

LITERATURA CORRENTE

CURRENT LITERATURE

ASPECTOS SOCIAIS

EL HASSAN, L.A.; KHALIL, E.A.; EL-HASSAN, A.M. Socio-cultural aspects of leprosy among the Masalit and Hawsa tribes in the Sudan. *Leprosy Rev.*, v.73, n.1, p.20-8, Mar., 2002.

Social and cultural factors influencing knowledge, attitudes and practices (KAP) towards leprosy in two communities in eastern Sudan were studied to determine their effects on treatment seeking and compliance. The study was qualitative using focus small group discussions, personal interviews and direct observation. The target populations were Masalit and Hawsa, the two main tribes in the area. Knowledge about the pathological cause of leprosy was lacking but the clinical manifestations were well recognized, particularly among the Masalit, in whom the disease is more common than the Hawsa. Among the Masalit there was a widely held belief that leprosy was caused by eating meat of the wild pig and a certain type of fish. The Hawsa, who are more devout Muslims, do not eat pig and associate leprosy with consumption of two types of fish. Between both tribes, the stigma of leprosy was not strong and the degree of rejection was more towards those with severe disease, particularly patients with ulcerated lesions and severe deformities. Patients were cared for by the family and lived in a separate hut within the families' housing compounds. In this remote area where medical services are scarce or nonexistent, those interviewed did not realize that leprosy was treatable by modern medicine. This influenced the treatment-seeking behaviour of patients, who were often treated by spiritual healers and other traditional medicine practices. With the introduction of multidrug therapy and health education of patients and society, many more patients are now seeking medical treatment, indicating a change in health seeking behaviour.

HELENE, L.M.; SALUM, M.J. [Social reproduction of leprosy: a study of patients profile with leprosy in the city of São Paulo]. A reprodução social da hanseníase: um estudo do perfil de doentes com hanseníase no Município de São Paulo. *Cad. Saúde Pública*, v.18, n.1, p.101-13, Jan-Feb., 2002.

This study discusses the relationship between work

and living conditions among leprosy patients enrolled in the São Paulo municipal public health system in 1996. Social patterns were studied based on the theory of social determination of the health-disease process. The main purpose of the study was to emphasize evidence of the disease determination network, seeking new knowledge to improve public policies on leprosy. Data were gathered from a sample of leprosy patients registered in the city's public health system. Although patients' families are characterized by a common social thread, different work/life possibilities allow for a classification of patients into three social groups. The majority belong to groups that are marginalized from social production, living in areas where social exclusion is more extreme, on the outskirts of the city. If the trends in this study persist, incident leprosy cases will result from the social exclusion of migrants from Brazil's Southeast and Northeast. The study also discusses the position of young people and female patients in the determination network of this infectious disease in the city of São Paulo.

CIRURGIA

DEBRAY, M.; HANSLIK, T.; AVANSI, M.A.; PABION, B.; LORTHOLARY, O. [Surgical decompression treatment of leprosy neuritis at the Bom-Pastor Hospital (Brazilian Amazonia)]. Traitement chirurgical de décompression des névrites lépreuses à l'hôpital Bom-Pastor (Amazonie brésilienne). *Rev. Med. Interne*, v.22, n.12, p.1188-95, Dec., 2001.

PURPOSE: Only leprosy resource centres undertake surgery for neuritis. Patients' accessibility to this surgical procedure is poor because these centres are often far from their homes. The aim of our work is to study the feasibility of neuritis surgery in the field. **METHODS:** A surgeon trained in this surgery was recruited by Bom-Pastor hospital in Brazilian Amazonia, which is located 400 km away from the leprosy resource centre. Patients operated from May 1996 to December 1997 were enrolled in this retrospective study. **RESULTS:** A total of 45 operations were carried out during 17 procedures on 13 patients, among which 12 were multibacillary cases. The decompression surgery was performed with a median delay of 1 year after leprosy diagnosis and 3.5 months after the neuritis diagnosis. Among 17 operations, 14 were

performed for painful neuritis of recent onset unsuccessfully treated with corticoids or recurring during the month after corticoids were withdrawn. The other three operations were performed for long-standing neuritis with paralysis and deformity. Pain was relieved in all the cases of recent neuritis, except for one patient who suffered from a serious steroid-dependant erythema nodosum leprosum. An improvement of motor function was observed in one out of three patients with long-standing neuritis. Adverse effects were few: a scar infection with a rapid recovery and a keloid scar. Two neurites recurred 2 and 10 months after the surgery. CONCLUSIONS: In an endemic leprosy region, field access to surgery for neuritis appears to prove real progress in the management of leprosy neuritis.

CLASSIFICAÇÃO

BRENNAN, P.J.; VISSA, V.D. Genomic evidence for the retention of the essential mycobacterial cell wall in the otherwise defective *Mycobacterium leprae*. *Leprosy Rev.*, v.72, n.4, p.415-28, Dec., 2001.

The obligate intracellularism of *Mycobacterium leprae* may be attributable to the effects of mutations in major metabolic areas due to a genome capable of encoding only about 1600 proteins. Yet cell wall biosynthesis capability remains relatively intact and comparisons with the genome of *Mycobacterium tuberculosis* provide insights into the genetic basis of a minimal mycobacterial cell wall.

COLE, S.T.; SUPPLY, P.; HONORÉ, N. Repetitive sequences in *Mycobacterium leprae* and their impact on genome plasticity. *Leprosy Rev.*, v.72, n.4, p.449-61, Dec., 2001.

About 2% of the genome of *Mycobacterium leprae* is composed of repetitive DNA. There are more than 26 extinct IS elements together with four families of dispersed repeats, present in five copies or more, RLEP (37 copies), REPLEP (15 copies), LEPREP (eight copies), and LEPRPT (five copies). Although there is no sequence similarity to known transposable elements, RLEP occurs predominantly at the 3'-end of genes and, in several cases, within pseudogenes, suggesting that it was capable of dissemination. Strikingly, on comparison of the genome sequences of *M. leprae* and the closely related tubercle bacillus, *Mycobacterium tuberculosis* H37Rv, many of these repetitive sequences were found at sites of discontinuity in gene order. Evidence is presented that loss of synteny, inversion and genome downsizing may have resulted from recombination between dispersed copies of these repetitive elements.

CORNIELJE, H.; NICHOLLS, P.G.; VELEMA, J.P. Avoiding misperceptions: classifying rehabilitation projects using letters rather than numbers. *Leprosy Rev.*, v.73, n.1, p.47-51, Mar., 2002.

A classification system proposed earlier of the many different known rehabilitation approaches and activities used a quantitative scoring system, thus giving the impression that projects with a higher score were better, more correct or more important than projects with a lower score. We therefore propose an alternative classification based on letters, so that a given combination of letters characterizes a particular type of project. The letters are derived from four dimensions: desired outcome of the intervention, participation of the clients in the rehabilitation process, the target group served and the services offered. Some examples are presented. The classification serves to analyse rehabilitation projects, to define policy and as a starting point for evaluation.

EIGLMEIER, K.; PARKHILL, J.; HONORÉ, N.; GARNIER, T.; TEKAIA, F.; TELENTI, A.; KLATSER, P.; JAMES, K.D.; THOMSON, N.R.; WHEELER, P.R.; CHURCHER, C.; HARRIS, D.; MUNGALL, K.; BARRELL, B.C.; COLE, S.T. The decaying genome of *Mycobacterium leprae*. *Leprosy Rev.*, v.72, n.4, p.387-98, Dec., 2001.

Everything that we need to know about *Mycobacterium leprae*, a close relative of the tubercle bacillus, is encrypted in its genome. Inspection of the 3.27 Mb genome sequence of an armadillo-derived Indian isolate of the leprosy bacillus identified 1,605 genes encoding proteins and 50 genes for stable RNA species. Comparison with the genome sequence of *Mycobacterium tuberculosis* revealed an extreme case of reductive evolution, since less than half of the genome contains functional genes while inactivated or pseudogenes are highly abundant. The level of gene duplication was approximately 34% and, on classification of the proteins into families, the largest functional groups were found to be involved in the metabolism and modification of fatty acids and polyketides, transport of metabolites, cell envelope synthesis and gene regulation. Reductive evolution, gene decay and genome downsizing have eliminated entire metabolic pathways, together with their regulatory circuits and accessory functions, particularly those involved in catabolism. This may explain the unusually long generation time and account for our inability to culture the leprosy bacillus.

EIGLMEIER, K.; SIMON, S.; GARNIER, T.; COLE, S.T. The integrated genome map of *Mycobacterium Ieprae*. *Leprosy Rev.*, v.72, n.4, p.462-9, Dec., 2001.

The integrated map of the *Mycobacterium Ieprae* genome unveiled for the first time the genomic organization of this obligate intracellular parasite. Selected cosmid clones, isolated from a genomic library created in the cosmid vector Lorist6, were identified as representing nearly the complete genome and were subsequently used in the *M. Ieprae* genome sequencing project. Now a new version of the integrated map of *M. Ieprae* can be presented, combining the mapping results from the Lorist6 cosmids with data obtained from a second genomic library constructed in an *Escherichia coli*-mycobacterium shuttle cosmid, pYUB18. More than 98% of the *M. Ieprae* genome is now covered by overlapping large insert genomic clones representing a renewable source of well defined DNA segments and a powerful tool for functional genomics.

MAEDA, S.; MATSUOKA, M.; NAKATA, N.; KAI, M.; MAEDA, Y.; HASHIMOTO, K.; KIMURA, H.; KOBAYASHI, K.; KASHIWABARA, Y. Multidrug resistant *Mycobacterium Ieprae* from patients with leprosy. *Antimicrob. Agents Chemother.*; 45(12):3635-9, Dec., 2001.

Sequences of the *folP1*, *rpoB*, and *gyrA* genes were analyzed for 88 isolates of *Mycobacterium Ieprae* from leprosy patients in Japan, Haiti, Indonesia, Pakistan, and the Philippines. Thirteen isolates (14.8%) showed representative mutations in more than two genes, suggesting the emergence of multidrug-resistant *M. Ieprae*.

CLÍNICA

CHAE, G.T.; LEE, S.B.; KANG, T.J.; SHIN, H.K.; KIM, J.P.; KO, Y.H.; KIM, S.H.; KIM, N.H. Typing of clinical isolates of *Mycobacterium Ieprae* and their distribution in Korea. *Leprosy Rev.*, v.73, n.1, p.41-6, Mar., 2002.

Although there is no genetic diversity in isolates of *Mycobacterium Ieprae*, the variance of tandem repeats in the *rpoT* gene was recently demonstrated. We have typed clinical isolates of *M. Ieprae* in Korea using difference of the tandem repeats in the *rpoT* gene. Among 69 patients, 65 Korean isolates (94.2%) demonstrated four copies of the 6 by tandem repeat (GACATC) in the *rpoT* gene, and incidences of three copies were found in only two Koreans and two foreigners (2.9%, respectively).

FERRARI, T.C.; ARAÚJO, M.G.; RIBEIRO, M.M. Hepatic involvement in lepromatous leprosy. *Leprosy Rev.*, v.73, n.1, p.72-5, Mar., 2002.

Hepatic involvement in a lepromatous leprosy (LL) patient is reported. The serum concentrations of aminotransferases were much higher than previously described in the leprosy literature. Other causes for hepatic damage were ruled out. Such hepatic involvement and elevation of aminotransferases have never been described in leprosy.

GROENEN, G. Trends in prevalence and case finding in the ALERT leprosy control programme, 1979-1999. *Leprosy Rev.*, v.73, n.1, p.29-40, Mar., 2002.

From 1979 to 1999, the ALERT leprosy control programme has covered a well-defined area in central Ethiopia using standardized case finding strategies. During this period, the leprosy prevalence has decreased more than 30-fold, there has been a 3-fold decrease in case detection and a 6-fold decrease in the case detection rate. The proportion of MB patients among new cases increased by around 80% and the proportion of children among new cases decreased by around 60%. Several factors may have contributed to these trends. The impact of the introduction of MDT and the shortening of the duration of the MB regimen are shown, but other factors are also discussed at length: an increase in the population of the area, cleaning up of the registers, changing case definitions, changes in staff motivation and fluctuations, even small ones, in case finding intensity and coverage. Do the observed trends reflect a reduction in the transmission of the leprosy infection? Because of the many confounding factors, it would be difficult to answer that question positively at present. Additional rigorous data collection and analysis is required.

KALUARACHCHI, S.I.; FERNANDOPULLE, B.M.; GUNAWARDANE, B.P. Hepatic and haematological adverse reactions associated with the use of multidrug therapy in leprosy—a five year retrospective study. *Indian J. Leprosy*, v.73, n.2, p.121-9, Apr-Jun., 2001.

This study analyses retrospectively some of the risks associated with the use of WHO-multidrug therapy (MDT) in Sri Lanka. Case records of 3,333 new cases of leprosy attending the Central Leprosy Clinic in Colombo during 1991-1995, were analysed for adverse drug reactions involving the liver and blood. There were 81 reports of suspected hepatic or haematological adverse reactions associated with the use of MDT, of which 39 were classified as haemolytic anaemia, 25 as toxic hepatitis, 2 as methaemoglobinaemia and 15 as anaemia. Dapsone, was

incriminated in the majority of adverse reactions (72%). Adverse drug reactions were more common in female than male subjects (55% vs 45%; $P < 0.5$), but there was no significant differences between the age groups. Majority of adverse reactions was seen within the first three months of initiation of MDT. This study in no way undermines the benefits of MDT but highlights the risks and suggests measures to minimize these risks.

KOSHY, S.; DANIEL, E.; KURIAN, N.; YOVAN, P. Pathogenesis of dry eye in leprosy and tear functions. *Int. J. Leprosy*, v.69, n.3, p.215-8, Sep., 2001.

Seventy-five leprosy patients and an equal number of age- and sex-matched controls were examined for tear functions, using Schirmer's test and tear break up time (BUT). There was no statistically significant difference in the Schirmer's test, but the tear BUT showed a statistically significant lower value of < 10 seconds in multibacillary patients compared to paucibacillary patients. Leprosy patients with lagophthalmos and decreased corneal sensation showed a lower value of tear BUT which was also statistically significant. This study shows that even though the quantity of tears is not affected, proper and prolonged wetting of the cornea is deficient in many leprosy patients.

KUMANO, K. [Leprosy reactions]. *Nihon Hansenbyo Gakkai Zasshi*, v.71, n.1, p.3-29, Fev., 2002.

In leprosy, the causative bacteria, *Mycobacterium leprae*, will not threaten the lives of the hosts directly because they proliferate only slowly in the Schwann cells of the peripheral nerves. It is the "reactions" which give the patients irreversible morbidity through the inflammatory damages to the peripheral nerves. Physicians should be aware of the possibility of the state of the "reaction" when they examine leprosy patients. They also should be aware of the possibility of leprosy and the state of the "reaction" when they examine patients with cutaneous lesions and/or peripheral nerve disturbances, because it may be the first presenting symptom of the disease. In this review, recent advances on the issue about the reactions are discussed including pathogenesis, immunology, clinical features, pathology, treatment and prevention.

RYAN, T.J.; JONES, R.L.; MORTIMER, P.S.; SINGH, G. Lymphatics in leprosy: relationship to elastic fibres and observations following intra-lesional injections of colloidal carbon. *Leprosy Rev.*; v.73, n.1, p.52-63, Mar., 2002.

An investigation of skin lymphatics in leprosy has been undertaken. Examination of 62 skin biopsies from 31 patients with various classifications of leprosy has revealed

dilated initial lymphatics within granulomas of lepromatous leprosy, but no significant abnormalities in non-lepromatous disease or in non-granulomatous skin. Colloidal carbon injected intra-lesionally failed to appear within granulomas, but could be seen in lymphatics in non-granulomatous dermis. Elastic fibres were also absent within granulomas. AFB were clearly identified within endothelial cells of initial lymphatics. We suggest lymphatic malfunction may be compartmental, existing only within the granulomas and not in the surrounding normal appearing dermis.

SANTOS, A.R.; BALASSIANO, V.; OLIVEIRA, M.L.; PEREIRA, M.A.; SANTOS, P.B.; DEGRAVE, W.M.; SUFFYS, P.N. Detection of *Mycobacterium leprae* DNA by polymerase chain reaction in the blood of individuals, eight years after completion of anti-leprosy therapy. *Mem. Inst. Oswaldo Cruz*; v.96, n.8, p.1129-33, Nov, 2001.

Thirty eight patients with indeterminate leprosy (HI), at least 4 to 6 years after discharge from multibacillary (MB) or paucibacillary (PB) schemes of anti leprosy multidrug therapy (MDT), were submitted to traditional diagnostic procedures for leprosy and to polymerase chain reaction (PCR) analysis of different clinical samples for detection of *Mycobacterium leprae* DNA. No significant difference was observed for any of the parameters analyzed between PB or MB schemes of treatment and no indications were found for more efficient outcome of HI using the MB scheme. Remarkably, 18 (54.5%) of the individuals were PCR positive in at least one of the samples: positivity of PCR was highest in blood samples and four individuals were PCR positive in blood and some other sample. Upon comparison of PCR results with clinical and histopathological parameters, no correlation was found between PCR-positivity and eventual relapse. This is the first report on detection of *M. leprae* DNA in PB patients, more than half a decade after completion of MDT, suggesting that live bacilli are present and circulating much longer than expected, although reinfection of the individuals can not be excluded. Overall, we feel that because of the high sensitivity of the assay, extreme care should be taken about association of PCR results, efficacy of treatment and disease status.

DIAGNÓSTICO

ANSHU; GANGANE, N.; VALHA, S.; SAMAL, N. Cytodiagnosis of erythema nodosum leprosum. A case report. *Acta Cytol.*, v.46, n.2, p.386-8, Mar-Apr., 2002.

BACKGROUND: The application of cytology in leprosy has been restricted to the evaluation of

morphologic and bacterial indices by slit skin smears to facilitate diagnosis of cases according to the Ridley-Jopling scale. Isolated reports have now documented the use of fine needle aspiration cytology (FNAC) in the diagnosis of leprosy. CASE: A 45-year-old male presented with the abrupt onset of multiple nodular eruptions all over the body. The clinical diagnosis was Sweet's syndrome. FNAC showed numerous neutrophils in a background of foamy macrophages. Special stains revealed the presence of a large number of fragmented acid-fast bacilli in the smears. A diagnosis of erythema nodosum leprosum (ENL) was made on FNAC. CONCLUSION: The presence of neutrophils in a characteristic milieu of foamy macrophages is seen in lesions of ENL. Such a picture should prompt the cytologist to use a modified Ziehl-Neelsen stain to demonstrate acid-fast bacilli, as ENL can present as an acute episode in patients without a previous diagnosis of leprosy.

GELUK, A.; VAN MEIJGAARDEN, K.E.; FRANKEN, K.L.; SUBRANTO, Y.W.; WIELES, B.; AREND, S.M.; SAMPAIO, E.P.; DE BOER, T.; FABER, W.R.; NAAFS, B.; OTTENHOFF, T.H. Identification and characterization of the ESAT-6 homologue of *Mycobacterium leprae* and T-cell cross-reactivity with *Mycobacterium tuberculosis*. *Infect Immun.*, v.70, n.5, p.2544-8, May, 2002.

In this paper we describe identification and characterization of *Mycobacterium leprae* ESAT-6 (L-ESAT-6), the homologue of *M. tuberculosis* ESAT-6 (T-ESAT-6). T-ESAT-6 is expressed by all pathogenic strains belonging to the *M. tuberculosis* complex but is absent from virtually all other mycobacterial species, and it is a promising antigen for immunodiagnosis of tuberculosis (TB). Therefore, we analyzed whether L-ESAT-6 is a similarly powerful tool for the study of leprosy by examining T-cell responses against L-ESAT-6 in leprosy patients, TB patients, and exposed or nonexposed healthy controls from areas where leprosy and TB are endemic and areas where they are not endemic. L-ESAT-6 was recognized by T cells from leprosy patients, TB patients, individuals who had contact with TB patients, and healthy individuals from an area where TB and leprosy are endemic but not by T cells from individuals who were not exposed to *M. tuberculosis* and *M. leprae*. Moreover, leprosy patients who were not responsive to *M. leprae* failed to respond to L-ESAT-6. A very similar pattern was obtained with T-ESAT-6. These results show that L-ESAT-6 is a potent *M. leprae* antigen that stimulates T-cell-dependent gamma interferon production in a large proportion of individuals exposed to *M. leprae*. Moreover, our results suggest that there is significant cross-reactivity between T-ESAT-6 and L-ESAT-6, which has implications for the use of ESAT-6 as tool for

diagnosis of leprosy and TB in areas where both diseases are endemic.

MAAS, M.; SLIM, E.J.; AKKERMAN, E.M.; FABER, W.R. MRI in clinically asymptomatic neuropathic leprosy feet: a baseline study. *int. J. Leprosy*, v.69, n.3, p.219-24, Sep., 2001.

This study was undertaken to analyze the magnetic resonance imaging (MRI) findings in the clinically asymptomatic neuropathic feet of leprosy patients. Since in the literature no MRI data are available concerning the asymptomatic neuropathic foot in leprosy, the interpretation of MRI examinations in clinically suspected neuropathic feet in leprosy is difficult. We examined 10 adult leprosy patients with clinically asymptomatic neuropathic feet. Inclusion criteria were a normal or near normal neuropathic foot, without signs of inflammation. All patients underwent an MRI protocol with the inclusion of two-point Dixon chemical shift imaging as fat suppression sequence. We found MRI changes in almost all patients. The most striking were the changes located in the region of the first metacarpophalangeal (MTP) joint. These changes ranged from degradation and interruption of the subcutaneous fat to effusion/synovitis in the first MTP joint. This study reveals significant MRI changes in clinically asymptomatic neuropathic feet in patients with leprosy. These changes may relate to the development of ulcerations. MRI may play an important role in detecting feet at risk and may influence clinical decision making.

EPIDEMIOLOGIA

BROUGH, M. Healthy imaginations: a social history of the epidemiology of Aboriginal and Torres Strait Islander health. *Med. Anthropol.*, v.20, n.1, p.65-90, 2001.

It is difficult to imagine Aboriginal and Torres Strait Islander health without the powerful descriptors of epidemiology. The statistical imagery of numerical tables, pie charts, and bar graphs have become a key element in the public presentation of Indigenous public health issues. Such quantitative measurements of health draw on the authority of neutral, objective science and are thus rarely questioned in terms of their social meaning. This paper traces the history of this imagery through the 20th century, providing a social account of epidemiological description. Historical notions such as social Darwinism, assimilation, and dangerous other are all seen to be woven into the epidemiological text. The enormous rise in the epidemiological description of Indigenous health problems in recent years needs to be analyzed as a social phenomenon and, in particular, as an aspect of emerging forms of governmentality. Finally, it is argued that such

analyses are needed in order to promote an anthropology of epidemiology and to avoid limiting medical anthropology to applications within epidemiology.

EJBKOWICZ, E; TSILMAN, B.; WEXLER, R.; COHEN, H.I. Leprosy in Israel: an imported disease—the support of histopathological examination for its detection. *Acta Histochem.*, v.103, n.4, p.433-6, Oct., 2001.

Leprosy is rare and non-endemic in Israel. Cases of leprosy are invariably imported by immigrants or foreign workers arriving from endemic areas. In view of the relative rarity of the disease, clinicians and pathologists are not always alert to the possibility of the disease or recognize potential symptoms. A case history is presented of a 31-year-old immigrant presenting symptoms of skin lesions and nodules on the hands and facial region, especially the ear lobe. Confirmation of the infection was provided by histopathology of suspected lesions stained for acid-fast bacilli (modified Fite-Faraco staining).

KUMAR, A.; GIRDHAR, A.; YADAV, V.S.; GIRDHAR, B.K. Some epidemiological observations on leprosy in India. *Int. J. Leprosy*, v.69, n.3, p.234-40, Sep., 2001.

This population sample survey conducted in rural and urban areas of the Agra District in India showed an active leprosy caseload of 60.1/10,000 in the rural and 39.1/10,000 in the urban areas against a targeted prevalence of < 1/10,000. The disease appeared to be widespread since almost 65% of the villages or urban pockets surveyed had at least one prevalent case of leprosy. Significantly larger numbers of leprosy patients were found among males, agricultural/manual workers, persons with no formal schooling, individuals living in unkept households with dirty surroundings, and among those living in dark and poorly ventilated houses. The epidemiological significance of this study reveals the endemic nature of leprosy in Agra and suggests the need to intensify and widen case-detection activities to achieve leprosy control.

SOUZA, W.V.; BARCELLOS, C.C.; BRITO, A.M.; CARVALHO, M.S.; CRUZ, O.G.; ALBUQUERQUE, M.F.; ALVES, K.R.; LAPA, T.M. [Empirical bayesian model applied to the spatial analysis of leprosy occurrence]. Aplicação de modelo bayesiano empírico na análise espacial da ocorrência de hanseníase. *Rev. Saude Publica*; v.35, n.5, p.474-80, Oct., 2001.

OBJECTIVE: To analyze the spatial distribution of leprosy, identify areas of potential case underreporting or high transmission risk, and to assess the ecological

association of leprosy distribution with multibacillary cases. **METHODS:** This study was carried out in 94 neighborhoods of Recife, Brazil. Data was obtained from the Ministry of Health's Disease Reporting System. An ecological approach with the empirical Bayesian method was applied for local rate flattening, using data from a neighborhood matrix. **RESULTS:** The mean annual occurrence was 17.3% of new cases in individuals under the age of 15 (28.3% corresponded to multibacillary forms), revealing an intense disease transmission. The spatial distribution of leprosy indicated three areas where there was a concentration of high detection rates and low-income neighborhoods. **CONCLUSIONS:** The Bayesian method allowed to reassess epidemiological indicators based on data from neighboring spatial units. This enabled to identify areas that should be prioritized in municipal control programs, either because of underreporting of cases or the higher number of occurrences related to multibacillary forms in individuals under 15.

IMUNOLOGIA

ADAMS, L.B.; SCOLLARD, D.M.; RAY, N.A.; COOPER, A.M.; FRANK, A.A.; ORME, I.M.; KRAHENBUHL, J.L. The study of *Mycobacterium leprae* infection in interferon-gamma gene—disrupted mice as a model to explore the immunopathologic spectrum of leprosy. *Infect. Dis.*, v.185, p.S1-8, Feb., 2002. Suppl 1.

Mycobacterium leprae infection was evaluated in interferon-gamma knockout (GKO) mice. At 4 months, growth of the bacilli in the footpads of GKO mice plateaued a log(10) higher than that in control mice. Control mice exhibited mild lymphocytic and histiocytic infiltrates, whereas GKO mice developed large, unorganized infiltrates of epithelioid macrophages and scattered CD4 and CD8 T cells. Flow cytometric analysis of popliteal lymph node cells demonstrated similar profiles of T cells; however, GKO cells exhibited an elevated proliferative response to *M. leprae* antigen. Expression of inducible nitric oxide synthase mRNA was decreased in GKO mice, whereas macrophage inflammatory protein-1 alpha and interleukin-4 and -10 mRNA expression were augmented. Control and GKO activated macrophages inhibited bacterial metabolism and produced nitrite. Thus, although deficient in an important Th1 cytokine, GKO mice possess compensatory mechanisms to control *M. leprae* growth and feature elements resembling mid-borderline leprosy in humans.

KURADE, N.; DHAMANASKAR, P.K.; JADHAV, V.H.; JADHAV, M.V. Protein profile in leprosy. *Indian J. Med. Sci.*, v.55, n.6, p.319-25, Jun., 2001.

Serum proteins and plasma fibrinogen were estimated in 103 patients in various groups of leprosy and 52 patients of reactional leprosy. Total proteins, serum globulin and fibrinogen showed significant rise while serum albumin showed fall over the immunological spectrum from TT to LL. Type II reactional leprosy similarly revealed significant rise in globulin and fibrinogen. The comparison of these parameters between most of the comparable groups of leprosy was statistically significant. ENL patients after complete subsidence of reaction and after steroid treatment showed significant decrease in these protein fractions, thus conferring some prognostic implication on these tests.

MODLIN, R.L. Learning from leprosy: insights into contemporary immunology from an ancient disease. *Skin. Pharmacol. Appl. Skin. Physiol.*, v.15, n.1-6, Jan-Feb., 2002.

Leprosy provides an ideal model to study immune responses in humans and in skin. Learning from leprosy, we have gained insight into mechanisms of host resistance and susceptibility to infection. New paradigms include the role of Th1/Th2 cytokines, the ability of CD1 to present nonpeptide antigens to T cells, the ability of microbial lipoproteins to stimulate antimicrobial activity in monocytes and the demonstration that T cells can mediate a direct antimicrobial activity through release of granulysin. Together, these findings provide a rationale for developing new strategies to treat and prevent infectious disease.

PARKASH, O. Progress towards development of immunoassays for detection of *Mycobacterium leprae* infection, employing 35kDa antigen: an update. *Leprosy Rev.*, v. 73, n.1, p.9-19, Mar., 2002.

The 35 kDa antigen of *Mycobacterium leprae* is a membrane component that contains both B and T-cell stimulating epitopes. Monoclonal antibodies, primarily specific to *M. leprae*, have been developed against this antigen. Moreover, this antigen has been genetically engineered. Using recombinant 35 kDa antigen and/or a monoclonal antibody against an epitope on 35 kDa, a variety of antibody/antigen detecting tests have been described for detection of *M. leprae* infection. 35 kDa protein also stimulates peripheral blood mononuclear cells (PBMCs) from the majority of paucibacillary (PB) patients. Approaches using combined antibody and T cell are discussed.

RAMBUKKANA, A.; ZANAI, G.; TAPINOS, N.; SALZER, J.L. Contact-dependent demyelination by *Mycobacterium leprae* in the absence of immune cells. *Science*, v.296, n.5569, p.927-31, May, 2002.

Demyelination results in severe disability in many neurodegenerative diseases and nervous system infections, and it is typically mediated by inflammatory responses. *Mycobacterium leprae*, the causative organism of leprosy, induced rapid demyelination by a contact-dependent mechanism in the absence of immune cells in an in vitro nerve tissue culture model and in Rag1-knockout (Rag1^{-/-}) mice, which lack mature B and T lymphocytes. Myelinated Schwann cells were resistant to *M. leprae* invasion but undergo demyelination upon bacterial attachment, whereas nonmyelinated Schwann cells harbor intracellular *M. leprae* in large numbers. During *M. leprae*-induced demyelination, Schwann cells proliferate significantly both in vitro and in vivo and generate a more nonmyelinated phenotype, thereby securing the intracellular niche for *M. leprae*.

ROOK, G.A.; LIGHTMAN, S.L.; HEIJNEN, C.J. Can nerve damage disrupt neuroendocrine immune homeostasis? Leprosy as a case in point. *Trends Immunol.*, v.23, n.1, p.18-22, Jan., 2002.

The crucial clinical problem in leprosy is the occurrence of acute inflammatory episodes that lead to nerve damage, even after the infecting organisms have been killed by antibiotics. We suggest that the instability of these inflammatory sites is attributable to a disturbance of the role that nerves play in the regulation of inflammation. The destruction of sensory C fibers and sympathetic innervation will remove anti-inflammatory feedback circuits. Moreover, diminishing levels of neuropeptides and changes in the cytokine profile will affect the cortisol-sensitivity of infiltrating T cells, and modulate the cortisol-cortisone shuttle so that the inflammatory site becomes resistant to physiological levels of anti-inflammatory adrenocortical steroids.

SPENCER, J.S.; MARQUES, M.A.; LIMA, M.C.; JUNQUEIRA-KIPNIS, A.P.; GREGORY, B.C.; TRUMAN, R.W.; BRENNAN, P.J. Antigenic specificity of the *Mycobacterium leprae* homologue of ESAT-6. *Infect. Immun.*, v.70, n.2, p.1010-3, Feb., 2002.

The sequence of the *Mycobacterium leprae* homologue of ESAT-6 shows only 36% amino acid correspondence to that from *Mycobacterium tuberculosis*. Anti-*M. leprae* ESAT-6 polyclonal and monoclonal

antibodies and T-cell hybridomas reacted only with the homologous protein and allowed identification of the B- and T-cell epitopes. The protein is expressed in *M. leprae* and appears in the cell wall fraction. Thus, *M. leprae* ESAT6 shows promise as a specific diagnostic agent for leprosy

YOGI, Y.; ENDOH, M.; BANBA, T.; KOBAYASHI, M.; KATOH, H.; SUZUKI, K.; NOMAGUCHI, H. [Susceptibility to *Mycobacterium leprae* of congenic hypertensive nude rat (SHR/NCrj-rnu) and production of cytokine from the resident peritoneal macrophages]. *Nihon Hansenbyo Gakkai Zasshi*, v.71, n.1, p.3945, Feb., 2002.

We have established a congenic hypertensive nude rat strain, SHR/NCrj-rnu, carrying nude (μ) and hypertension genes which was produced using females of the SHR/NCrj rat and males of the F344/NJcl nude rat by cross-intercross system for 12 generations. We demonstrated the susceptibility to *M. leprae* infection of SHR/NCrj-rnu rats as compared with F344/NJcl-rnu rats. SHR/NCrj- μ rats were highly susceptible to *M. leprae*, and the SHR/NCrj-rnu rats of both sexes showed massive swelling of legs due to multiplication of *M. leprae*. However, F344/NJcl-rnu rats of both sexes revealed very poor susceptibility to *M. leprae*. There was a wide difference in the susceptibility to *M. leprae* between the SHR/NCrj-rnu and the F344/NJcl-rnu rats. We also examined the cytokine production. The resident peritoneal macrophages of SHR/NCrj-rnu rats produced IL-1 alpha, IL-6, IL-10 and TNF alpha, whereas those of F344/NJcl-rnu rats produced only TNF alpha.

OFTALMOLOGIA

ALMEIDA, Edmundo Frota de; ALMEIDA, Luciana Negrão Frota de. O uso de lentes intra-oculares em pacientes portadores de hanseníase / Use of intraocular lenses in patients with leprosy. *Arq. bras. Oftalmol.*, v.;64, n.6, p.541-543, Nov-Dez., 2001.

Objetivo: Avaliar as alterações oculares decorrentes da cirurgia de catarata com implante de lentes intra-oculares (LIO) em pacientes portadores de mal de Hansen (MH) e compará-las às dos pacientes não-portadores de Hanseníase. Métodos: Neste estudo, 122 olhos de 80 pacientes portadores de MH e 71 olhos de 71 pacientes não hansenianos foram submetidos à facectomia extracapsular e/ou à facoemulsificação com implante de LIO e examinados periodicamente durante o pós-operatório. Resultado:Foram constatadas alterações oculares decorrentes da cirurgia e da presença da LIO mais freqüentes no grupo portador de

hanseníase. Conclusão: O uso da LIO em pacientes com hanseníase, mesmo ocorrendo algumas alterações inflamatórias, é indicado devido ao benefício que propicia a esses pacientes em face das mutilações decorrentes da doença. (AU).

PREVENÇÃO E CONTROLE

HALDER, A.; MISHRA, R.N.; HALDER, S.; MAHATO, L.; SAHA, A.K. Impact of modified leprosy elimination campaign in a MDT pilot project district of India. *Indian J. Public Health*, v.45, n.3, p.88-92, Jul-Sep., 2001.

A study was carried out based upon the data available from National Leprosy Eradication Program of Purulia district in West Bengal. The result showed that the disease was in a declining trend up to the year 1998 and was inclining during the year 1998-1999 due to more case detection through MLEC-I, then followed by declining trend during the year 2000 as it was observed by MLEC-II. Single skin lesion rate was higher, MB rate was same and reduced deformity rate indicates early detection of cases due to better awareness of the community about the disease.

LAPA, Tiago Maria; XIMENES, Ricardo Arraes de Alencar; SILVA, Nilza Nunes; SOUZA, Wayner Vieira de; ALBUQUERQUE, Maria de Fátima Pessoa Militão; CAMPOZANA, Gisele. Vigilância da hanseníase em Olinda, Brasil, utilizando técnicas de análise espacial / Leprosy surveillance in Olinda, Brazil, using spatial analysis techniques. *Cad. saúde pública*, v.17, n.5, p.1153-62, Set.-Out., 2001.

Contribui-se com o sistema de Vigilância Epidemiológica em nível local por meio de análise espacial em razão do predomínio do caráter urbano da hanseníase em nosso meio e por sua distribuição não homogênea - em parte, pela forma de ocupação e transformação do espaço urbano. Trabalha-se o conceito de risco coletivo pela definição de micro-áreas homogêneas mediante o indicador de carência social, verificando-se sua coerência com padrões da distribuição da hanseníase obtidos da base de dados do SINAN para o Município de Olinda no período 1991-96. Para cada estrato, definido segundo níveis semelhantes dos indicadores, foi calculado o coeficiente de detecção médio para o período. Ao exame da associação entre carência social (risco) e coeficiente de detecção de hanseníase obteve-se coeficiente de explicação de 66,1 por cento no modelo multiplicativo, acrescido para 84,3 por cento com a variável renda. Para atender à lógica de intervenção, definiram-se estratos de alto, médio e baixo risco nos distritos sanitários e área programática. A

construção desses mapas mostrou-se útil a instrumentalizar o planejamento em nível local.(AU).

MURTHY, B.N.; SUBBIAH, M.; BOOPATHI, K.; RAMAKRISHNAN, R.; GUPTE, M.D. Lot quality assurance sampling (LQAS) for monitoring leprosy elimination in an endemic district in Tamilnadu. *Indian J. Leprosy*; v.73, n.2, p.111-9, Apr-Jun., 2001.

This paper examines whether the health administration can use lot quality assurance sampling (LQAS) for identifying high prevalence areas for leprosy for initiating necessary corrective measures. The null hypothesis was that leprosy prevalence in the district was at or above ten per 10,000 and the alternative hypothesis was that it was at or below five per 10,000. A total of 25,500 individuals were to be examined with 17 as an acceptable maximum number of cases (critical value). Two-stage cluster sample design was adopted. The sample size need not be escalated as the estimated design effect was 1. During the first phase, the survey covered a population of 4,837 individuals out of whom 4,329 (89.5%) were examined. Thirty-five cases were detected and this number far exceeded the critical value. It was concluded that leprosy prevalence in the district should be regarded as having prevalence of more than ten per 10,000 and further examination of the population in the sample was discontinued. LQAS may be used as a tool by which one can identify high prevalence districts and target them for necessary strengthening of the programme. It may also be considered for certifying elimination achievement for a given area.

MUSTAFA, T.; BJUNE, T.G.; JONSSON, R.; PANDO, R.H.; NILSEN, R. Increased expression of fas ligand in human tuberculosis and leprosy lesions: a potential novel mechanism of immune evasion in mycobacterial infection. *Scand. J. Immunol.*, v.54, n.6, p.630-9, Dec., 2001.

To study the location and mechanism of apoptosis within the human tuberculosis (TB) and leprosy lesions, parallel sections were analyzed for mycobacterial antigens (M.Ag), Fas ligand (FasL), Fas, CD68 and Mac387 by immunohistochemistry, and apoptotic cells by the terminal deoxynucleotidyl-transferase-mediated dUTP-digoxigenin nick end labelling method. Cutaneous leishmaniasis and foreign body granulomas were analyzed for comparison. The heavily infected macrophages in multibacillary TB and leprosy granulomas very strongly expressed FasL, indicating that a mycobacterial infection can induce an increased expression of FasL in a population of infected macrophages, which may protect

them from the attack of Fas-expressing lymphocytes. However, macrophages with high levels of leishmania amastigotes did not selectively express FasL, suggesting that this phenomenon is specific for the mycobacteria. Interestingly, in the well-formed TB granulomas, 84% of the multinucleated giant cells strongly expressed FasL. The expression of Fas was weak (34%) or absent. A higher number (33%) of epithelioid cells expressed FasL than Fas (23%). Lymphocytes were scanty among the epithelioid cells. The frequency of apoptotic cells was higher in the epithelioid cells (0.25%) than the mononuclear cells in the mantle zone (0.14%). Thus, the epithelioid cells and the multinucleated giant cells by virtue of the increased expression of FasL may make these granulomas an immune privileged site for mycobacteria.

PETERS, E.J.; ANSA, V.O.; IMANANAGHA, K.K.; ANTIA, E.A. Time of presentation for treatment and profile of deformities among leprosy patients in South Eastern Nigeria. *West Afr. J. Med.*, v.20, n.4, p.237-41, Oct-Dec, 2001.

A 10 year review of leprosy patients seen at Leprosy Hospital Ekpene Obom in South Eastern Nigeria (1988-1997) was carried out to evaluate the effect of early identification and treatment of leprosy patients in the limitation of deformities among them. A total of 2,597 patients comprising 1,714 (66%) males and 883 (34.0%) females formed subjects for the study. Of these 288(11.1%) were aged 15 and below while 2,309 (88.9) were above 15 years. Their case records were thoroughly reviewed noting the duration of disease before presentation, type and location of deformity as well as the type of leprosy. Though there was a steady decline in the total number of leprosy patients seen over the study period as well as a decrease in the mean duration of illness before presentation, approximately 19% of patients still had deformities at presentation, a figure much lower than those reported by other workers. Analysis of the pattern of deformities shows that most patients 71.2% presented with affection of the upper and lower limbs with consequent functional disability. We conclude that early treatment is an effective means of reducing the prevalence of deformity and thus disability from leprosy. More effective implementation of health education and treatment programmes initiated by the W.H.O should further reduce the scourge of leprosy in our community.

PORTER, J.D.; KESSEL, A.S. Needing to know? Ethical dilemmas in leprosy treatment and control. Erratum In: *Leprosy Rev.*, v.72, n.4, p.478, Dec., 2001. *Leprosy Rev.*, v.72, n.3, p.246-9, Sep., 2001.

A young man presents to your local clinic in a leprosy

endemic country with a small patch of discoloured skin on his right forearm. The diagnosis is clear. You start to explain, but the man stops you: he doesn't want to hear more, just requests the medicine. But you are 'in conflict', and not just by the desire to discuss the situation more fully with your patient before prescribing a drug. The local public health team, of which you are a part, is currently evaluating the impact on the community's health of a patient education programme which necessitates informing all new leprosy cases of their diagnosis. What should you do? And can bio-ethics help?

TERAPÊUTICA

CAMBAU, E.; BONNAFOUS, P.; PERANI, E.; SOUGAKOFF, W.; JI, B.; JARLIER, V. Molecular detection of rifampin and ofloxacin resistance for patients who experience relapse of multibacillary leprosy. *Clin. Infect. Dis.*; v.34, n.1, p.39-45, Jan., 2002.

Molecular detection of rifampin resistance (*rpoB* analysis) in *Mycobacterium leprae* was determined for 49 patients who experienced relapse of multibacillary leprosy and for 34 untreated patients. Molecular detection of ofloxacin resistance (*gyrA* analysis) was determined for the 12 patients who experienced relapse and who had received ofloxacin. Results of molecular tests were compared with the reference susceptibility test in the mouse footpad. Overall, the efficiency of molecular detection—that is, positive DNA amplification—was 95%, whereas that of the *in vivo* test was 55% ($P < .001$). Results of molecular detection and *in vivo* test were fully concordant when both were available—that is, for 35 rifampin-sensitive cases of leprosy (no *rpoB* mutation), 4 ofloxacin-sensitive cases (no *gyrA* mutation), 11 rifampin-resistant cases (*rpoB* missense mutations), and 1 ofloxacin-resistant case (*gyrA* mutation). *rpoB* and *gyrA* analysis appears to be an effective method for detection of rifampin and ofloxacin resistance in patients with leprosy.osy.

CHAE, G.T.; KIM, M.I.; KANG, T.J.; LEE, S.B.; SHIN, H.K.; KIM, J.P.; KO, Y.H.; KIM, S.H.; KIM, N.H. DNA-PCR and RT-PCR for the 18-kDa gene of *Mycobacterium leprae* to assess the efficacy of multi-drug therapy for leprosy. *J. Med. Microbiol.*, v.51, n.5, p.417-22, May, 2002.

DNA-PCR and reverse transcription (RT)-PCR for the 18-kDa protein of *Mycobacterium leprae* were used to examine the efficacy of multi-drug therapy (MDT) in leprosy. MDT was administered for 0-24 months. Fourteen (63.6%) of 22 patients showed positive PCR results after treatment for 12 months and the positive results decreased to 30% after 24 months of MDT. These results

did not correlate with the bacterial index (BI) or the IgM antibody titre for the phenolic glycolipid (PGL)-1. One-dimensional densitometric analysis of agarose gels from PCR from the longitudinal study showed a gradual reduction of the 360-bp band after 12-24 months of MDT. RT-PCR for mRNA of the 18-kDa protein successfully tracked bacterial RNA changes in the biopsies and confirmed a decrease in the RNA of *M. leprae* in patients after MDT for 12 months. Thus, DNA- and RT-PCR for the 18-kDa protein of *M. leprae* are effective in assessing the efficacy of MDT for leprosy.

DE SARKAR, A.; KAUR, I.; RADOTRA, B.D.; KUMAR, B. Impact of combined Mycobacterium w vaccine and 1 year of MDT on multibacillary leprosy patients. *Int. J. Leprosy*, v.69, n.3, p.187-94, Sep., 2001.

A total of 20 bacteriologically positive multibacillary (MB) leprosy patients older than 18 years of age with a bacterial index (BI) of 2+ or greater were given standard World Health Organization multiple drug therapy (MDT-MB) for 12 consecutive months plus four intradermal doses of Mycobacterium w vaccine at 3 monthly intervals (Study group). Twenty age-matched MB patients were given WHO/MDT alone (Control group). The patients of both groups were followed up for 1 year. Improvements in the patients were periodically monitored by clinical (Ramu's score), bacteriological (SSS), histopathological (skin biopsy) and immunological (lepromin conversion) parameters. Study group patients showed more significant improvements in all parameters except for lepromin conversion compared to patients in the Control group. The incidence of type 1 reaction was more in the Study group (30% vs 10%), while the incidence of type 2 reaction was more in the Control group (25% vs 15%). Neuritis associated with reactions was seen more often in the Control group compared to the Study group (20% vs 10%). The addition of Mycobacterium w vaccine as an adjunct to the 1-year WHO/MDT regimen appears to be significantly more beneficial in MB leprosy patients with a high initial BI compared to WHO/MDT given alone. Studies on larger numbers of patients with extended follow up will be in order.

GROSSET, J.H.; COLE, S.T. Genomics and the chemotherapy of leprosy. *Leprosy Rev.*, v.72, n.4, p.429-40, Dec., 2001.

The information deduced from the genome sequence of *Mycobacterium leprae* is of immense value for the chemotherapy of leprosy. Knowing the complete set of genes, enzymes and proteins allows us to understand why some drugs are without effect whereas

others are fully active. It may also enable better use to be made of existing drugs, such as beta-lactams, and opens new avenues for the development of novel compounds. *M. leprae* is relatively susceptible to a wide range of drugs, unlike the highly related tubercle bacillus, and several new multidrug regimens are in clinical trials. Genomics provides a number of possible explanations for this broader susceptibility as some of the genes encoding enzymes involved in antibiotic inactivation have decayed whereas the number of transporters available to contribute to drug efflux is considerably lower than in *Mycobacterium tuberculosis*. Several leads for new drug targets have been uncovered.

HONORÉ, N.; ROCHE, P.W.; GROSSET, J.H.; COLE, S.T. A method for rapid detection of rifampicin-resistant isolates of *Mycobacterium leprae*. *Leprosy Rev.*, v.72, n.4, p.441-B, Dec., 2001.

A genotypic method for predicting rifampicin resistance in *Mycobacterium leprae* has been developed and rigorously tested on mouse footpad-derived and clinical specimens. A series of immobilized oligonucleotide capture probes can discriminate between

wild type and mutant *rpoB* alleles, and positive controls are available for the most frequent mutation affecting Ser425. Two different non-radioactive detection formats have been tested with comparable success in both an industrialized and a developing country. The standardized procedure could now be used in a prospective study of potential rifampicin resistance among multibacillary patients.

SALAZAR, J.J.; SERRANO, G.G.; LEON-QUINTERO, G.I.; TORRES-MENDOZA, B.M. Use of topical ketanserin for the treatment of ulcers in leprosy patients. *Indian J. Leprosy*, v.73, n.2, p.103-10, Apr-Jun., 2001.

A comparative study was carried out in which 66 leprosy patients with ulcers were randomly divided in two groups of 33 patients each: Group A (experimental group) was treated with ketanserin gel (2%) and group B with clioquinol cream and/or Lassar paste during a three month period. At the end of the study, when ulcer sizes in the two groups were compared, the group treated with topical ketanserin showed superior results ($p < 0.001$ using Kolmogorov-Smirnov's test). We conclude that the drug is useful as coadjuvant treatment for healing ulcers in these patients.