expression in LL and TL. **METHODS:** Skin biopsies from 40 leprosy patients (LL, n = 20; TL, n = 20) were used to determine by immunohistochemistry and automated morphometry the percentage of COX-2 immunostained cells. **RESULTS:** Most COX-2-positive cells were macrophages; their percentages in the inflammatory infiltrate located in the papillary dermis, reticular dermis and periadnexally were significantly higher in LL than TL (P < 0.001 by Student's t-test). **CONCLUSIONS:** The high expression of COX-2 in LL may be related to high prostaglandin production contributing to T-cell anergy.

MAEDA, S.M.; ROTTA, O.; MICHALANY, N.S.; CAMARGO, Z.P.; SUNDERKÖTTER, C.; TOMIMORI-YAMASHITA, J. Comparison between anti-PGL-I serology and Mitsuda reaction: clinical reading, microscopic findings and immunohistochemical analysis. *Lepr Rev.*, v.74, n.3, p.263-74, Sep., 2003.

The lepromin test, serum IgM antibodies against *Mycobacterium leprae* and in situ observations of T cell subsets in biopsies of Mitsuda reaction using monoclonal antibodies were performed on 44 untreated leprosy patients belonging to various classifications of the disease. The Mitsuda reaction was assessed clinically and histologically after 28 days. Clinical reading and histological analysis of Mitsuda reaction showed good agreement. The high positivity in clinical reading correlated with compact granulomas in histology. There is a graduation of Mitsuda reaction that follows the immunological spectrum of the disease. The histological study of Mitsuda reaction is valuable to confirm the immunological condition in doubtful clinical reaction. Anti-PGL-I IgM levels correlated with disease classification, increasing from the tuberculoid towards the lepromatous pole of the disease spectrum. There was an inverse correlation between serum IgM antibody levels and clinical and histological reading of Mitsuda reaction. There were no statistical difference in quantities and distribution of CD4+ and CD8+ T cells in all Mitsuda reactions. The pattern of cellular content of Mitsuda reaction could not be related to the T cells.

## INFECCÃO EXPERIMENTAL

JOB, C.K.; MCCORMICK, G.T.; SCOLLARD, D.M.; TRUMAN, R.W. Electron microscopic appearance of lepromatous foodpads of nude mice. *Int J Lepr.*, v. 71, n.3, p.231-9, Sep. 2003.

Footpad lesions of 3 nude mice infected by *Mycobacterium leprae* were studied at 9, 12, and 14 months after inoculation with light and electron microscope. The lesions were somewhat similar to those found in nodules in polar lepromatous leprosy. Striated muscles rather than nerves were the preferred site of the growth of *M. leprae*. Yet, *M. leprae* were identified in Schwann cells and endothelial cells, singly and in clumps. *M. leprae* filled macrophages, and free *M. leprae* were found in large numbers in the endoneurium without producing any significant demyelination.

## LABORATÓRIO

RADA, E.; MARZAL, M.; ARANZAZU, N.; CONVIT, J. Incremento de óxido nítrico en el suero y sobrenadantes de cultivo de células mononucleares de pacientes con la enfermedad de Hansen en estado reaccional tipo II. [Increase in nitric oxide concentrations in serum and mononuclear cell cultures from patients with Type II reaction state of Hansen's disease]. *Invest Clin.*, v.44, n.2, p.129-36, Jun. 2003.

The word "reaction" is used in leprosy to describe signs and symptoms of acute inflammation. Type II reactions, including erythema nodosum leprosum (ENL) occur in the multibacillary forms of Hansen's disease. Nitric oxide (NO) could play a role in the response of the host, where a high NO production would be involved in acute inflammatory processes. In this paper we evaluate NO production in serum and in the supernatants of mononuclear cell cultures (MNCC), measured indirectly by Griess' method. The results obtained in serum showed that 52% of patients with ENL (15/29) had a production over 30 microM, distributed as follows: 8/15 had a mean concentration of 36.38 +/- 25.71 microM; 1/15, 70.5 microM and 6/15 had a mean concentration greater than 100 microM (205.97 +/- 5 microM). Forty eight percent presented nitrite and nitrate levels lower than 30 microM (18.93 +/- 6.15). Only supernatants of mononuclear cell cultures from ENL patients collected at 120 hours of incubation presented NO production levels higher than 10 microM +/- 6.53, as compared with the supernatants from the stable polar forms of the disease (lepromatous leprosy and tuberculoid leprosy), where values were 2.52 microM +/- 1.18 and 2.69 microM +/- 1.07, respectively. These preliminary results show a different metabolic activity in the group of patients with Type II reaction state (ENL).

## NEUROFISIOLOGIA

MALAVIYA, G.N. Sensory perception in leprosy-neurophysiological correlates. *Int. J. Lepr.*, v.71, n.2, p.19-24, Jun. 2003.

The loss of sensation in skin lesions, and in a palm or sole that has been innervated by peripheral nerve trunks, is characteristic of leprosy. Detection of early nerve trunk involvement depends on demonstrating sensory loss. Newer developments in neurological sciences have made fresh interpretations of the observed sensory abnormalities in leprosy-affected persons possible. Some of these observations are described in this review, and their implications discussed.

MARQUES, W.; FOSS, N.T.; ARRUDA, A.P.; BARREIRA, A.A. Near-nerve potential in lepromatous leprosy. *Muscle Nerve*; v.28, n.4, p.460-3, Oct., 2003.

In leprosy, sensory action potentials (SAPs) may be normal in spite of clinical sensory loss. This may result from the early involvement of small nerve fibers, which have potentials that are not detected in routine studies. To evaluate this possibility, we used a near-nerve recording technique that records potentials from nerve fibers as small as 4-6 microm in diameter. We hypothesized that this technique might increase the sensitivity of nerve conduction studies in detecting leprosy neuropathy. We found the technique to be useful for recording conduction abnormalities in recently diagnosed patients, including those with preserved sensation, suggesting that axonal loss may be the underlying mechanism. Contrary to our hypothesis, however, recording the late SAP components did not improve the sensitivity of nerve conduction studies. We suggest that the late components having normal conduction velocities may be generated by either regenerating or remyelinating abnormal fibers, which have an electrophysiological behavior similar to that of normal 4-6-microm-diameter fibers.

## NEUROLOGIA

CROFT, R.P.; NICHOLLS, P.G.; STEYERBERG, E.W.; RICHARDUS, J.H.; WITHINGTON, S.G.; SMITH, W.C. A clinical prediction rule for nerve function impairment in leprosy patients-revisited after 5 years of follow-up. *Lepr Rev*; v. 74, n.1, p.35-41, Mar. 2003.

Nerve function impairment (NFI) commonly occurs during or after chemotherapy in leprosy. We previously described a clinical prediction rule to estimate the risk of NFI occurring within 2 years of diagnosis, based on 2510 patients who are followed up in the Bangladesh Acute Nerve Damage Study (BANDS). This prediction rule assigns new leprosy patients to one of three risk groups based on leprosy group and the presence or absence of NFI at registration. Updated data

with up to 5 years of follow-up showed that 95% of all NFI occurred within 2 years. This study confirms the validity of the rule and supports the conclusion that there is little value for the detection of NFI in extending follow-up beyond 2 years.

KOELEWIJN, L.F.; MEIMA, A.; BROEKHUIS, S.M.; RICHARDUS, J.H.; MITCHELL, P.D.; BENBOW, C.; SAUNDERSON, P.R. *Sensory testing in leprosy: comparison of ballpoint pen and monofilaments. Comentários: Erratum In: Lepr Rev.* v.74, n.2, p.192, Jun; 2003 *Lepr Rev*; v.74, n.1, p.42-52, Mar. 2003

The 10 g monofilament has been replaced by the ballpoint pen in routine sensory testing of nerves in leprosy control in Ethiopia. Results of sensory testing between the ballpoint pen and different monofilaments on hands and feet were compared. Ballpoint pen underdiagnosis of loss of sensation was defined to occur when the pen was felt and the monofilament was not. Differences were evaluated both for individual test points (test point level) and for the test points of extremities collectively (extremity level). An extremity (either a hand or a foot) was defined as having sensory nerve function impairment (SNFI) if a supplying nerve had SNFI, which was the case when sensation was absent in two or more test points in the area supplied by that nerve. At test point level, the percentages with ballpoint pen underdiagnosis relative to the 2, 10, 20 and 50 g monofilaments were 40, 21, 9 and 7%, respectively, in the hands, and 47, 30, 15 and 7% in the feet. Ballpoint pen underdiagnosis percentages of SNFI at extremity level were 32, 18, 8 and 9% in the hands, and 37, 26, 14 and 6% in the feet. The risk of ballpoint pen underdiagnosis appears to be higher in extremities without visible damage. In conclusion, substantial levels of underdiagnosis of sensory loss with the ballpoint pen were observed. However, the consequences for the prognosis of treatment with corticosteroids in patients with the more subtle sensation loss noted here need to be established. Development and testing of guidelines is a prerequisite for the use of the ballpoint pen.

TURKOF, E.; RICHARD, B.; ASSADIAN, O.; KHATRI, B.; KNOLLE, E.; LUCAS, S. Leprosy affects facial nerves in a scattered distribution from the main trunk to all peripheral branches and neurolysis improves muscle function of the face. *Am J Trop Med Hyg*; v. 68, n.1, p.81-8, Jan. 2003.

Current literature rejects nerve release in leprosy facial neuropathy and states that lesions are restricted to the peripheral zygomatic branches. Since there are approximately 500,000 patients with this disease throughout the world, we wanted to clarify the precise location of facial nerve's affection and the benefit of neurolysis. Our study showed that in patients with leprosy, the facial nerve's main trunk, the peripheral zygomatic branches, and all other branches were affected. Follow-up showed improvement in lagophthalmos and in

misreinnervation, with no improvement in the control cohort. Nerve release improves muscle function in leprosy facial neuropathy, provided surgery is performed on all affected segments. Intraoperative electroneurodiagnostics is an effective tool for detecting the most proximal site of lesion and ensuring effective surgery.

ULVI, H.; YOLDAS, T.; YIGITER, R.; MÜNGEN, B. R-R interval variation and the sympathetic skin response in the assessment of the autonomic nervous system in leprosy patients. *Acta Neurol Scand*; v.107, n.1, p.42-9, Jan.2003.

**OBJECTIVES:** The aim of this study was to evaluate possible autonomic nervous system (ANS) dysfunction in leprosy patients with the sympathetic skin response (SSR) and the heart rate (R-R) interval variation (RRIV) measurements which are easy and reliable methods for evaluation of autonomic functions. **MATERIAL AND METHODS:** We studied 37 lepromatous leprosy patients (mean age: 38 +/- 17 years, range 23-62 years, 20 females and 17 males) and 35 age-matched healthy subjects (mean age: 34.19 +/- 12.74 years, range 24-48 years, 20 females and 15 males). Non-invasive bedside tests (orthostatic test, Valsalva ratio), R-R interval variation (RRIV) during at rest and deep breathing, the SSR latency and amplitude from both palms, and nerve conduction parameters were studied in all the subjects. **RESULTS:** The mean values of RRIV in leprosy patients during at rest [mean RRIV in patients, 17.42 +/- 8.64% vs controls, 22.71 +/- 3.77% (P < 0.05)] and during deep breathing [mean RRIV in patients, 21.64 +/- 9.08% vs controls, 30.70 +/- 5.99% (P < 0.005)] was significantly lower compared with the controls. The mean latency of SSR in leprosy patients [mean SSR latency in patients, 1.72 +/- 1.13 ms vs controls, 1.30 +/- 0.41 ms (P < 0.05)] was significantly prolonged compared with the controls. The mean amplitude of SSR in leprosy patients [mean SSR amplitude in patients, 0.54 +/- 0.57 microV vs controls, 1.02 +/- 0.56 microV (P > 0.05)] was smaller compared with the controls, but this difference was not significant. The mean Valsalva ratio in leprosy patients [mean in patients, 1.11 +/- 0.13 vs controls, 1.16 +/- 0.07 (P > 0.05)] was smaller compared with the controls, but not statistically significant. The mean difference of systolic and diastolic blood pressure between supine rest and during standing in leprosy patients were higher compared with the controls [mean systolic pressure in patients, 7 +/- 6 mmHg vs controls, 6 +/- 8 mmHg (P > 0.05) and mean diastolic pressure in patients, 3 +/- 3 mmHg vs controls, 3 +/- 2 mmHg (P > 0.05)], but they did not reach statistical significance. Furthermore, lower RRIV and the prolonged SSR latencies in leprosy patients were closely correlated to some parameters of sensorimotor nerve conduction and each other [median nerve distal latency and RRIV, r = -0.67 (P < 0.05), ulnar nerve distal latency and RRIV, r = -0.59 (P < 0.05), RRIV and SSR latency,

r = -0.33 (P < 0.02)]. These data indicate that leprosy patients have the functional abnormalities of ANS. **CONCLUSION:** We conclude that combined use of these two tests, both of which can be easily and rapidly performed in the electromyogram (EMG) laboratory using standard equipment, allows separate testing of parasympathetic and sympathetic function, and are very sensitive methods in assessing of ANS function in peripheral neuropathy in leprosy patients.

## OFTALMOLOGIA

COLODETTI, S.C.Z.; COLODETTI, L.S.D.; MORAES JÚNIOR, H.V.M. Estudo das alterações oculares em pacientes hansenianos provenientes de área hiperendêmica (Município de Sooretama, Espírito Santo) / Ocular manifestations in leprosy patients at the hyperendemic area of the Southeast Brazil. *Rev. bras. oftalmol*; v.62, n.7, p.516-523, jul. 2003.

**Objetivo:** Estimar a frequência de alterações oftalmológicas em pacientes hansenianos de controle ambulatorial em Município hiperendêmico em Hanseníase no norte do Estado do Espírito Santo (Sooretama). **Local:** Posto de saúde da prefeitura do Município de Sooretama. **Materiais e Métodos:** Trinta e nove pacientes hansenianos, provenientes do Programa de Controle de Hanseníase do Município de Sooretama no ano de 2001, foram submetidos a exame oftalmológico de acordo com protocolo pré-estabelecido. Os dados obtidos e os dados referentes a doença foram cruzados e analisados estatisticamente. **Resultados:** Dos 39 pacientes avaliados, vinte e um casos (53,85 por cento) eram da forma Indeterminada, 13 casos (33,33 por cento) da forma Dimorfa, 4 casos (10,26 por cento) da forma Tuberculóide e 1 caso da forma Virchowiana. A acuidade visual foi melhor que 0,8 em 74,35 por cento dos olhos e em nenhum caso a baixa de acuidade visual foi atribuída diretamente a Hanseníase. A alteração ocular mais freqüentemente encontrada foi a madarose parcial de supercílios com 12 casos (30,77 por cento), seguida pela hiposecreção lacrimal com 7 casos (17,94 por cento) e madarose parcial de cílios com 6 casos (15,38 por cento). A hipoestesia corneana e catarata ocorreram em 5 casos (12,82 por cento). Triquiase, opacidades corneanas e ceratite puntata ocorreram em 3 casos (7,69 por cento). Esclerite foi observada em 2 casos (5,13 por cento). Não foram observados neste estudo: entrópico, ectrópico, eritema nodoso, dacriossistite, madarose total, corneoescleral roll, episclerite, anestesia corneana, espessamento de nervos corneanos, vascularização, úlceras corneanas, precipitados ceráticos, nódulos irianos, sinéquias, esférulas hansenóticas, irite aguda e crônica. **Conclusão:** A baixa frequência das manifestações oftalmológicas graves foi atribuída a alta prevalência da forma Indeterminada da Hanseníase.(AU).

DANIEL, E.; KOSHY, S.; JOSEPH, G.A.; RAO, P.S. Ocular complications in incident relapsed borderline lepromatous and lepromatous leprosy patients in South India. *Indian J Ophthalmol.*, v.51, n.2, p.155-9, Jun. 2003.

**PURPOSE:** To determine the magnitude of ocular complications that present in incident cases of relapsed borderline lepromatous (BL) and lepromatous leprosy (LL) patients. **METHOD:** From 1991 to 1997, all new BL and LL patients who had relapsed from an earlier disease, detected by active case finding in the geographically defined area of Gudiyattam taluk, were invited for ocular examination after their leprosy status was confirmed clinically and histopathologically. **RESULTS:** Sixty relapsed lepromatous patients, 45 male and 15 females, were examined. Fifty-two patients had relapsed after receiving only dapsone monotherapy, 4 after receiving paucibacillary multi-drug therapy (PB-MDT) preceded by dapsone mono-therapy and 4 after only PB-MDT. Three (5%) patients had lagophthalmos, 1 (1.6%) patients each had ectropion and trichiasis, 32 (53%) patients had impaired corneal sensation in both eyes, 2 (3.3%) patients each had corneal opacity (associated with reduced vision), corneal nerve beading, punctate keratitis, keratic precipitates, and iris atrophy, 4 (6.6%) patients had cataract associated with decreased vision, 1 (1.6%) patient had blocked naso-lacrimal duct and 13 (21.7%) patients had pterygium. Seven (12%) patients had a visual acuity of 6/18 or less, 4 (6.7%) patients had 6/60 or less and one patients had vision below 3/60. General ocular complications rather than leprosy-related ocular complications were responsible for reduced vision. Lagophthalmos was associated with increased duration of the disease ( $P = 0.009$ ), Grade II deformity ( $P = 0.001$ ), punctate keratitis ( $P < 0.001$ ) and cataract ( $P < 0.001$ ). Beaded corneal nerves were associated with lepromatous leprosy ( $P < 0.001$ ) and high mycobacterial infection ( $P = 0.05$ ). Patients whose initial disease was categorised as BL and LL had greater impairment of vision ( $P = 0.037$ ), more iris atrophy ( $P = 0.013$ ), increased keratic precipitates ( $P = 0.013$ ) and more corneal nerve beading ( $P = 0.013$ ), when compared with the group comprising Tuberculoid-tuberculoid (TT), Borderline-tuberculoid (BT) and Intermediate (IND). **CONCLUSION:** This first report on ocular complications in relapsed lepromatous patients demonstrates that general and leprosy-related ocular complications occur in these patients. However, they are not in excess of those reported in other leprosy groups. Borderline and lepromatous leprosy patients tend to have had more ocular complications than patients with tuberculoid leprosy.

DHALIWAL, U.; MOHANTY, S.; BHATTACHARYA, S.N. Erythema nodosum leprosum and orbital involvement. *Int. J. Lepr.*, v.71, n.1, p.10-3, Mar. 2003.

This is the first report of ENL involving the orbit in a

lepromatous patients with recurrent ENL, receiving MDT. Severe injury to the eye ensued, in spite of continued ENL and appropriate treatment of the reaction.

THOMAS R; THOMAS S; MULIYIL J Prevalence of glaucoma in treated multibacillary Hansen's disease. *J Glaucoma*,v. 12, n.1, p.16-22, Feb. 2003

**PURPOSE:** To determine the prevalence of glaucoma in a population of patients with multibacillary Hansen disease who had completed treatment. **PATIENTS AND METHODS:** The authors examined 386 of 446 patients with treated multibacillary Hansen's disease residing in a geographically limited area. A complete ophthalmic examination including slit-lamp, applanation tonometry, gonioscopy, ophthalmoscopy, and stereobiomicroscopic examination of the optic disc was performed in all subjects. Glaucoma suspects were invited to the base hospital for further examination including automated perimetry. **RESULTS:** The overall prevalence of glaucoma was 3.6% (CI 1.9-5.3); 1.3% had primary open-angle glaucoma, 7% were primary angle-closure suspects (occludable angles), 1.8% had primary angle-closure glaucoma, and 0.5% had secondary glaucoma. **CONCLUSION:** The prevalence of primary glaucoma in patients with treated multibacillary Hansen's disease was similar to that in the general population, and secondary glaucoma was rare.

YAN, L.; ZHANG, G.; ZHENG, Z.; LI, W.; YE, G. A survey of blindness and poor vision in leprosy patients. *Chin Med J (Engl)*, v.116, n.5, p.682-4, May 2003.

**OBJECTIVE:** To determine the prevalence, cause and distributions of blindness and poor vision in patients with leprosy. **METHODS:** An epidemiological survey of blindness and poor vision among 1045 cases of leprosy was carried out in Taixing City of Jiangsu Province, China. **RESULTS:** The prevalence of bilateral blindness was 7.67%, unilateral blindness 4.4%, bilateral poor vision of various degrees 9.28% and unilateral poor vision 5.84%. The prevalence of eye complications varied significantly among different groups of patients; females had a higher prevalence than males, multibacillary patients higher than paucibacillary patients, and in-patients higher than out-patients. Corneal disease was the most common cause of blindness in study groups, followed by iritic disease and cataract; while the main cause of poor vision was cataract, then corneal and iritic diseases. Treatable blindness accounted for 62.7% of the cases and treatable poor vision for 88.6% of the patients studied. 56.62% of cases with eye complications expressed their willingness to be treated. **CONCLUSIONS:** Although prevention and treatment of low vision and blindness in leprosy patients is very hard, it is necessary for doctors and medical workers to make clear of the factors to cause low vision and blindness, especially those in

leprosy patients so that some measures for prevention and treatment of the disease could be taken accordingly.

## PATOLOGIA

NAYAK, S.V.; SHIVARUDRAPPA, A.S.; MUKKAMIL, A.S. Role of fluorescent microscopy in detecting *Mycobacterium leprae* in tissue sections. *Ann Diagn Pathol.*, v.7, n.2, p.78-81, Apr. 2003.

We compared the sensitivity of the fluorescent method with that of the modified Fite-Faraco method in the detection of *Mycobacterium leprae* in tissue sections. Fifty-six skin biopsies were obtained from patients having leprosy, particularly the paucibacillary type. Minor alterations were made in the deparaffinization and staining technique, as compared with Kuper and May's method, to obtain optimum fluorescence. Of 56 biopsies studied, 39 showed organisms by the fluorescent method and only 25 showed organisms by the modified Fite-Faraco method. The fluorescent method was found to be more advantageous than the modified Fite-Faraco method, particularly in paucibacillary cases. Fluorescent microscopy has the advantage of speed and ease of screening and reduces observer fatigue. Bacillary positivity rates were higher in the fluorescent method than in the modified Fite-Faraco method in each type of leprosy.

## PREVENÇÃO E CONTROLE

KALK, A. A cooperação entre uma ONG e os Estados "anfitriões" no controle da hanseníase na América Latina. [Cooperation between an NGO and "host" states in the control of leprosy in Latin America] *Cad Saude Publica.*, v.19, n.2, p.663-6, 2003.

The proliferation of nongovernmental organizations (NGOs) can be considered the result of the inability of the current democratic system to perform all the tasks desired by its citizens. Although NGOs often do quite positive work, they tend to diminish governmental power and are capable of interfering in the internal affairs of other countries. In this context, there are efforts to control their activities, and this control can produce both negative effects (blocking the defense of human rights) and positive ones (correcting the lack of coordination in the work by NGOs). NGOs working with the control of leprosy have a long history of cooperation with "host" states in Latin America. In the worst cases they work in a vacuum left by the state. In a country like Brazil, where the government prioritizes the control of Hansen's disease and community participation in the political process - NGOs generally work "in harmony" with national authorities. The most useful contribution to state efforts has been the technical and financial support for training health personnel, supervision, and awareness-raising campaigns. Thus, the NGO becomes "quasi-governmental" in performing its tasks.

SHUMIN, C.; DIANGCHANG, L.; BING, L.; LIN, Z.; XIOULU, Y. Assessment of disability, social and economic situations of people affected by leprosy in Shandong Province, People's Republic of China. *Lepr Rev.*, v.74, n.3, p.215-21, Sep. 2003.

With the decline in prevalence of leprosy, social and economic rehabilitation (SER) has become a major priority in leprosy control programme in Shandong Province. In the preparative phase of an SER programme, a province-wide survey was conducted with a semi-structured questionnaire in order to provide policy makers and programme managers with some basic information on the disability, and social and economic situation of the people affected by leprosy. This paper presents the results of a study in the people affected by leprosy living in the communities.

## REABILITAÇÃO

BRANDSMA, J.W. 26th Kellersberger Memorial Lecture. Lessons from leprosy rehabilitation for general rehabilitation. *Ethiop Med J.*, v.41, n.1, p.77-87, 2003.

Leprosy is primarily a disease of skin and peripheral nerves. Because of nerve function impairment, leprosy patients may develop primary nerve related impairments such as, loss of sensation and weakness or paralysis. These primary impairments may lead to secondary impairments such as ulceration and contractures. Many other diseases and disorders present with similar impairments as seen in leprosy e.g. diabetes and peripheral nerve injuries. Nerve function assessment and ulcer prevention and treatment are areas that have been researched in leprosy but these research findings are not yet commonly known and adopted in diseases and disorders that 'relate' to leprosy. Rehabilitation is a relatively new field in medicine and not (well) developed in many developing countries. Rehabilitation requires an integrated approach from different disciplines and professionals. As for other medical specialty fields, rehabilitation demands evidence based practice.

## REABILITAÇÃO-CIRURGIA

BARI, M.M. Surgical reconstruction of leprotic foot drop. *Mymensingh Med J.*, v.12, n.1, p.11-2, Jan. 2003.

We have operated 152 patients for correction of foot-drop due to leprosy from March 1992 to July 1999. The method used was circumtibial transfer of the tibial is posterior to the tendons of extensor hallucis longus and the extensor digitorum longus in the foot together with lengthening of the Achilles tendon. The results were satisfactory in 135 of these cases as judged by adequate restoration of heel-toe gait and of active dorsiflexion. The follow up period ranged from 6 months to 8 years. Inadequate post-operative physiotherapy was the reason for unsatisfactory results in seventeen cases.



MALAVIYA, G.N. Radial half of extensor carpi radialis longus tendon as graft to elongate muscle tendon unit for correction of finger clawing. *Plast Reconstr Surg.*, v.111, n.6, p.1914-7, May, 2003.

In 12 patients, the extensor carpi radialis longus muscle tendon unit was elongated using the radial half of the parent tendon so that it could reach the site of new insertion, the A1-A2 pulley of flexor sheath or lateral bands, after routing the transfer through the carpal tunnel. The tendon was of appropriate thickness and could be split into two halves to be used as a graft. Further splitting of the tendon into four tails was possible. The transferred slips retained adequate strength to activate the fingers after the operation. It is suggested that splitting of the extensor carpi radialis longus tendon to use one half as a tendon graft be considered in patients in whom extensor carpi radialis longus transfer is planned to correct finger clawing. This technique is simple, needs minor modification in the sequence of operative steps, reduces operating time, and saves the patient from postoperative discomfort, muscle herniation, and scarring at the donor site (usually the thigh).

OOMMEN, A.T.; MANNAM, E.; PARTHEEBARAJAN, S.; SAMUEL, S. Excision arthroplasty: an effective method in the management of plantar ulcers with metatarsophalangeal joint infection in anaesthetic feet. *Lepr Rev.*, v.74, n.1, p.63-7, Mar. 2003.

The cases of 30 patients with septic arthritis of the metatarsophalangeal (MTP) joints as a complication of plantar ulceration in leprosy who underwent excision arthroplasty and primary closure of the plantar ulcer were reviewed. Twenty-two of these patients were male. The commonest site of MTP joint involvement was the first MTP joint. The average longitudinal diameter of ulcers was 2cm, and most ulcers were oval in shape. Diagnosis was made on the basis of signs of infection over the MTP joint, discharge from the ulcer and examination with a probe. Infection in the joint ranged from simple synovial discharge to seropurulent or purulent discharge. Treatment involved excision arthroplasty of the MTP joint, excision of the ulcer with primary closure of the plantar incision and dorsal or lateral drainage depending upon the direction in which the infection extended. In two patients, the plantar wound could not be closed as it was too large. Healing of the plantar incision took 2 weeks in 12 patients and 3 weeks in 14 patients. In four patients, healing did not occur by primary intention. In a follow up of 1-2 years, there was no recurrence in 24 patients, while four patients had recurrent simple ulceration. Two patients were lost to follow up. Review of the results of this procedure dealing with septic arthritis of MTP joints secondary to plantar ulceration shows that primary healing of the plantar incision could be achieved in 3 weeks. With regard to recurrence, even though only four out of 28 ulcers treated by this procedure recurred, other contributing factors should be considered in a

prospective control study to support the view that this procedure has contributed to non-recurrence.

OZKAN, T.; OZER, K.; YUKSE, A.; GULGONEN, A. Surgical reconstruction of irreversible ulnar nerve paralysis in leprosy. *Lepr Rev.*; v.74, n.1, p.53-62, Mar. 2003.

Twenty-five patients with irreversible leprotic ulnar nerve palsy having undergone lumbrical replacement with two different tendon transfer techniques were assessed 6-120 months after surgery. Nineteen patients were reconstructed with the flexor digitorum four-tail procedure (FDS-4T), and six with Zancolli's lasso procedure (ZLP). Mean paralysis times were 103 months for FDS-4T, and 68 months for ZLP. Mean age of the patients was 36 years (21-57). Grip strength measurements, improvement in active range of motion at the PIP joints, patients' ability to open and close their hands fully, as well as sequence of phalangeal flexion, were noted. Mean grip strength measurements during follow-up were 76% of the contralateral extremity in the FDS-4T group and 82% in the ZLP group. Comparison of the follow-up grip strength with the preoperative value revealed 1% improvement in the FDS-4T group and 20% in the ZLP group. Claw hand deformity was completely corrected in 12 patients in FDS-4T group, and in five patients in the ZLP group. Residual flexion contracture remained in five patients after surgery. Swan-neck deformity subsequently developed in seven fingers. Age, sex, mean follow-up and surgical technique did not relate statistically to the functional outcome. However, preoperative extensor lag of the PIP joint and mean paralysis time significantly affected the functional outcome. ZLP was found to be a more effective procedure in restoring grip strength, whereas FDS-4T was more effective in correcting claw hand deformity.

RICHARD, B.M. Location of the extracranial extent of leprosy facial nerve pathology may allow leprosy facial palsy to be reanimated by free muscle transfer. *Br J Plast Surg.*, v.56, n.1, p.14-9; discussion 20, 2003.

Leprosy is a mycobacterial nerve and skin infection, which can be eradicated by antibiotics. Some patients affected by leprosy, once cured, have residual nerve impairment with paralysis and sensory neuropathy. A series of patients with facial nerve paralysis, investigated using clinical, histological and electrophysiological techniques, demonstrated that the nerve pathology was distal to the section of main trunk prior to its bifurcation. Facial reanimation was achieved with a free gracilis-muscle transfer, coapting its motor nerve to the ipsilateral facial nerve trunk proximal to the site of the leprosy pathology, with a moderate clinical result.

## TERAPÊUTICA

De CARSALADE, G.Y.; ACHIRAFI, A.; FLAGEUL, B. Pentoxifylline in the treatment of erythema nodosum leprosum. *J Dermatol*; v. 30, n.1, p.64-8, Jan. 2003.

Erythema nodosum leprosum (ENL) is a well-known serious complication affecting 10% of lepromatous multibacillary leprosy patients. In the chronic form, its morbidity may be considerable. Thalidomide and systemic steroids are the two current effective drugs for the management of ENL. However, their use in endemic countries is often difficult and hazardous, and a search for new therapies is needed. We report our experience on the effects of pentoxifylline, a methylxanthine derivative, which has recently been suggested as a possible effective treatment for ENL attacks.

DHOPLÉ, A.M.; NAMBA, K. In vivo susceptibility of *Mycobacterium leprae* to sitafloxacin (DU-6859a), either singly or in combination with rifampicin analogues. *Int J Antimicrob Agents*; v.21, n.3, p.251-5, Mar. 2003.

The antimicrobial effects of sitafloxacin (DU-6859a) against *Mycobacterium leprae*, either singly or in combination with either rifampicin, rifabutin or KRM-1648, were studied using a mouse footpad assay technique and the results were compared with those obtained with ofloxacin. When used singly, the minimum concentrations of sitafloxacin and ofloxacin needed to inhibit completely the growth of *M. leprae* were 25 and 100 mg per kg body weight per day, respectively, and the effects were bactericidal. Both sitafloxacin and ofloxacin exhibited excellent synergistic effects when combined with either rifabutin or KRM-1648, but not with rifampicin. Thus, incorporation of sitafloxacin and rifabutin (or KRM-1648) in the multidrug regimen for treating leprosy patients is suggested.

GORDON, J.N.; GOGGIN, P.M. Thalidomide and its derivatives: emerging from the wilderness. *Postgrad Med J*, v.79, n.929, p.127-32, 2003

Forty years on from its worldwide withdrawal, thalidomide is currently undergoing a remarkable renaissance as a novel and powerful immunomodulatory agent. Over the last decade it has been found to be active in a wide variety of inflammatory and malignant disorders where conventional therapies have failed. Recently, considerable progress has been made in elucidating its complex mechanisms of action, which include both anticytokine and antiangiogenic properties. However, in addition to its well known teratogenic potential, it has a significant side effect profile that leads to cessation of treatment in up to 30% of subjects. In response to this, two new classes of potentially safer and non-teratogenic derivatives have

recently been developed. This review summarises the biological effects, therapeutic applications, safety profile, and future potential of thalidomide and its derivatives.

ISHII, N. Recent advances in the treatment of leprosy. *Dermatol Online J*; v.9, n.2, p.5, Mar. 2003.

Leprosy, a chronic infectious disease caused by *Mycobacterium leprae*, was identified by G. H. A. Hansen in 1873. The different clinical presentations of the disease are determined by the quality of the host immune response. The bacteria have affinity for the peripheral nerves and are likely the cause of neuropathy, a cardinal manifestation of the disease. WHO recommends a protocol of multidrug therapy (MDT), which effectively controls the disease, hence contributing to the global elimination program. Early detection of leprosy and treatment by MDT are the most important steps in preventing deformity and disability.

MATSUOKA, M.; KASHIWABARA, Y.; LIANGFEN, Z.; GOTO, M.; KITAJIMA, S. A second case of multidrug-resistant *Mycobacterium leprae* isolated from a Japanese patient with relapsed lepromatous leprosy. *Int J Lepr*, v.71, n.3, p.240-3, 2003.

Emergence of drug resistant strains of *Mycobacterium leprae* was reported soon after the introduction of dapsone (diamino-diphenyl sulphone, DDS) for leprosy treatment (6, 10, 11). Three cases of multidrug-resistant strains of *M. leprae* have been reported recently (2, 8, 9, 13). In order to prevent multiple drug resistant strains of *M. leprae* from developing, current leprosy control strategies are based on early detection of cases and treatment with multidrug therapy (MDT) as recommended by the World Health Organization (WHO). We report here the identification of a multidrug-resistant strain of *M. leprae* from a patient who received inadequate therapy for leprosy. The drug resistant profile of the isolated strain was confirmed by the mouse footpad method and the identification of mutations in genes previously shown to be associated with resistance to each drug was made.

MURRAY, C.K.; JOYCE, M.P.; LONGFIELD, R.N. Short report: Treatment failure in Hansen's disease. *Am J Trop Med Hyg*; v.68, n.2, p.233-4, Feb. 2003.

Areas of low endemicity of Hansen's disease, such as Texas, California, and Hawaii, exist due to immigration and rare autochthonous infections. Managing this disease in these areas of low endemicity is difficult, especially in observing for relapse. The accurate diagnosis of relapse is imperative so that appropriate therapy can be promptly reinstated and unnecessary treatment can be avoided. To assess treatment failures in an area of low endemicity, we retrospectively

evaluated 113 patients with Hansen's disease treated in southern Texas. Of 57 patients who completed therapy, 11 were later restarted on medications for this disease for presumed relapse. However, nine of the 11 were found not to have true relapses of Hansen's disease. The accurate diagnosis of relapse of this disease is essential not only in the individual patient but also for prospective treatment trials to establish best practices.

NORMAN, G.; JOSEPH, G.; EBENEZER, G.; RAO S.P.; JOB, C.K. Secondary rifampin resistance following multi-drug therapy—a case report. *Int. J. Lepr.*, v.71, n.1, p.18-21, Mar. 2003.

This is the first report of secondary resistance to rifampin following MDT in a patient with prolonged, but irregular treatment. Repeated mouse foot-pad studies demonstrated resistance to dapsone after several years of monotherapy, and following subsequent MDT the studies demonstrated the development of resistance to rifampin.

OKAFOR, M.C. Thalidomide for erythema nodosum leprosum and other applications. *Pharmacotherapy*, v.23, n.4, p.481-93, Apr. 2003.

Thalidomide, administered as a sedative and antiemetic decades ago, was considered responsible for numerous devastating cases of birth defects and consequently was banned from markets worldwide. However, the drug remarkably has resurfaced with promise of immunomodulatory benefit in a wide array of immunologic disorders for which available treatments were limited. It is approved by the Food and Drug Administration for erythema nodosum leprosum (ENL). Although the relative paucity of leprosy and ENL worldwide may perceivably limit interest in and knowledge about thalidomide, increasing numbers of new and potential uses expand its applicability widely beyond ENL. Thalidomide, an inhibitor of tumor necrosis factor  $\alpha$ , is the best known agent for short-term treatment of ENL skin manifestations, as well as postremission maintenance therapy to prevent recurrence. For this indication, it is effective as monotherapy and as part of combination therapy with corticosteroids. Studies of thalidomide in chronic graft-versus-host disease showed benefit in children and adults as treatment, but not as prophylaxis. The agent has been administered successfully for treatment of cachexia related to cancer, tuberculosis, and human immunodeficiency virus infection, although evidence of efficacy is inconclusive. Thalidomide monotherapy effectively induced objective response in trials in patients with both newly diagnosed and advanced or refractory multiple myeloma. Combination therapy with thalidomide and corticosteroids was also effective in these patients, as well as in treatment of aphthous and genital ulcers. Limited evidence supports the

drug's benefit in treatment of Kaposi's sarcoma. Other thalidomide applications include Crohn's disease, rheumatoid arthritis, and multiple sclerosis. Somnolence, constipation, and rash were the most frequently cited adverse effects in studies, but thalidomide-induced neuropathy and idiopathic thromboembolism were critical causes for drug discontinuation. Thalidomide is still contraindicated in pregnant women, women of childbearing age, and sexually active men not using contraception. Clinicians should be conversant with thalidomide in ENL (its primary application) in the natural course of leprosy, as well as in the agent's other applications.

PERRI, A.J.; HSU, S. A review of thalidomide's history and current dermatological applications. *Dermatol Online J*; v.9, n.3, p.:5, Aug. 2003.

Once abandoned because of devastating teratogenic effects, thalidomide has reemerged as an alternative treatment in many dermatologic diseases. In 1998, thalidomide became FDA approved for the acute treatment and suppression of the cutaneous manifestations of erythema nodosum leprosum (ENL). ENL is a systemic disorder that typically occurs after several years of antileprosy treatments, usually for lepromatous leprosy. Off-label uses for thalidomide include: aphthous stomatitis, Behçet disease, pyoderma gangrenosum, chronic discoid lupus erythematosus, systemic lupus erythematosus, lichen planus, prurigo nodularis and sarcoidosis. This review examines the background, pharmacokinetics, mechanism of action, side-effects, and indications of thalidomide.

SHAW, I.N.; CHRISTIAN, M.; JESUDASAN, K.; KURIAN, N.; RAO, G.S. Effectiveness of multidrug therapy in multibacillary leprosy: a long-term follow-up of 34 multibacillary leprosy patients treated with multidrug regimens till skin smear negativity. *Lepr Rev.*, v.74, n.2, p.141-7, Jun. 2003.

The World Health Organization (WHO) Field Trials of multidrug therapy (MDT) started at Schieffelin Leprosy Research and Training Centre (SLR & IC), Karigiri, India in December 1981. The patients were treated with two MDT regimens. The first (regimen A) consisted of 600mg rifampicin and 300mg of clofazimine given under supervision on 2 consecutive days monthly, 225mg injection of acedapsone bimonthly and dapsone 100mg daily. The second regimen (regimen B) was the conventional MDT (WHO/MDT), rifampicin 600mg and clofazimine 300mg supervised once a month, dapsone 100mg and clofazimine 50mg daily, unsupervised. Both the regimens were administered for a minimum period of 2 years or until skin smear negativity, whichever occurred later. Thirty-four newly detected previously untreated MB patients, 16 of whom received regimen A and 18 regimen B, were reassessed. Both regimens were well accepted and well tolerated by the patients. Clofazimine discoloration was the only adverse effect of MDT

seen in these patients. After completion of treatment with MDT, the patients were followed up for a total duration of 466 person-years with a mean of 13.7 +/- 1.4 years per patient. No relapse was seen.

SHETTY, V.P.; WAKADE, A.V.; GHATE, S.; PAI, V.V.; GANAPATI, R.; ANTIA, N.H. Viability and drug susceptibility testing of *M. leprae* using mouse footpad in 37 relapse cases of leprosy. *Int. J. Lepr.*; v.71, n.3, p.210-7, Sep. 2003.

*Mycobacteria leprae* isolates obtained from 37 referral relapse cases of leprosy (37 skin and 10 nerve biopsy samples) received during the years 1994-2001, were tested for viability and drug sensitivity in the mouse footpad. A significant *M. leprae* yield in the footpads of control mice was obtained, with 32/47 (68%) isolates (from 26 cases) thus confirming viability. Of the 28 isolates successfully drug tested, 6 (21%) were resistant to one or more drugs. All except one, were multidrug treated cases (5/24 = 21%). One of the isolates was resistant to all three drugs, i.e., dapsone (di-aminodiphenyl sulphone, DDS), rifampin (RFP), and clofazimine (CLF). Two were resistant to two drugs, i.e., DDS and RFP, and each of the others were mono resistant to DDS, RFP, or CLF. Notably, one of the isolates that showed combined resistance to DDS and RFP was derived from a borderline tuberculoid case. Also, in one case skin and nerve showed that discordance viz: *M. leprae* derived from skin were resistant to RFP, while those derived from nerve tested sensitive to all three drugs, indicating tissue related difference.

TADESSE, A.; TAYE, E.; SANDOVAL, F.; SHANNON, E.J. Thalidomide does not modify the ability of cells in leprosy patients to incorporate [3H]-thymidine when incubated with *M. leprae* antigens. *Lepr Rev.*, v.74, n.3, p.206-14, Sep. 2003.

The immune response in reversal reaction, (RR) and in erythema nodosum leprosum (ENL) is characterized in vitro by an enhancement in lymphocyte blast transformation against *M. leprae*. As thalidomide is an effective treatment for ENL, this study assessed the effect of this drug on these phenomena. Mononuclear cells from patients attending the clinic at ALERT and from healthy staff were cultured for 5 days with integral *M. leprae* (IMI), or a modified Dharmendra antigen (Dhar), or PPD from *M. tuberculosis*. In one set of cultures, thalidomide was

added once at the initiation of the culture; in the other set thalidomide was added a second time (2x), 18 h prior to harvesting the cells. The mononuclear cells, in the absence of thalidomide, from healthy staff, borderline tuberculoid patients (BT) and BT patients in RR (BT/RR) incorporated [3H]-thymidine best when cultured with PPD > Dhar > *M. leprae*. The cells from patients with ENL did not respond well to the *M. leprae* antigens. Thalidomide (2x) enhanced proliferation to Dhar in the BTRR group (Wilcoxon signed rank test,  $P < 0.05$ ). No significant changes occurred for the other groups. Comparing PPD-stimulated cells treated with thalidomide once to those treated with thalidomide twice, thalidomide (2x) suppressed incorporation of [H3]-thymidine by the PPD-stimulated ( $P < 0.05$ ) as well as IMI-stimulated ( $P < 0.05$ ) cells in the healthy staff group. In the Dhar-stimulated cells from the healthy staff thalidomide significantly suppressed TNF-alpha ( $P < 0.05$ ). A mixed effect was seen within and between the other groups, but there was a trend for thalidomide to suppress TNF-alpha induced by the *M. leprae*, Dhar and PPD antigens.

USTIANOWSKI, A.P.; LOCKWOOD, D.N. Leprosy: current diagnostic and treatment approaches. *Curr Opin Infect Dis.*; v.16, n.5, p.21-7, Oct. 2003.

PURPOSE OF REVIEW: Leprosy remains an important problem globally and leprosy patients may present to physicians outside leprosy endemic areas. We review the recent biological and clinical advances in leprosy. RECENT FINDINGS: Sequencing the genome has been a major biological advance and will open up new possibilities for research. The three cardinal criteria (anaesthetic skin patches, thickened nerves and acid-fast bacilli in skin smears) have not yet been bettered. Multidrug therapy for leprosy is highly effective with low relapse rates though the optimal duration of therapy for multibacillary patients is unclear. Nerve damage remains a significant problem (in some series only 50% responding to steroid therapy). New treatments for leprosy reactions are needed. Stigma remains a problem but is being combated by patient groups. SUMMARY: Far from being eliminated as a public health problem, leprosy still causes a considerable long-term morbidity in both the developing and developed world. New treatments for leprosy reactions are needed and the optimal length of multidrug therapy required further research.