

### ANTROPOLOGIA / SOCIAL / ESTIGMA

**Borg J, Larsson S. Assistive devices for people affected by leprosy: underutilised facilitators of functioning?.** *Lepr Rev.* 2009 Mar; 80(1):13-21.

**OBJECTIVES:** People affected by leprosy and their families face social and economic problems. The focus of interventions is often on prevention of disabilities and socioeconomic rehabilitation. The objective of this study was to explore to what extent the potential of assistive devices to facilitate activities and participation of people affected by leprosy has been utilised. **DESIGN:** Published literature was reviewed and the findings analysed. **RESULTS:** Considerable attention has been given to the protecting role of assistive devices. The focus of assistive devices facilitating functioning has been on mobility aspects of self-care and domestic life. **CONCLUSIONS:** The findings indicate that the potential of assistive devices to facilitate activities and participation in life areas such as work and employment is still waiting to be utilised on a broad scale.

**Nations MK, Lira GV, Catrib AM. Stigma, deforming metaphors and patients' moral experience of multibacillary leprosy in Sobral, Ceará State, Brazil.** *Cad Saude Publica.* 2009 Jun; 25(6):1215-24.

In response to the call for a new Science of Stigma, this anthropological study investigates the moral experience of patients diagnosed with severe multibacillary leprosy. From 2003 to 2006, fieldwork was conducted in the so-called 'United-States-of-Sobral', in Ceará State, Northeast Brazil. Sobral is highly endemic for leprosy, despite intensified eradication efforts and a 30% increase in primary care coverage since 1999. Of 329 active leprosy cases at two public clinics, 279 multibacillary patients were identified and six information-rich cases selected for in-depth ethnographic analysis, utilizing illness narratives, key-informant interviews, home visits, participant-observation of clinical consultations and semi-structured interviews with physicians. A 'contextualized semantic interpretation' revealed four leprosy metaphors: a repulsive rat's disease, a racist skin rash, a biblical curse and lethal leukemia. Far from value-free pathology, the disease is imbued

with moral significance. Patients' multivocalic illness constructions contest physicians' disease discourse. 'Skin Spot Day' discriminates more than educates. Patients' 'non-compliance' with effective multi-drug therapy is due to demoralizing stigma more than a rejection of care. 'Social leprosy' in Northeast Brazil deforms patients' moral reputations and personal dignity.

**Fukamizu Y, En J, Kano T, Arikawa I. Power of music that moves mind and body music therapy in the Hansen's disease sanatorium in Japan.** *Nihon Hansenbyo Gakkai Zasshi.* 2009 Feb; 78(1): 35-9.

Average age of residents living in National sanatorium Hoshizuka-Keiaien where people have past history of Hansen disease is around 80 years old at present, and many of them spend their whole days in watching TV or sleeping almost alone in their rooms. Therefore music therapy was introduced in order to improve their daily activities in our sanatorium. Singing, listening to music, playing the musical instruments, and dancing were performed, either in a group or individually. Reactivation of their brain function such as recollection, sense of unity and relaxation were expected. Improvement of cardiopulmonary function was also expected. Solidarity and relaxed state were observed by being with the other participants in the group therapy. For example, when using musical instruments, some participants with hesitation tried to use their instruments, and had good performance. They seemed to be satisfied and became confident with the musical instruments. Then their confidence and satisfaction activated the group. After the sessions, mutual conversation increased. These processes obtained a synergy effect, which means that a group affects of individuals at first and next alteration of individual behavior influences the group. We could observe a better effect in their motivation and activity in their daily life in the individual therapy. The music therapy was applied to the senior participants by the music therapist in this study. The participants could easily reinforce their mind and body through this therapy. Music therapy will be continued for the improvement of quality of life of residents in the sanatorium.

Nations MK, Lira GV, Catrib AMF. Stigma, deforming metaphors and patients' moral experience of multibacillary leprosy in Sobral, Ceará State, Brazil. *Cad. saúde pública jun.* 2009; 25(6):1215-24.

In response to the call for a new Science of Stigma, this anthropological study investigates the moral experience of patients diagnosed with severe multibacillary leprosy. From 2003 to 2006, fieldwork was conducted in the so-called "United-States-of-Sobral", in Ceará State, Northeast Brazil. Sobral is highly endemic for leprosy, despite intensified eradication efforts and a 30 percent increase in primary care coverage since 1999. Of 329 active leprosy cases at two public clinics, 279 multibacillary patients were identified and six information-rich cases selected for in-depth ethnographic analysis, utilizing illness narratives, key-informant interviews, home visits, participant-observation of clinical consultations and semi-structured interviews with physicians. A "contextualized semantic interpretation" revealed four leprosy metaphors: a repulsive rat's disease, a racist skin rash, a biblical curse and lethal leukemia. Far from value-free pathology, the disease is imbued with moral significance. Patients' multivocalic illness constructions contest physicians' disease discourse. "Skin Spot Day" discriminates more than educates. Patients' "non-compliance" with effective multi-drug therapy is due to demoralizing stigma more than a rejection of care. "Social leprosy" in Northeast Brazil deforms patients' moral reputations and personal dignity.

### **BIOLOGIA MOLECULAR**

Matsuoka M. Recent advances in the molecular epidemiology of leprosy.

*Nihon Hansenbyo Gakkai Zasshi.* 2009 Feb; 78(1): 67-73.

Recent advances in the molecular epidemiology of leprosy through genotyping of variable number tandem repeats (VNTRs) and single nucleotide polymorphisms (SNPs) are described. VNTRs with a broad range of diversity are useful genotyping tools for analyzing transmission in community areas, and SNPs and VNTRs with a small degree of variation are favorable for investigating the global transmission of leprosy. We expect that the

transmission of leprosy can be fully analyzed by the application of these new methodologies.

Robbins G, Tripathy VM, Misra VN, Mohanty RK, Shinde VS, Gray KM, et al. Ancient skeletal evidence for leprosy in India (2000 B.C.). *PLoS One.* 2009 May 27;4(5):e5669.

**BACKGROUND:** Leprosy is a chronic infectious disease caused by *Mycobacterium leprae* that affects almost 250,000 people worldwide. The timing of first infection, geographic origin, and pattern of transmission of the disease are still under investigation. Comparative genomics research has suggested *M. leprae* evolved either in East Africa or South Asia during the Late Pleistocene before spreading to Europe and the rest of the World. The earliest widely accepted evidence for leprosy is in Asian texts dated to 600 B.C. **METHODOLOGY/PRINCIPAL FINDINGS:** We report an analysis of pathological conditions in skeletal remains from the second millennium B.C. in India. A middle aged adult male skeleton demonstrates pathological changes in the rhinomaxillary region, degenerative joint disease, infectious involvement of the tibia (periostitis), and injury to the peripheral skeleton. The presence and patterning of lesions was subject to a process of differential diagnosis for leprosy including treponemal disease, leishmaniasis, tuberculosis, osteomyelitis, and non-specific infection. **CONCLUSIONS/SIGNIFICANCE:** Results indicate that lepromatous leprosy was present in India by 2000 B.C. This evidence represents the oldest documented skeletal evidence for the disease. Our results indicate that Vedic burial traditions in cases of leprosy were present in northwest India prior to the first millennium B.C. Our results also support translations of early Vedic scriptures as the first textual reference to leprosy. The presence of leprosy in skeletal material dated to the post-urban phase of the Indus Age suggests that if *M. leprae* evolved in Africa, the disease migrated to India before the Late Holocene, possibly during the third millennium B.C. at a time when there was substantial interaction among the Indus Civilization, Mesopotamia, and Egypt. This evidence should be impetus to look for additional skeletal and molecular evidence of leprosy in India and Africa to confirm the African origin of the disease.

Ávila JFT, Colorado CL, Gamboa LA, Araujo MJ, Franco CLI, Guerrero, MIG. Genotipificación de *Mycobacterium leprae* colombiano para la determinación de patrones de transmisión de la enfermedad / Genotyping Colombian *Mycobacterium leprae* for determining disease transmission patterns. *Rev. salud pública* feb. 2009; 11(1):3-13.

Objetivo: Evaluar la variabilidad de VNTR (variable-number tandem repeat) de *Mycobacterium leprae* de pacientes colombianos con y sin tratamiento previo para identificar posibles fuentes de infección y entender los patrones de transmisión de la enfermedad. Metodología Estudio transversal descriptivo, en donde mediante un muestreo electivo a conveniencia se tomaron 161 biopsias de pacientes multibacilares de lepra, que habían sido solicitadas para diagnóstico y seguimiento de la enfermedad, de las cuales se realizó extracción de ADN de *M. leprae* y usando la técnica de PCR para VNTRs de *M. leprae* estandarizada, se establecieron los genotipos y los diferentes clusters mediante el agrupamiento apareado UPGMA. Resultados En las 161 muestras totales se hallaron 22 genotipos VNTRs diferentes, de las cuales 100 muestras (62,1 por ciento) pertenecían al genotipo único VNTRU, y de los genotipos restantes, los mayoritarios, es decir los que dieron lugar a formación de grupos o clusters fueron VNTR17 (5,6 por ciento), VNTR20 (4,3 por ciento), VNTR18 (4,3 por ciento), VNTR14 (4,3 por ciento) y VNTR13 (3,7 por ciento). Conclusión En este estudio se evidencia por análisis de agrupamiento que se pueden detectar clones con diferente grado de virulencia/agresividad, lo cual implica la necesidad de incrementar varias de las actividades del programa de control que darán como resultado la verdadera disminución de la transmisión del microorganismo.

### BIOQUÍMICA

Ascenzi P, Marinis E, Visca P, Ciaccio C, Coletta M. Peroxynitrite detoxification by ferryl *Mycobacterium leprae* truncated hemoglobin O. *Biochem Biophys Res Commun*. 2009 Mar 6; 380(2): 392-6.

During infection, *Mycobacterium leprae* is faced with the host macrophagic environment limiting the growth of

the bacilli. However, (pseudo-)enzymatic detoxification systems, including truncated hemoglobin O (MI-trHbO), could allow this mycobacterium to persist in vivo. Here, kinetics of peroxynitrite (ONOOH/ONOO(-)) detoxification by ferryl MI-trHbO (MI-trHbO-Fe(IV)=O), obtained by treatment with H<sub>2</sub>O<sub>2</sub>, is reported. Values of the second-order rate constant for peroxynitrite detoxification by MI-trHbO-Fe(IV)=O (i.e., of MI-trHbO-Fe(III) formation; k<sub>on</sub>), at pH 7.2 and 22.0 degrees C, are 1.5x10<sup>4</sup> M<sup>-1</sup> s<sup>-1</sup>, and 2.2x10<sup>4</sup> M<sup>-1</sup> s<sup>-1</sup>, in the absence of and presence of physiological levels of CO<sub>2</sub> (approximately 1.2x10<sup>-3</sup> M), respectively. Values of k<sub>on</sub> increase on decreasing pH with a pK<sub>a</sub> value of 6.7, this suggests that ONOOH reacts preferentially with MI-trHbO-Fe(IV)=O. In turn, peroxynitrite acts as an antioxidant of MI-trHbO-Fe(IV)=O, which could be responsible for the oxidative damage of the mycobacterium. As a whole, MI-trHbO can undertake within the same cycle H<sub>2</sub>O<sub>2</sub> and peroxynitrite detoxification

### CIRURGIA / REABILITAÇÃO / INCAPACIDADES

Gonçalves SD, Sampaio RF, Antunes CM. Predictive factors of disability in patients with leprosy. *Rev Saude Publica*. 2009 Apr; 43(2): 267-74.

OBJECTIVE: To analyze predictive factors in the progression of the disability grade in patients with leprosy. METHODS: A retrospective cohort study followed up 595 patients with disability registered at a healthcare unit in the city of Belo Horizonte (Southeastern Brazil) from 1993 to 2003. Patients' sociodemographic and clinical information was collected from the respective medical records. Comparisons were made between the disability grade upon admission and at the end of treatment using a marginal homogeneity test. To determine factors associated with progression in the disability grade, univariate analysis (linear trend chi-square test) was employed, as well as multivariate analysis by means of the algorithm Chi-square Automatic Interaction Detector. RESULTS: Among the cases in which the disability grade was recorded upon admission and upon discharge, 43.2% of the patients who had grade 1 in the first assessment progressed to grade 0. Among those who began with grade 2, 21.3% progressed to grade 0 and 20% pro-

gressed to grade 1. In the univariate analysis, the variables that proved to be statistically associated with progression in the disability grade were: neuritis, time elapsed until the occurrence of neuritis, number of damaged nerves, type of physiotherapy treatment and higher dose of prednisone. In the multivariate analysis, the main factor associated with the progression of disability was the disability grade upon admission. **CONCLUSIONS:** The results showed the importance of an early diagnosis of neuropathy as well as the efficient association of pharmacological and non-pharmacological treatment, through disability prevention techniques and adequate doses of steroid.

**Rath S, Selles RW, Schreuders TA, Stam HJ, Hovius SE. A randomized clinical trial comparing immediate active motion with immobilization after tendon transfer for claw deformity. J Hand Surg Am. 2009 Mar; 34(3): 488-94.**

**PURPOSE:** Immobilization after tendon transfers has been the conventional postoperative management. A recent study indicated beneficial effects of an immediate active motion protocol (IAMP) after tendon transfer for claw deformity correction compared with effects in a historical cohort. In this study, we further tested this hypothesis in a randomized clinical trial comparing the effectiveness of the IAMP with that of conventional immobilization. **METHODS:** Fifty supple claw hand deformities were randomized postoperatively into 2 equal groups for IAMP and immobilization. Therapy began on the second postoperative day for the IAMP group and on the twenty-second postoperative day for the immobilization group. The primary outcome measures were deformity correction, active range of motion of digits, tendon transfer insertion pullout, and time until discharge from rehabilitation. Secondary outcome measures were swelling, pain, hand strength, and dexterity. Both groups were compared at discharge from rehabilitation and at the last clinical follow-up (at least 1 year postoperatively). **RESULTS:** Assessments were available for all 50 patients at discharge and for 23 patients in each group at follow-up. The average follow-up was 18 months for the IAMP group and 17 months for the im-

mobilization group. Deformity correction, range of motion, swelling, dexterity, and hand strength were similar for both groups at discharge and a follow-up. There was no evidence of tendon insertion pullout in any patient of either group. Relief of pain was achieved significantly earlier with IAMP. Morbidity was reduced by, on average, 22 days with IAMP. **CONCLUSIONS:** We found that the immediate active motion protocol is safe and has similar outcomes compared with those of immobilization, with the added advantage of earlier pain relief and quicker restoration of hand function. Immediate motion after tendon transfer can significantly reduce morbidity and speed up the rehabilitation of paralytic limbs, and it may save expense for the patients.

**Van Veen NH, Schreuders TA, Theuvenet WJ, Agrawal A, Richardus JH. Decompressive surgery for treating nerve damage in leprosy. Cochrane Database Syst Rev. 2009 Jan 21;(1): CD006983.**

**BACKGROUND:** Leprosy causes nerve damage which may result in nerve function impairment and disability. Decompressive surgery is used for treating nerve damage, although the effect is uncertain. **OBJECTIVES:** To assess the effects of decompressive surgery on nerve damage in leprosy. **SEARCH STRATEGY:** We searched the Cochrane Neuromuscular Disease Group Trials Register (November 2007), the Cochrane Central Register of Controlled Trials (The Cochrane Library Issue 4, 2007), MEDLINE (from January 1950 to November 2007), EMBASE (from January 1980 to November 2007), AMED (from January 1985 to November 2007), CINAHL (from January 1982 to November 2007) and LILACS (from January 1982 to November 2007) in November 2007. We checked reference lists of the studies identified, the Current Controlled Trials Register ([www.controlled-trials.com](http://www.controlled-trials.com)), conference proceedings and contacted trial authors. **SELECTION CRITERIA:** Randomised and quasi-randomised controlled trials of decompressive surgery for nerve damage in leprosy. **DATA COLLECTION AND ANALYSIS:** The primary outcome was improvement in sensory and motor nerve function after one year. Secondary outcomes were improvement in nerve function after two years, change in nerve pain and tenderness, and adverse events. Two authors inde-

pendently extracted data and assessed trial quality. We contacted trial authors for additional information. We collected adverse effects information from the trials and non-randomised studies. **MAIN RESULTS:** We included two randomised controlled trials involving 88 people. The trials examined the added benefit of surgery over prednisolone for treatment of nerve damage of less than six months duration. After two years follow-up there was no significant difference in nerve function improvement between people treated with surgery plus prednisolone or with prednisolone alone. Adverse effects of decompressive surgery were not adequately described. **AUTHORS' CONCLUSIONS:** Decompressive surgery is used for treating nerve damage in leprosy but evidence from randomised controlled trials does not show a significant added benefit of surgery over steroid treatment alone. Well-designed randomised controlled trials are needed to establish the effectiveness of the combination of surgery and medical treatment compared to medical treatment alone.

**Van Veen NH, Schreuders TA, Theuvenet WJ, Agrawal A, Richardus JH. Decompressive surgery for treating nerve damage in leprosy. A Cochrane review. Lepr Rev. 2009 Mar; 80(1):3-12.**

**OBJECTIVE:** Decompressive surgery is used for treating nerve damage in leprosy. We assessed the effectiveness of decompressive surgery for patients with nerve damage due to leprosy. **METHODS:** A broad search strategy was performed to find eligible studies, selecting randomised controlled trials (RCTs) comparing decompressive surgery alone or plus corticosteroids with corticosteroids alone, placebo or no treatment. Two authors independently assessed quality and extracted data. Where it was not possible to perform a meta-analysis, the data for each trial was summarised. **RESULTS:** We included two randomised controlled trials involving 88 people. The trials examined the added benefit of surgery over prednisolone for treatment of nerve damage of less than 6 months duration. After 2 years follow-up there was no significant difference in nerve function improvement between people treated with surgery plus prednisolone or with prednisolone alone. Adverse effects of decompression surgery were

not adequately described. **CONCLUSIONS:** Evidence from randomised controlled trials does not show a significant added benefit of surgery over steroid treatment alone. Well-designed randomised controlled trials are needed to establish the effectiveness of the combination of surgery and medical treatment compared to medical treatment alone.

**Malaviya GN. Fracture of calcaneum following drop foot surgery--a case report. Lepr Rev. 2009 Mar; 80(1):77-80.**

The usual protocol for correction of drop foot in leprosy, a consequence of damage to the common peroneal nerve, is a tendon transfer, immobilisation to heal the tendon juncture and post-operative exercises to put the transfer into use. Tarsal disintegrations have been reported in literature in drop foot patients when the transferred tendons were inserted into the bone making a drill hole to ensure firm anchorage. Such disintegrations are rarely seen these days because bony insertion of the tendon transfers is not performed in the leprosy-affected foot. We report here a case of drop foot that developed a fracture of the calcaneum during the post-operative period after tibialis posterior two tail transfer (to tibialis anterior and extensor digitorum longus) along with lengthening of the tendoachillis. The case is interesting in the sense that osteoporosis and walking strains resulted in a fracture of the body of the calcaneum which healed with conservative treatment and controlled mobilisation of the patient.

**Anand S, Neethiodiss P, Xavier JW. Intra and post operative complications and visual outcomes following cataract surgery in leprosy patients. Lepr Rev. 2009 Jun; 80(2):177-86.**

**OBJECTIVES:** The occurrence of intra and post operative complications was compared in different groups of leprosy patients. The association between post operative and intra operative complications was studied, and how visual outcomes were affected by these complications. We also share our medical management and surgical

techniques that might help minimise intra operative complications and improve visual outcomes. DESIGN: A retrospective analysis of 1024 cataract operations in 786 leprosy patients over an 11 year period from 1995 to 2006 at Kothara Community Hospital, a rural hospital belonging to The Leprosy Mission Trust India, located in the Amravati district of Maharashtra. RESULTS: 3.5% of eyes had intra operative complications and 22% of eyes had post operative complications, with no appreciable difference in incidence of intra operative complications in the various groups of patients studied. Post operative uveitis was higher in the MB (3.2%), smear positive (6.5%), UT (6%), eyes with leprosy related ocular disease (6.4%) and lepra reaction (12%) groups. Overall, eyes with leprosy related complications and eyes operated on during lepra reactions had more post operative complications compared to the group without. Visual outcomes for eyes with intra and post operative complications were poorer than the groups without. CONCLUSIONS: Cataract surgery in the hands of a careful and well trained surgeon, who is familiar with ocular leprosy and can modify the surgical technique as necessary, is safe and associated with minimal intra operative and post operative complications.

**Ebenso J, Velema JP. Test-retest reliability of the Screening Activity Limitation and Safety Awareness (SALSA) scale in North-West Nigeria. *Lepr Rev.* 2009 Jun; 80(2):197-204.**

INTRODUCTION: The present study examines the inter-tester and intra-tester reliability of the recently developed scale for Screening of Activity Limitation and Safety Awareness (SALSA) in North-West Nigeria. The scale was developed through collaborative research in five countries around the world. METHODOLOGY: One hundred and three people affected by leprosy from three states in North-West Nigeria participated in the study. A Hausa translation of the 20-item SALSA questionnaire was used by four trained health staff to interview the participants. Seventy-five paired interviews were conducted where the second interview was administered by a different interviewer from the first at intervals of 4-76 days (median 52). Twenty-eight paired interviews were conducted,

both by the same interviewer, at intervals of 52-71 days (median 63). RESULTS: Inter-tester reliability: All 20 items had Kappa's ranging from 0.45-0.8; 15 items had Kappa's > 0.6; 8 items had Kappa's > 0.7. Intra-tester reliability: All 20 items had Kappa's ranging from 0.51-1; 15 items had Kappa's > 0.6; 12 items had Kappa's > 0.7. For inter-tester reliability, the first interview had a mean SALSA score of 36.5 (95% CI = 34.96-38.05). The second interview had a mean of 35.02 (95% CI = 35.01-37.99). For intra-tester reliability, the mean SALSA scores of first and second interviews were 27.36 (95% CI = 24.36-30.36) and 26.68 (95% CI = 23.93-29.43), respectively. CONCLUSIONS: The Hausa translation of SALSA has an acceptable reliability in Nigeria provided the interviewers are well trained.

**Gonçalves SD, Sampaio RF, Antunes CMF. Fatores preditivos de incapacidades em pacientes com hanseníase. *Rev. saúde pública* abr. 2009; 43(2):267-74.**

OBJETIVO: Analisar os fatores preditivos na evolução do grau de incapacidade em pacientes com hanseníase. MÉTODOS: Foram analisados dados de coorte retrospectiva, que acompanhou 595 pacientes com incapacidades, registrados em uma unidade de saúde de Belo Horizonte (MG), de 1993 a 2003. Informações sociodemográficas e clínicas dos pacientes foram coletadas dos respectivos prontuários. Comparou-se o grau de incapacidade na admissão e no final do tratamento por meio do teste de homogeneidade marginal. Para identificar os fatores associados à evolução do grau de incapacidade foram utilizadas as análises univariada (teste qui-quadrado de tendência linear) e multivariada pelo algoritmo Chi-square Automatic Interaction Detector. RESULTADOS: Dos casos com registro de grau de incapacidade na admissão e na alta, observou-se que 43,2 por cento que tinham grau 1 na primeira avaliação evoluíram para grau 0. Dos que apresentavam grau 2, 21,3 por cento passaram a ter grau 0 e 20 por cento passaram a grau 1. Na análise univariada as variáveis que se mostraram estatisticamente associadas à evolução no grau de incapacidade foram: neurite, tempo até a ocorrência de neurite, número de nervos acometidos, tipo de tratamento fisioterápico e maior dose de prednisona. Na análise multivariada, o principal fator que se associou à evolução do grau de

incapacidade foi o grau de incapacidade na admissão. **CONCLUSÕES:** Os resultados mostraram a importância do diagnóstico precoce de neuropatia, assim como da eficiente associação das intervenções medicamentosas e não-medicamentosas por meio das técnicas de prevenção de incapacidade e dosagens adequadas de corticoterapia.

**Oliveira RA, Cunha MGS, Talhari S, Cunha PAS. Avaliação neurofuncional no pré e pós-operatório de neurólise no dano neural devido à hanseníase. Fisioter. Brás jan.-fev. 2009; 10(1):15-20.**

O presente estudo teve como objetivo analisar, por meio do exame neurofuncional, a eficácia da cirurgia de neurólise em pacientes com neurite hansênica. Tratou-se de um estudo prospectivo, do tipo descritivo. Teve como universo de estudo a população portadora de neurite hansênica do Estado do Amazonas, tratada na FUAM-AM. Foram selecionados 27 participantes os quais foram triados para cirurgia eletiva de neurólise no período de outubro de 2004 a janeiro de 2005, correspondendo a 64 cirurgias eletivas. Foi realizada uma avaliação neurofuncional pré-operatória compreendendo o teste de força muscular manual, teste de sensibilidade pelos estesiômetros de Semmes-Weinstein, avaliação da dor por meio de escala analógica visual e classificação do grau de incapacidade. A mesma avaliação foi repetida um mês após a cirurgia. Os principais nervos operados foram, em ordem decrescente, medial e ulnar, fibular comum e tibial posterior. A forma clínica mais comum entre os mesmos foi a virchowiana (67 por cento), seguida da dimorfa-virchowiana (19 por cento), tuberculóide (7 por cento) e dimorfa-tuberculóide (7 por cento). Setenta e quatro por cento dos pacientes operados encontravam-se em alta clínica e 26 por cento ainda realizavam tratamento por poliquimioterapia. A principal queixa apresentada foi dor (55 por cento). Em relação ao grau de incapacidade, 70 por cento apresentaram grau I e 30 por cento apresentaram grau II. No pós-operatório, foi relatada melhora da dor em 64 por cento das cirurgias, 30 por cento não apresentaram alteração e 6 por cento apresentaram piora. Cinquenta e seis por cento dos nervos com comprometimento motor não apresentaram melhora, 32 por

cento melhoraram em até um grau e 12 por cento apresentaram piora em até um grau. Trinta e quatro por cento dos pacientes apresentaram melhora da sensibilidade, e 66 por cento se mostraram com quadro inalterado.

**Shah AR, Zeitler D, Wise JB. Nasal reconstruction of the leprosy nose using costal cartilage. Otolaryngol Clin North Am. 2009 Jun; 42(3):547-55.**

Leprosy is a chronic granulomatous infection of the skin and peripheral nerves that often leads to gross deformation of the nasal skeleton and subsequent formation of a saddle-nose deformity. Reconstruction of the nose following *Mycobacterium leprae* infection has challenged surgeons for centuries. As a result, a number of different techniques have been attempted with varying outcomes. This article describes the case and surgical treatment of a 37-year old female who presented with a subtotal nasoseptal perforation and saddle-nose deformity secondary to previous infection with leprosy. Reconstruction was achieved via an open septorhinoplasty approach using autologous costal cartilage grafts, yielding a successful postoperative result.

#### **CLÍNICA**

**Thomas M, Emmanuel M. A case of advanced lepromatous leprosy with rhino-oro-laryngological involvement in the post-elimination era. Indian J Lepr. 2009 Apr-Jun;81(2): 81-2.**

A patient presenting with symptoms and signs of congestive heart failure was incidentally found to be in advanced stage of leprosy. He had multiple lepromatous nodules over the entire body. The oral mucosa was yellowish with a matte appearance and the palate had a site ready to perforate. Nasal cavity revealed a small septal perforation with overlying crusts suggesting advanced rhinitis. Diagnosis of lepromatous leprosy was confirmed on histology. This case report emphasizes the existence of pockets of highly bacilliferous cases that continue to be a source of infection within the community and highlights the need for enhanced health education.

**Leal AM, Foss NT. Endocrine dysfunction in leprosy. Eur J Clin Microbiol Infect Dis. 2009 Jan; 28(1): 1-7.**

Leprosy is still an endemic disease, especially in Third World countries, and, because of migration, it still persists in Europe and the United States. The disease affects the peripheral nerves, skin, and multiple internal organs, making its clinical recognition difficult. In particular, the endocrine manifestations caused by leprosy have been underestimated, even by specialists. The endocrine changes present in leprosy include hypogonadism, sterility, and osteoporosis. In addition, the spectral immune nature of leprosy offers an attractive model to investigate the pathogenetic correlation between the patterns of inflammation in the poles of its spectrum and the hormonal disarrangements observed in this disease. It is important that those involved in leprosy management be aware of the potential endocrine changes and their treatment to address the disease in all of its aspects. In this article, we review the findings on endocrine dysfunction in leprosy, including a survey of the literature and of our own work.

**Benard G, Sakai-Valente NY, Trindade MAB. Concomitant lucio phenomenon and erythema nodosum in a leprosy patient: clues for their distinct pathogeneses. Am J Dermatopathol. 2009 May; 31(3):288-92.**

Lepromatous leprosy patients may develop necrotic lesions, usually in the context of Lucio phenomenon (LP) or severe erythema nodosum (EN). The clinical and histopathological characteristics of the necrotic manifestations of both entities may eventually be confounded. We describe a patient with lepromatous leprosy who developed, since the 4th month of her first pregnancy, recurrent necrotic lesions in lower limbs, which, at the postpartum, worsened and led to partial destruction of ears and nose. In addition, she referred painful nodes on upper limbs since 1 year before pregnancy and intermittent swelling and tenderness of the ankles, which together with a right tibial and ulnar neuritis led to the diagnosis of, erythema nodosum leprosum (ENL). The histopathology of a biopsy of the upper limb (ENL) revealed a dermal-hypodermal inflammation with vasculitis and vascular lumen narrowing, whereas biopsy of the lower limb (LP) revealed small

vessels with fibrin thrombi on the superficial layer of the dermis without inflammatory infiltrate and no evidence of vasculitis. Thus, besides having several different clinical features, LP and ENL result from different pathogenetic mechanisms. The histopathological and clinical features distinguishing both entities are proposed. This distinction is important because decrease in bacillary load through multidrug therapy is the main target in LP, whereas in ENL, concomitant reduction of the reaction by means of thalidomide or high-dose steroids is recommended.

**Menezes VM, Sales AM, Illarramendi X, Miranda A, Gonçalves MM, Gutierrez-Galhardo MC, et al. Leprosy reaction as a manifestation of immune reconstitution inflammatory syndrome: a case series of a Brazilian cohort. AIDS. 2009 Mar 13; 23(5):641-3.**

Several case reports have demonstrated that the immune reconstitution inflammatory syndrome induces reversal reaction in HIV and leprosy-coinfected patients. The present study describes 10 cases of immune reconstitution inflammatory-associated reversal reaction. The patients evolved satisfactorily despite presenting a more severe form of the disease and the fact that three required an additional use of corticoids. The present study, the largest case series published to date, demonstrates that leprosy reaction is a manifestation of immune reconstitution.

**Prabhu S, Shenoi SD, Pai SB, Sripathi H. Erythema nodosum leprosum as the presenting feature in multibacillary leprosy. Dermatol Online J. 2009 Jun 15; 15(6):15.**

Leprosy is an ancient disease that has survived into the modern ages despite an intense effort to eliminate it worldwide. Here we report a case of a 32-year-old woman who had recurrent painful nodules of six months duration. Because of a lack of lesions suggestive of leprosy, she was initially diagnosed to have cutaneous vasculitis and erythema nodosum. However, because of the persistent nature of her condition she was later detected to have leprosy and erythema nodosum leprosum (ENL) with the aid of simple diagnostic tests.



Santos AP, Selles BR, Ayres EL, Xavier MH, Rochoael MC. A man with erythematous nodules: what is the diagnosis? Lepromatous leprosy. *Dermatol Online J.* 2009 Jun 15; 15(6):10.

A 65-year-old man presented with an approximately 5-year history of cutaneous nodules of the arms and legs. In addition, physical examination revealed bilateral thickening of ulnar and tibial nerves, distal weakness with hallux extension and finger abduction, and distal hypoesthesia of the left hallux. Histopathological analysis of the skin biopsy specimen showed a dense inflammatory infiltrate in the hypodermis, characterized by vacuolated macrophages containing multiple organisms. The Fite stain was positive confirming the diagnosis of multibacillary leprosy.

Kaliyadan F, Bhaskaran M, Dharmaratnam AD, Manoj J, Sreekanth G. Anti-phospholipid syndrome preceding a diagnosis of lepromatous leprosy. *Dermatol Online J.* 2009 Jun 15; 15(6):4.

A 64-year-old male, with known anti-phospholipid syndrome (APS), which had been diagnosed two years previously, presented to our department with asymptomatic papules over his trunk. Histopathological examination confirmed the diagnosis of lepromatous leprosy. We present this as a case of APS, preceding a diagnosis of lepromatous leprosy.

Kar HK, Sharma P, Bhardwaj M. Borderline tuberculoïd leprosy with upgrading Type 1 reaction in a HIV seropositive patient, after antiretroviral therapy: an immune reconstitution inflammatory syndrome. *Leprosy Rev.* 2009 Mar; 80(1):85-8.

A case of borderline tuberculoïd (BT) leprosy with upgrading Type 1 reaction, in a HIV seropositive patient, 7 weeks after starting highly active antiretroviral therapy, as an immune reconstitution inflammatory syndrome (IRIS), is reported.

## DIAGNÓSTICO

King K, Browning JC, Metry DW, Prestigiacomo J, Scollard D, Schutze GE, et al. Leprosy and international adoption: a case report and review of diagnostic and treatment dilemmas. *Pediatr Infect Dis J.* 2009 Apr; 28(4):322-5.

Hansen disease, commonly known as leprosy, is uncommon in the United States and poses difficult diagnostic and treatment challenges. A 10-year-old girl was adopted from Ethiopia with a history of "multibacillary leprosy" and "multidrug treatment" for 12 months. Three months after her arrival in the United States and 4 months after treatment was completed, she presented with new papules and plaques on her left nose and ear. Herein, we present her case and review current treatment options in leprosy in children and the management of immunologic reactions.

Daniel S, Arunthathi S, Rao PS. Impact of integration on the profile of newly diagnosed leprosy patients attending a referral hospital in South India. *Indian J Lepr.* 2009 Apr-Jun; 81(2): 69-74.

This article compares the clinical profile of new untreated leprosy patients attending a referral hospital (The Schieffelin Institute for Health Research & Leprosy Centre, formerly known as SLR&TC, Karigiri, South India, in post-integration period (2005-2007) with that during the pre-integration period (1995-1996). A total of 529 patients--259 in pre-integration and 270 in post-integration period--were seen at this hospital. The clinical data culled from records for the earlier period were compared with data gathered prospectively for the latter period and was analyzed using SPSS software. The results showed a significant increase in the mean age of registration, percent multibacillary (clinical criteria) and grade 2 disabilities in post-integration period. Increase in proportion of cases with grade 2 deformities is a matter of concern and suggests continued need for referral hospitals for their management and also population based overall assessment whether actual numbers with deformities have increased or it is peculiar to a tertiary care hospital where the cases with problems may be coming. As the

proportion of bacteriological positive cases was not found to change, it is a positive sign of effective coverage in the post-integration scenario in this population.

**Sapkota BR, Neupane KD, Maharjan RK. Single lesion multibacillary leprosy, a treatment enigma: a case report. J Med Case Reports. 2009 Jan 13; 3:8.**

**INTRODUCTION:** Leprosy exhibits a wide spectrum of presentation, varying from the tuberculoid to the lepromatous pole, with immunologically unstable borderline forms in-between, depending upon the immune status of the individual. The clinical system of classification for the purpose of treatment includes the number of skin lesions and nerves involved as the basis for classifying the patients into multibacillary and paucibacillary. **CASE PRESENTATION:** A 20-year-old man belonging to a moderately endemic leprosy area in the Terai region of Nepal reported a large single, hypopigmented, well defined anaesthetic lesion on his left thigh extending to his knee which had been present for 2 years. There was no other nerve involvement. Clinical diagnosis was tuberculoid leprosy and immunological lateral flow test for anti-Phenolic glycolipid-I antibody was positive. Six months of paucibacillary multidrug treatment was advised immediately. However, the patient was reclassified as multibacillary on the basis of a positive skin smear and appropriate treatment of 24 months multibacillary multidrug regimen was commenced after only 1 week. Slit skin smear examination for *Mycobacterium leprae* from the lesion revealed a bacterial index of 4+ while it was negative from the routine sites. Histopathological examination from skin biopsy of the lesion further supported the bacterial index of the lesion granuloma which was 2+ and the patient was diagnosed as borderline tuberculoid. Bacteriological, histological, and immunological findings of this patient were borderline tuberculoid leprosy and he should have been treated with multibacillary regimen from the beginning. Five months after commencement of treatment, the patient developed a lepra reaction of Type 1 or reversal reaction with some nerve function impairment and enlargement of the lateral popliteal nerve of the left leg. This reversal reaction was managed by standard oral prednisolone whilst continuing the multibacillary multidrug regimen.

**CONCLUSION:** This case illustrates and emphasizes the importance of slit-skin smear and biopsy as routine in all new cases to help differentiate multibacillary from paucibacillary for correct treatment. It further suggests that there are factors yet undetermined which play a significant role in determining the host response to *M. leprae* which is a remaining challenge in this disease.

**Kaur I, Dogra S, De D, Saikia UN. Histoid leprosy: a retrospective study of 40 cases from India.**

**BACKGROUND:** Rare variants of leprosy pose a diagnostic challenge even to astute clinicians and histoid leprosy is one such form of disease with unique clinical and histopathological features. There are very few large series on this entity, mainly reported from India. **OBJECTIVES:** To study the epidemiological and clinical characteristics of patients with histoid leprosy. **METHODS:** We undertook this retrospective study including patients registered with the leprosy clinic of our tertiary care referral centre from January 1991 to December 2006. Data regarding demographic details, clinical features, treatment, complications and course following treatment were extracted from the records of the leprosy clinic. **RESULTS:** The incidence of histoid leprosy among the registered patients of our clinic was 1.8% (40 of 2150). There was a significant male preponderance with a male/female ratio of 5.7 : 1. The anatomical areas of involvement were thighs/buttocks (67.5%), arms (62.5%), back (52.5%), face (47.5%), forearms (47.5%) and legs (35%) in descending order of frequency. This variety of leprosy was found most commonly in patients with a primary diagnosis of lepromatous leprosy (40%). De novo histoid lesions, i.e. lesions of histoid leprosy developing without evidence of lesions of other types of leprosy in the Ridley-Jopling classification, appeared in 12.5% of patients only. Only three patients had received antileprosy treatment before presentation. Episodes of erythema nodosum leprosum (ENL) had occurred in 40% of patients, although only one patient manifested ENL after the diagnosis of histoid leprosy. The disease responded satisfactorily to the respective World Health Organization multidrug therapy regimens in all except in one patient who relapsed with borderline lepromatous leprosy. **CONCLUSIONS:** As the bacillary load is very high in these patients, they can form

a potential reservoir of the infection in the community especially in the postleprosy elimination era. Contrary to the earlier belief in the dapsone era, most of our patients manifested disease without any history of inadequate or incomplete antileprosy therapy.

**Landais C, Graffin B, Leyral G, Boyé T, Carli P, Carsuzaa F. Lepromatous leprosy revealed by a swollen hands syndrome. *Med Mal Infect.* 2009 Jan; 39(1) :55-6.**

Osteoarticular pathology in leprosy is common and described at all stages, but rarely as the most evident clinical manifestation. We report a case of borderline lepromatous leprosy with initial and disabling hands edema. The swollen hands syndrome is probably due to chronic *Mycobacterium leprae* tenosynovitis.

**Nery JA, Schreuder PA, Mattos PC, Mendonça LV, Tardi RT, Mello S, et al. Hansen's disease in a general hospital: uncommon presentations and delay in diagnosis. *J Eur Acad Dermatol Venereol.* 2009 Feb; 23(2): 150-6.**

**BACKGROUND:** The question was raised as to why 'obvious' signs of leprosy, Hansen's disease (HD), are often missed by medical doctors working in a HD endemic area. **METHODS:** This study describes a small sample of patients who were diagnosed with HD during their hospital admission and not before. The discussion is whether the typical early signs and symptoms of HD are just not recognized, or whether unusual presentations confuse the attending physician. **RESULTS:** A total of 23 HD patients were hospitalized during the study period, of which 6 (26%) were only diagnosed with HD during their admission. All were classified as lepromatous leprosy (LL) with a history of signs and symptoms of HD. In nearly all patients, a suspicion of HD might have been raised earlier if a careful history and dermato-neurological examination had been done. **CONCLUSIONS:** Multibacillary (MB) HD, especially close to the lepromatous end of the spectrum, may mimic other diseases, and the patient can not be diagnosed without a biopsy or a slit skin smear examination. Clinicians working in a HD endemic area (Rio de Janeiro) do not always include HD in their differential

diagnosis, especially when the clinical presentation is unusual. HD should be considered in all patients with skin lesions not responding to treatment, especially when they have neurological deficits, and live or have lived in an HD endemic area. Due to the increase in global travel and immigration, doctors in low endemic areas need to consider HD as a possible diagnosis.

**Bang PD, Suzuki K, Phuong T, Chu TM, Ishii N, Khang TH. Evaluation of polymerase chain reaction-based detection of *Mycobacterium leprae* for the diagnosis of leprosy. *J Dermatol.* 2009 May; 36(5):269-76.**

Because *Mycobacterium leprae* cannot be cultivated in vitro, laboratory diagnosis of leprosy is generally made by microscopic and histopathological examination. The objective of the present study was to evaluate the sensitivity and utility of polymerase chain reaction (PCR) to detect *M. leprae* in comparison with other conventional methods for diagnosis such as split skin smears, histopathology and serodiagnosis. PCR amplification of the *M. leprae*-specific 16S ribosomal RNA was compared to other methods. Samples included 37 multibacillary (MB) patients with a positive bacteriological index (BI), 32 newly diagnosed paucibacillary (PB) patients whose BI were negative and 30 plaque psoriasis patients not residing in leprosy endemic areas as controls. The sensitivity of PCR was 30 fg of *M. leprae* DNA, which is equivalent to the DNA from 8.3 bacilli. The detection rate in MB and PB were 100% and 50%, respectively; the specificity was 100%. Semiquantitative evaluation of PCR correlated well with BI, but not with the morphological index (MI) nor with the serum antibody against phenolic glycolipid-1 (PGL-1). PCR detection of *M. leprae* targeting 16S ribosomal RNA was specific and more sensitive than conventional methods, and can contribute to early and accurate diagnosis of leprosy.

Kimura M, Sakamuri RM, Groathouse NA, Rivoire BL, Gingrich D, Krueger-Koplin S, et al. Rapid variable-number tandem-repeat genotyping for *Mycobacterium leprae* clinical specimens. *J Clin Microbiol*. 2009 Jun; 47(6):1757-66

*Mycobacterium leprae* is the noncultivable pathogen of leprosy. Since the genome sequence of an isolate of *M. leprae* has become available, multiple-locus variable-number tandem-repeat (VNTR) analysis (MLVA) has been explored as a tool for strain typing and identification of chains of transmission of leprosy. In order to discover VNTRs and develop methods transferable to clinical samples, MLVA was applied to a global collection of *M. leprae* isolates derived from leprosy patients and propagated in armadillo hosts. PCR amplification, agarose gel electrophoresis, and sequencing methods were applied to DNA extracts from these infected armadillo tissues ( $n = 21$ ). We identified polymorphisms in 15 out of 25 short-tandem-repeat (STR) loci previously selected by in silico analyses of the *M. leprae* genome. We then developed multiplex PCR for amplification of these 15 loci in four separate PCRs suitable for fluorescent fragment length analysis and demonstrated STR profiles highly concordant with those from the sequencing methods. Subsequently, we extended this method to DNA extracts from human clinical specimens, such as skin biopsy specimens ( $n = 30$ ). With these techniques, mapping of multiple loci and differentiation of genotypes have been possible using total DNA extracts from limited amounts of clinical samples at a reduced cost and with less time. These practical methods are therefore available and applicable to answer focused epidemiological questions and to allow monitoring of the transmission of *M. leprae* in different countries where leprosy is endemic.

Melo NM, Gomes PL, Patrocinio JA, Naves MFM, Diniz SA, Fleury RN, et al. Contribution of nasal biopsy to leprosy diagnosis. *Am J Rhinol Allergy*. 2009 Mar-Apr;23(2): 177-80.

**BACKGROUND:** The nasal mucosa plays the main role as the entry and the exit of leprosy bacilli and the nasal involvement may precede the skin lesions by several

years. Nasal biopsy has been used in research but its clinical application has not been described. We evaluated the contribution of the nasal biopsy for the diagnosis of leprosy and its correlation to skin biopsy and skin smear in untreated patients. **METHODS:** We evaluated changes in nasal biopsy in 227 leprosy patients. Patients were clinically classified and skin and nasal biopsies and skin smear were performed. **RESULTS:** Nasal biopsy showed positivity in 100% of the lepromatous spectrum decreasing toward the tuberculoid (TT) pole. Patients with TT or indeterminate forms did not present any nasal alterations, showing that they are the true paucibacillary forms. Also, the nasal biopsies of two patients were the only exam to show positivity. The bacillary index of the nasal biopsy was strongly correlated to skin biopsy and slit-skin smear. Additionally, the agreement among the exams was good, revealing the reliability of the nasal biopsy in leprosy diagnosis. **CONCLUSION:** The present study showed a rate of 48% of positivity in nasal biopsy of untreated patients, correlating well with skin biopsy and skin smear. Thus, the method in leprosy diagnosis and clinical form classification has shown great reliability.

Gomes FG, Marques W, Foss NT, Santana LA, Frade MA. Tactile threshold detection in leprosy patients with an electronic algometer. *J Neurosci Methods*. 2009 May 15; 179(2):319-22.

**OBJECTIVE:** To propose an electronic method for sensitivity evaluation in leprosy and to compare it to the Semmes-Weinstein monofilaments. **METHODS:** Thirty patients attending the Dermatology outpatient clinic of HCFMRP-USP were consecutively evaluated by both the electronic aesthesiometer and Semmes-Weinstein monofilaments on hand and foot test points. The intraclass correlation coefficient (ICC) was calculated to determine the variability of the electronic measures and the Kappa coefficient was calculated to determine the agreement between methods according to their categories (altered and non-altered tactile sensitivity). **RESULTS:** The ICC was approximately 1, demonstrating repeatability. The Kappa coefficient showed more than 75 and 63% agreement on the hand and foot points, respectively. The mean agreement between the 2 methods for the 7

points of the right and left hand was 77.14 and 75.71%, respectively. The mean agreement for all 10 points was 74.33 and 63.66% on the right and left foot, respectively. In cases of disagreement the detection of altered tactile sensitivity by the electronic esthesiometer on the right and left foot was 90.91 and 84.25%, respectively, with no detection by the monofilaments. **CONCLUSION:** The results suggest that the electronic esthesiometer is a reliable and easy application, capable of evaluating alterations of tactile sensitivity in leprosy patients.

**Khambati FA, Shetty VP, Ghate SD, Capadia GD. Sensitivity and specificity of nerve palpation, monofilament testing and voluntary muscle testing in detecting peripheral nerve abnormality, using nerve conduction studies as gold standard; a study in 357 patients. Lepr Rev. 2009 Mar; 80(1):34-50.**

**OBJECTIVE:** To determine sensitivity and specificity of clinical tools viz. nerve palpation (NP), monofilament (MF), and voluntary muscle testing (VMT), for assessing peripheral nerve function impairment (NFI) in leprosy, using nerve conduction studies (NCS) as gold standard. **STUDY POPULATION AND METHODS:** 357 untreated multibacillary (MB) leprosy patients were assessed using above tests. The nerves assessed were left and right ulnar, median, radial cutaneous, sural, common peroneal and posterior tibial. The concordance between the clinical and NCS tests was done for each nerve. The sensitivity and specificity of clinical tests for detecting nerve impairment was determined, using NCS as gold standard. Analysis was performed using SPSS version 10.0. **RESULTS:** The sensitivity of NP ranged between 71% to 88% for all nerves, except the median (43%) and sural (59%) nerves. Specificity was > 60% for all, but low for ulnar (34%) and common peroneal (40%) nerves. The specificity of MF testing was > 80% and of VMT assessment was >90% for all nerves. The sensitivity of MF testing ranged between 35-44%, while of VMT assessment was very low i.e. 4-5%, the maximum was for the ulnar nerve (25%). Detection sensitivity of MF testing and VMT assessment improved two fold when combined with NP and was closely comparable to NCS test findings. **CONCLUSIONS:** Both MF testing and VMT assessment showed good specificity, but moderate to low sensitivity. NP was less specific but

more sensitive than MF testing and VMT assessment. Combining NP with MF testing and VMT assessment gives a two fold improvement in the sensitivity for assessing nerve damage and could therefore serve as the most useful clinical tools for diagnosis of leprosy and detecting nerve damage at field level.

**Van Veen NH, Roberts AE, Mahato ME, Velema JP. Evaluation of simplified tests for the diagnosis of nerve function impairment in leprosy: the Sensory Motor Screening (SMS) study. Lepr Rev. 2009 Mar; 80(1):51-64.**

**OBJECTIVE:** Rapid and simple tests for diagnosing nerve function impairment (NFI) in leprosy are required in integrated settings. We examined whether simplified tests performed by newly trained general health workers (GHWs) have comparable diagnostic accuracy to the reference test conducted by experienced physiotherapists. **DESIGN:** This multi-centre study from India and Bangladesh evaluated three simplified tests named: ILEP Learning Guide Two (M2), Indian dance (M3), and a questionnaire (M4) in 408 people affected by leprosy. Sensitivity (Se) and specificity (Sp) of the three tests were calculated using the full assessment (M1) as reference. Se and Sp were calculated at both whole body and individual nerve levels: whether any NFI and if single NFI (voluntary muscle testing of lid gap, eye closure, little finger out, thumb up and foot up, sensory testing of hands and of feet) was present. **RESULTS:** M2 had 83% Se and 69% Sp, M3 had 76% Se and 84% Sp and M4 had 85% Se and 46% Sp in diagnosing any NFI. At the level of single NFI, M2 was most or similarly accurate in diagnosing single NFIs with highest prevalence (ST feet, ST hands, little finger out, thumb up), compared to M3 and M4. **CONCLUSIONS:** ILEP Learning Guide Two (M2) and Indian dance (M3) were found to be the most accurate simplified tests for diagnosing the presence of NFI compared to the reference. M2 was the most useful test, because of greatest accuracy for most of the common types of NFI and inclusion of sensory testing of the hands. M2 is considered to be a useful tool in the hands of GHWs with time constraints in integrated settings.

Jamjoom M, Sultan AH. Diagnosis of clinical samples spotted on FTA cards using PCR-based methods. *J Egypt Soc Parasitol.* 2009 Apr; 39(1):227-46.

The broad clinical presentation of Leishmaniasis makes the diagnosis of current and past cases of this disease rather difficult. Differential diagnosis is important because diseases caused by other aetiologies and a clinical spectrum similar to that of leishmaniasis (e.g. leprosy, skin cancers and tuberculosis for CL; malaria and schistosomiasis for VL) are often present in endemic areas of endemicity. Presently, a variety of methods have been developed and tested to aid the identification and diagnosis of Leishmania. The advent of the PCR technology has opened new channels for the diagnosis of leishmaniasis in a variety of clinical materials. PCR is a simple, rapid procedure that has been adapted for diagnosis of leishmaniasis. A range of tools is currently available for the diagnosis and identification of leishmaniasis and Leishmania species, respectively. However, none of these diagnostic tools are examined and tested using samples spotted on FTA cards. Three different PCR-based approaches were examined including: kDNA minicircle, Leishmania 18S rRNA gene and PCR-RFLP of Intergenic region of ribosomal protein. PCR primers were designed that sit within the coding sequences of genes (relatively well conserved) but which amplify across the intervening intergenic sequence (relatively variable). These were used in PCR-RFLP on reference isolates of 10 of the most important Leishmania species: *L. donovani*, *L. infantum*, *L. major* & *L. tropica*. Digestion of PCR products with restriction enzymes produced species-specific restriction patterns allowed discrimination of reference isolates. The kDNA minicircle primers are highly sensitive in diagnosis of both bone marrow and skin smears from FTA cards. Leishmania 18S rRNA gene conserved region is sensitive in identification of bone marrow smear but less sensitive in diagnosing skin smears. The intergenic nested PCR-RFLP using P5 & P6 as well as P1 & P2 newly designed primers showed high level of reproducibility and sensitivity. Though, it was less sensitive than kDNA minicircle primers, but easily discriminated between Leishmania species.

Trindade MAB, Varella TCN, Cisneros CGC, Moura AKA, Bottini V. Delayed diagnosis of multibacillary leprosy: a report of eight cases. *Braz. j. infect. Dis apr.* 2009; 13(2):155-7.

Leprosy is an important public health problem in Brazil. However, this disease is still poorly diagnosed in its early stages, leading to permanent disability and disfigurement. We examined eight patients with clinical and histological diagnosis of multibacillary leprosy who were being treated for other diseases for about three years without clinical hypothesis of leprosy. These cases illustrate the importance of medical education and public information about leprosy's signs and symptoms for prompt recognition and treatment, which are necessary to prevent permanent disabilities and eradicate the disease.

Batista KT, Araújo HJ, Paz Júnior AC. *Biópsia do nervo sural: técnica, indicações e resultados.* *Rev. Bras. Cir. Plást.* abr.-jun. 2009; 24(2):158-61.

A biópsia de nervo pode ser útil no diagnóstico de neuropatias periféricas quando não for possível determinar a causa por métodos convencionais como eletromiografia ou testes de sensibilidade. Nós revisamos as indicações desse procedimento, descrevemos a técnica e discutimos os resultados.

### **EDUCAÇÃO**

Berry BS, Devapitchai KS, Raju MS. Knowledge about persons with disability act (1995) among health care professionals dealing with persons affected by disabilities. *Indian J Lepr.* 2009 Jan-Mar; 81(1): 5-11.

To assess the level of awareness about the different provisions of the persons with Disability Act (1995) among the health care professionals, 201 health care professionals dealing with the disabled persons from different parts of India were interviewed using structured interview checklist. The data were analysed through statistical package of social sciences software. Chi-square test were applied on the variables and the P values were

ascertained. The results show that 48.3% knew about administration hierarchy, 53.7% of respondents were aware of the free education available for the disabled, 68.5% were aware of the employment scheme, 62.7% about poverty alleviation schemes, 59.2% know about the traveling benefits, 56.2% of professionals were aware of the benefits for people with low vision. Only 29.9% of respondents knew about provisions to overcome architectural barriers. 43.8% of them knew about the least disability percentage whereas only 28.4% were aware of research and manpower schemes. Regarding affirmative action, 32.17% told correctly and 52.7% of the professionals responded correctly with respect to non-discrimination schemes. The level of awareness among the professionals working in rural regions is lower with regard to administration hierarchy and poverty alleviation schemes. Informations regarding disabled friendly environments and research and manpower development were found to be low among respondents of all professions which need to be effectively intervened. Gender did not show any influence with respect to the components of the act. The study showed that there is an ample need for educational interventions among the health care professionals in all socio-demography. Inclusion of PWD Act in the curriculum of medical schools as a topic in conferences and workshops for health care professionals are suggested.

**Santos AK, Monteiro S, Rozemberg B. Meanings and use of educational materials on Hansen disease according to public health officials in the Municipality of Rio de Janeiro, Brazil. *Cad Saude Publica*. 2009 Apr; 25(4): 857-67.**

This article reflects on the communications processes in the Hansen Disease Control Programs under the Unified National Health System (SUS) in Brazil, analyzing how professionals at two public health services in Rio de Janeiro perceive the educational materials on the disease. The article discusses how analysis of printed materials favors negotiation of prevailing meanings and practices on Hansen disease in the programs. Thirty-eight different educational materials were analyzed (produced from 1993 to 2005 by governmental and nongovernmental

institutions) through two focus groups with program staff. Six materials were examined during the focus groups. The findings showed the communications processes are vertical and fragmented, with an emphasis on campaigns, centralized production of materials, homogenization of target publics, and a focus on biomedical knowledge. Horizontal and participatory activities were uncommon. A gap was identified between the institutionalization of the discourse on Hansen disease as an alternative to leprosy terminology and its circulation and uptake among different social actors.

**Bajaj DR, Matlani BL, Soomro FR, Iqbal MP. Knowledge, attitude and practices regarding leprosy among general practitioners at Hyderabad. *J Coll Physicians Surg Pak*. 2009 Apr;19(4): 215-8.**

**OBJECTIVE:** To assess the level of knowledge, social attitude towards patients, and diagnostic and management capabilities of general practitioners (KAP) regarding leprosy, practicing at Hyderabad, Pakistan. **STUDY DESIGN:** Cross-sectional study. **PLACE AND DURATION OF STUDY:** Hyderabad, Sindh, Pakistan, during October to December 2007. **METHODOLOGY:** A pre-tested and well-structured questionnaire consisting of 54 questions was administered to general practitioners working at various areas in Hyderabad. The questions were grouped under different headings and covered clinical features, common and uncommon presentations, complications, referral practices and stigma. The sum of correct answers marked by doctors was taken to classify the respondents. The doctors who responded correctly for upto 10 questions were assigned level 1 (poor), from 11 to 25: level 2 (average), from 26 to 40: level 3 (good), while those who marked correct answers for more than 40 questions were assigned level 4 (excellent). Chi-square test was used to determine significance at  $p < 0.05$ . **RESULTS:** A total of 200 doctors were surveyed. Fourteen doctors (7%) had poor knowledge of disease (number of correct answers less than 10), 32 (16%) had average (number of correct answers between 11 and 25), 140 (70%) doctors good (number of correct answers between 26 and 40) while 14 (7%) had excellent (number of correct answers more than 40) knowledge of the disease. **CONCLUSION:**

There is inconsistency and deficiencies in the knowledge, referral pattern and treatment of leprosy among general practitioners, which needs to be improved by conducting awareness activities.

**Santos AK, Monteiro S, Rozemberg B. Significados e usos de materiais educativos sobre hanseníase segundo profissionais de saúde pública do Município do Rio de Janeiro, Brasil. Cad. saúde pública abr. 2009; 25(4): 857-67.**

O artigo objetiva refletir sobre os processos comunicativos de Programas de Controle de Hanseníase (PCH) do Sistema Único de Saúde (SUS), por meio da análise da recepção de materiais educativos por profissionais de dois serviços de saúde pública no Rio de Janeiro, Brasil. O trabalho discute em que medida a análise de impressos favorece a negociação dos sentidos e das práticas sobre hanseníase vigentes nos PCH. Foram analisados 38 materiais produzidos entre 1993 a 2005, por instituições governamentais e não-governamentais e realizados dois grupos focais com profissionais atuantes no PCH. Durante os grupos focais 6 materiais foram examinados. Os resultados revelaram a verticalidade e fragmentação nos processos comunicativos, expressas pela: ênfase em campanhas, produção centralizada, homogeneização dos públicos e conteúdos e privilégio dado ao saber biomédico. As atividades horizontais e participativas não eram comuns. Foi identificada uma lacuna entre a institucionalização do discurso da hanseníase, como alternativa à terminologia da lepra, e a sua circulação e consumo entre os diferentes atores sociais.

**Trindade MA, Varella TC, Cisneros CG, Bottini V, Moura AK. Delayed diagnosis of multibacillary leprosy: a report of eight cases. Braz J Infect Dis. 2009 Apr;13(2):155-7.**

Leprosy is an important public health problem in Brazil. However, this disease is still poorly diagnosed in its early stages, leading to permanent disability and disfigurement. We examined eight patients with clinical and histological diagnosis of multibacillary leprosy who were

being treated for other diseases for about three years without clinical hypothesis of leprosy. These cases illustrate the importance of medical education and public information about leprosy's signs and symptoms for prompt recognition and treatment, which are necessary to prevent permanent disabilities and eradicate the disease.

### **ENFERMAGEM / PREVENÇÃO**

**Duarte MTC, Ayres JÁ, Simonetti JP. Consulta de enfermagem: estratégia de cuidado ao portador de hanseníase em atenção primária. Texto & contexto enferm jan. mar. 2009; 18(1):100-7**

Objetivou-se analisar instrumento de consulta de enfermagem utilizado no atendimento de portadores de hanseníase e identificar as principais necessidades de saúde e as ações de enfermagem propostas. Fizeram parte desta pesquisa 37 usuários, sendo 27 em poliquimioterapia e 10 em seguimento pós-alta medicamentosa. A coleta de dados ocorreu no período de dezembro de 2003 a dezembro de 2006, por meio dos instrumentos de consulta de enfermagem - Caso Novo e Consulta de Seguimento, baseados no processo de enfermagem proposto por Horta com adaptações. Fez-se uso da estatística descritiva para a análise dos mesmos. Conclui-se que o instrumento foi potente na identificação de necessidades das diversas esferas que se relacionam ao processo saúde-doença, facilitando intervenções conjuntas com a equipe multiprofissional, contribuindo para a prevenção de agravos, especialmente das incapacidades físicas, com a melhoria da saúde dos indivíduos, bem como com a educação em saúde destes e de seus familiares.

**Gonçalves CC, Lacerda AF, Santos Júnior HPO. Exergando além de uma mancha indolor - com a palavra: o portador de hanseníase. Nursing (São Paulo) jan. 2009; 11(128): 40-5.**

Trata-se de um estudo descritivo qualitativo, aplicado a 30 hanseníacos usuários do SUS, que objetivou identificar o que mudou na vida desses após a descoberta da Hanseníase e qual a importância dada pelos mesmos



ao apoio familiar, após essa descoberta. Utilizou-se a entrevista semi-estruturada e em seguida aplicou-se em análise de dados, a técnica de análise de conteúdo de Bardin. As percepções apreendidas organizaram-se em torno da hanseníase como sinônimo de Câncer e Aids e da vivência com a desilusão. Também circularam idéias relativas ao apoio familiar contrapondo o estigma da doença e a necessidade de esconder o diagnóstico.

**Silva FRF, Costa ALRC, Araújo LFS, Bellato R. Prática de enfermagem na condição crônica decorrente de hanseníase. Texto & contexto enferm abr.-jun. 2009; 18(2): 290-7.**

Objetivou-se compreender como se efetiva a prática de atendimento de enfermagem na prevenção da hanseníase e suas complicações, de modo a responder aos princípios da integralidade e resolutividade em duas unidades da Estratégia Saúde da Família na Regional de Saúde Diamantino-MT. Trata-se de pesquisa na modalidade estudo de caso, de natureza qualitativa, realizada no ano de 2007. A composição do corpus de análise compreendeu a observação direta das práticas de atendimento de enfermagem; produção de imagem das mesmas e análise documental. A análise dos dados evidenciou a relevância da prática de atendimento de enfermagem para os serviços de saúde. Também observou-se que essa prática é realizada de forma compartilhada com os demais membros da equipe de saúde, apontando para uma nova forma de atuar da enfermagem na qual há a possibilidade de ampliar a compreensão das necessidades de saúde das pessoas e propiciar a integralidade da atenção em saúde.

#### **EPIDEMIOLOGIA / DETECÇÃO / CONTROLE / PREVALÊNCIA**

**Shen J, Wang Y, Zhou M, Li W. Analysis on value of household contact survey in case detection of leprosy at a low endemic situation in China. Indian J Dermatol Venereol Leprol. 2009 Mar-Apr; 75(2):152-6.**

**BACKGROUND:** Leprosy is at a low endemic situation in China, the value of house contact survey in case detec-

tion of leprosy becoming a dispute. **AIMS:** To evaluate the value of household contact survey in the case detection of leprosy at a low endemic situation in China. **METHODS:** A study was carried out using a designed questionnaire in a retrospective method to analyze the value of household contact survey in case detection in Southwest and East China. **RESULTS:** A total of 2135 index leprosy patients were collected from January 1, 1996 to December 31, 2005 in six provinces of China. The number of index patients accounted for 22.0 and 14.1% of newly registered patients in the Southwest and East of China, respectively. The household contact survey (36.1%) and the skin clinic (62.0%) ranked first in methods of case detection in Southwest and East China, respectively. Within 5 years after primary leprosy patients were detected, 24.8 and 16.1% of the index patients in Southwest China and East China had been detected, respectively. **CONCLUSION:** The authors conclude that at the time of a low leprosy endemic situation, the household contact survey is still a useful method for case detection in China.

**Ishii N, Mori S, Nagaoka Y, Suzuki K. Report of the Ninth meeting of the WHO Technical Advisory Group of Leprosy Control. Nihon Hansenbyo Gakkai Zasshi. 2009 Feb; 78(1):75-88.**

The Ninth meeting of the WHO Technical Advisory Group (TAG) on Leprosy Control was held in Cairo, Egypt on 6th and 7th March 2008. The meeting was chaired by Professor W.C.S. Smith and attended by national leprosy programme managers from Brazil, the Democratic Republic of Congo, Cambodia, Egypt, Iran, India, Nigeria and Thailand. In addition, several experts and members of the Technical Commission of the International Federation of Anti-Leprosy Associations (ILEP) also attended the meeting.

**Suzuki K, Nagaoka Y, Mori S, Ishii N. Global leprosy situation, beginning of 2008. Nihon Hansenbyo Gakkai Zasshi. 2009 Feb; 78(1):25-34.**

The epidemiological situation of leprosy is reported by the health division of each country to WHO. The reported

data is collected by WHO and is immediately run on the Weekly Epidemiological Record. On this latest edition, data from the beginning of 2008 was reported. In almost all of the highly endemic countries, control activities have been integrated within the general healthcare system. However, maintaining political interest and mobilizing the necessary funds to implement activities in the field are challenges for many national programmes as the burden of disease declines further.

**Ezzedine K, Malvy D, Beylot C, Longy-Boursier M. Autochthonous leprosy in metropolitan France presenting with a diffuse infiltration of the face and febrile illness. *Int J Dermatol.* 2009 Jan; 48(1): 69-72.**

Leprosy is now considered in Western Europe as a strictly imported disease. A case of presumed locally acquired diffuse lepromatous leprosy was observed in a native-Portuguese woman living in France who developed an acute febrile presentation with extensive cutaneous signs.

**Imbiriba EB, Basta PC, Pereira Edos S, Levino A, Garnelo L. Leprosy in indigenous populations of Amazonas State, Brazil: an epidemiological study in the counties of Autazes, Eirunepé and São Gabriel da Cachoeira (2000 to 2005). *Cad Saude Publica.* 2009 May; 25(5):972-84.**

In 2005, Amazonas State, Brazil, showed hyperendemic leprosy detection coefficients and prevalence with medium endemicity. Although this State has the largest indigenous population in Brazil, there are no data on the leprosy profile in these groups. This study aimed to describe and analyze the epidemiological characteristics of leprosy case reporting in the municipalities (counties) of Autazes, Eirunepé, and São Gabriel da Cachoeira, comparing indigenous and non-indigenous findings according to target variables. A total of 386 cases reported to SINAN from 2000 to 2005 were analyzed. Mean detection rates were 3.55, 14.94, and 2.13/10,000 (among non-indigenous) and 10.95, 1.93, and 0.78/10,000 (among indigenous peoples) in Autazes, Eirunepé, and São Gabriel da Cachoeira, respectively. Paucibacillary cases predominated among

both indigenous and non-indigenous populations; however, dimorphous cases represented one-third of notifications. Despite coverage limitations and underreporting, the findings suggest that leprosy is a major public health problem for indigenous populations in Amazonas State. Classification according to race/ethnicity has been a useful tool for solving health inequalities.

**Kerketta AS, Bulliyya G, Babu BV, Mohapatra SS, Nayak RN. Health status of the elderly population among four primitive tribes of Orissa, India: a clinico-epidemiological study. *Z Gerontol Geriatr.* 2009 Feb; 42(1): 53-9.**

Primitive tribal groups (PTGs) are the most marginalised and vulnerable communities in India. Clinico-epidemiological studies on morbidity patterns among the elderly primitive tribe members are essential to recommend special intervention programmes to improve the health of the elderly in these communities. A community-based cross-sectional study was carried out among the elderly populations of four different PTGs, namely Langia Saora (LS), Paudi Bhuiyan (PB), Kutia Kondh (KK) and Dongria Kondh (DK) living in the forests of Orissa, India. Clinical and anthropometric data were collected using standard methods and haemoglobin was estimated by the cyanomethaemoglobin method. The average number of illnesses per person was 3.0. Common disabilities like vision and hearing impairment and mobility-related problems were found in considerable numbers. Gastrointestinal problems like acid peptic disease were found among 2.6% to 20% of cases. Non-specific fever was marked in 10.2% to 24.2% of individuals. The iodine deficiency disorder, namely goitre, was found among 4.2% to 6.0% of individuals. Diseases of the respiratory tract, like upper and lower respiratory tract infection, asthma, tuberculosis and leprosy, were found in small numbers. The prevalence of hypertension among males and females was 31.8% and 42.2%, respectively. The LS had the highest prevalence of hypertension (63% among men and 68% among women). With regard to anaemia status, severe anaemia was marked in 70% of males and 76.7% of females in the LS, while in other groups the prevalence of severe anaemia ranged from 15% to 33%. Although the prevalence of severe anaemia in other tribal communi-

ties is lower than in the LS, mild to moderate anaemia was found to range from 60% to 80%. The present study revealed a high prevalence of physical disabilities with both non-communicable as well as communicable diseases among the elderly primitive tribal members. This warrants the implementation of a special health care strategy to reduce suffering at this crucial age and improve quality of life.

**Penna ML, Oliveira MLWDR, Penna G. Spatial distribution of leprosy in the Amazon region of Brazil. *Emerg Infect Dis.* 2009 Apr; 15(4): 650-2.**

To detect areas with increased case-detection rates, we used spatial scan statistics to identify 5 of 10 clusters of leprosy in the Amazon region of Brazil. Despite increasing economic development, population growth, and road infrastructure, leprosy is endemic to this region, which is a source of case exportation to other parts of Brazil.

**Penna G, Pinto LF, Soranz D, Glatt R. High incidence of diseases endemic to the Amazon region of Brazil, 2001-2006. *Emerg Infect Dis.* 2009 Apr; 15(4):626-32.**

In Brazil, reportable diseases are the responsibility of the Secretariat of Health Surveillance of the Brazilian Federal Ministry of Health. During 2001-2006, to determine incidence and hospitalization rates, we analyzed 5 diseases (malaria, leishmaniasis [cutaneous and visceral], dengue fever, leprosy, and tuberculosis) that are endemic to the Amazon region of Brazil. Data were obtained from 773 municipalities in 3 regions. Although incidence rates of malaria, leishmaniasis, tuberculosis, and leprosy are decreasing, persons in lower socioeconomic classes with insufficient formal education are affected more by these diseases and other health inequalities than are other population groups in the region.

**Varkevisser CM, Lever P, Alubo O, Burathoki K, Idawani C, Moreira TM, et al. Gender and leprosy: case studies in Indonesia, Nigeria, Nepal and Brazil. *Lepr Rev.* 2009 Mar; 80(1):65-76.**

There appear to be regional differences in gender ratios of leprosy patients being diagnosed and treated. In Asian countries, more men than women are registered whilst in Africa female patients outnumber males. The Netherlands Leprosy Relief (NLR) therefore initiated research into factors underlying these regional gender differences. Between 1997 and 1999, leprosy control teams in Indonesia, Nigeria, Nepal and Brazil supported by social/public health scientists, conducted comparative exploratory research. They looked at three groups of potential explanatory factors: biological, socio-cultural/economic and service-related. The studies were partially quantitative (analysis of the records of patients who according to prescription could have completed treatment) and partially qualitative (interviews/focus group discussions with patients, their relatives, community members and health staff on perceptions of leprosy, its socio-economic consequences, treatment and cure). Biological factors appeared similar in the four countries: irrespective of the M/F ratio, more men than women were registered with multibacillary (MB) leprosy. Strong traditions, the low status of women, their limited mobility, illiteracy and poor knowledge of leprosy appeared to be important sociocultural factors explaining why women were under reporting. Yet, accessible, well reputed services augmented female participation and helped to diminish stigma, which in three out of the four societies seemed greater for women than for men. These positive effects could still be higher if the services would enhance community and patient education with active participation of patients and ex-patients themselves.

**Imbiriba EB, Basta PC, Pereira ES, Levino A, Garnelo L. Hanseníase em populações indígenas do Amazonas, Brasil: um estudo epidemiológico nos municípios de Autazes, Eirunepé e São Gabriel da Cachoeira (2000 a 2005). *Cad. Saúde Pública* maio 2009; 25(5):972-84**

O Estado do Amazonas, Brasil, apresentou, em 2005, coeficientes hiperendêmicos de detecção de hanseníase e prevalência de média endemicidade. O estado detém a maior população indígena no país, mas inexistem informações sobre o perfil da hanseníase nesses grupos. O estudo objetivou a descrição e análise das caracterís-

ticas epidemiológicas das notificações de hanseníase nos municípios de Autazes, Eirunepé e São Gabriel da Cachoeira, comparando achados entre indígenas e não indígenas, segundo variáveis de interesse. Foram analisados os casos notificados no SINAN, no período de 2000 a 2005. Do total de 386 casos notificados, verificaram-se coeficientes médios de detecção de 3,55, 14,94 e 2,13/10 mil (entre os não indígenas) e de 10,95, 1,93 e 0,78/10 mil (para os indígenas), para Autazes, Eirunepé e São Gabriel da Cachoeira, respectivamente. Houve predomínio de casos paucibacilares em indígenas e em não indígenas, no entanto, a forma dimorfa representou 1/3 das notificações. Apesar das limitações de cobertura e do sub-registro, os achados sugerem que a hanseníase representa importante problema de saúde pública para os indígenas no Amazonas. A classificação segundo óraça/etnicidade se constituiu em ferramenta útil para elucidar desigualdades em saúde

#### **FONOAUDIOLOGIA**

**Quintas VG, Salles PV, Costa VC, Alvarenga EA, Miranda ICC, Attoni TM. Achados fonoaudiológicos na hanseníase: considerações teóricas. Rev. Soc. Bras. Fonoaudiol 2009; 14(4): 560-64.**

A hanseníase é uma doença que tem altos níveis de incidência no Brasil. De origem bacteriana crônica, com alta infectividade e baixa patogenicidade, tem como hospedeiro primário o homem e como agente etiológico o *Mycobacterium leprae*. O bacilo de Hansen, como também é conhecido o agente, se acumula principalmente na pele, nos nervos periféricos e pares cranianos, levando a diversas lesões cutâneas, também à perda da condução neural e, conseqüentemente, a severas alterações anatômicas e funcionais nas extremidades do corpo, como membros e região orofacial. De acordo com estas premissas, foi realizada uma revisão da literatura com intuito de mostrar a fisiopatologia da doença e sua classificação de acordo com as suas manifestações. Desta forma, a literatura, por intermédio de alguns estudos, mostrou que esta doença pode provocar alterações que comprometem significativamente a voz, a audição, os órgãos fonoarticulatórios e as funções estomatognáticas, tornando-se assim, de grande relevância à Fonoaudiologia.

#### **GENÉTICA**

**Akama T, Suzuki K, Tanigawa K, Kawashima A, Wu H, Nakata N, et al. Whole-genome tiling array analysis of *Mycobacterium leprae* RNA reveals high expression of pseudogenes and noncoding regions. J Bacteriol. 2009 May; 191(10): 3321-7.**

Whole-genome sequence analysis of *Mycobacterium leprae* has revealed a limited number of protein-coding genes, with half of the genome composed of pseudogenes and noncoding regions. We previously showed that some *M. leprae* pseudogenes are transcribed at high levels and that their expression levels change following infection. In order to clarify the RNA expression profile of the *M. leprae* genome, a tiling array in which overlapping 60-mer probes cover the entire 3.3-Mbp genome was designed. The array was hybridized with *M. leprae* RNA from the SHR/NCrj-rnu nude rat, and the results were compared to results from an open reading frame array and confirmed by reverse transcription-PCR. RNA expression was detected from genes, pseudogenes, and noncoding regions. The signal intensities obtained from noncoding regions were higher than those from pseudogenes. Expressed noncoding regions include the *M. leprae* unique repetitive sequence RLEP and other sequences without any homology to known functional noncoding RNAs. Although the biological functions of RNA transcribed from *M. leprae* pseudogenes and noncoding regions are not known, RNA expression analysis will provide insights into the bacteriological significance of the species. In addition, our study suggests that *M. leprae* will be a useful model organism for the study of the molecular mechanism underlying the creation of pseudogenes and the role of microRNAs derived from noncoding regions.

**Messias-Reason I, Kremsner PG, Kun JF. Functional Haplotypes that Produce Normal Ficolin-2 Levels Protect against Clinical Leprosy. J Infect Dis. 2009 Mar 15; 199(6): 801-4.**

Host factors have been shown to play a significant role in the susceptibility to and clinical outcome of leprosy. Here, we analyze polymorphisms of the gene encoding

ficolin-2 (FCN2), which is a soluble pattern-recognition molecule. A total of 158 patients with leprosy and 210 healthy control subjects from Brazil were investigated. Polymorphisms in the promoter and exon 8 of FCN2 were assessed by DNA sequencing. The distribution of functional FCN2 haplotypes among patients was significantly different from that among the control subjects ([Formula: see text]). These results unveil an immunogenetic role for ficolin-2 in the host response against *M. leprae*.

**Félix JSV, Salazar SGC, Velázquez RC, Maldonado JGR, Villalobos HR. Association between the TaqI polymorphism of the vitamin D receptor gene and lepromatous leprosy in a Mexican population sample. Salud Publica Mex. 2009 Jan-Feb; 51(1): 59-61.**

**OBJECTIVE:** To establish the association of the vitamin D receptor gene TaqI polymorphism with lepromatous leprosy (LL) in individuals from Sinaloa, Mexico. **MATERIAL AND METHODS:** A 740 bp fragment was amplified from the VDR gene in DNA samples of 71 patients with LL and 144 controls in the Hospital General de Culiacán during 2004-2007. Polymorphism was identified through TaqI endonuclease. **RESULTS:** A significant increase in the genotype TT of the VDR gene was observed in patients when compared to controls ( $p = 0.040$ ;  $OR = 1.82$ ). **CONCLUSIONS:** Our data support the association between the TT genotype and susceptibility to LL in this Mexican population.

**Pereira AC, Souza VNB, Cardoso CC, Dias-Baptista IM, Parelli FP, Venturini J, et al. Genetic, epidemiological and biological analysis of interleukin-10 promoter single-nucleotide polymorphisms suggests a definitive role for -819C/T in leprosy susceptibility. Genes Immun. 2009 Mar; 10(2): 174-80.**

Leprosy is a complex infectious disease influenced by genetic and environmental factors. The genetic contributing factors are considered heterogeneous and several genes have been consistently associated with susceptibility like PARK2, tumor necrosis factor (TNF), lymphotoxin-alpha (LTA) and vitamin-D receptor (VDR).

Here, we combined a case-control study (374 patients and 380 controls), with meta-analysis (5 studies; 2702 individuals) and biological study to test the epidemiological and physiological relevance of the interleukin-10 (IL-10) genetic markers in leprosy. We observed that the -819T allele is associated with leprosy susceptibility either in the case-control or in the meta-analysis studies. Haplotypes combining promoter single-nucleotide polymorphisms also implicated a haplotype carrying the -819T allele in leprosy susceptibility (odds ratio (OR)=1.40;  $P=0.01$ ). Finally, we tested IL-10 production in peripheral blood mononuclear cells stimulated with *Mycobacterium leprae* antigens and found that -819T carriers produced lower levels of IL-10 when compared with non-carriers. Taken together, these data suggest that low levels of IL-10 during the disease outcome can drive patients to a chronic and unprotective response that culminates with leprosy.

**Goulart LR, Goulart IM. Leprosy pathogenetic background: a review and lessons from other mycobacterial diseases. Arch Dermatol Res. 2009 Feb;301(2): 123-37.**

Leprosy is a disease caused by *Mycobacterium leprae* that initially affects the peripheral nervous system with patients exhibiting contrasting clinical, immunological, and pathological manifestations despite minimal genetic variation among bacilli isolates. Its clinical manifestations are related to *M. leprae* survival, innate and acquired immune responses, and interactions between host and bacterial proteins, preventing their invasion and infection, or promoting their development and pathogenesis. The complex molecular interactions in affected individuals influenced by the pathogenetic background will be explored in this review. However, the great genetic diversity imposes difficulty for understanding disease development, and it is likely that many factors and metabolic pathways regulating the immense and contrasting symptomatology will yet be revealed. Four pathways may play a central role in leprosy, including the TLR/LIR-7, VDR, TNF-alpha, and TGF-beta1 for which a large amount of gene polymorphisms have been described that could potentially affect the clinical outcome. Cross-

talk pathways may significantly change the course of the disease, depending on the specific disequilibrium of genic homeostasis, which is highly dependent on the environment, antigens that are presented to the host cell, and specific polymorphisms that interact with other genes, external factors, and pathogen survival, culminating in leprosy occurrence. Currently, the microarray-based genomic survey of gene polymorphisms, multiple gene expression analyses, and proteomic technologies, such as mass spectrometry and phage display applied in the discovery of antigens, represent a great potential for evaluating individual responses of leprosy patients and contacts to predict the outcome and progression of the disease. At present, none of the genes is good prognostic marker; however, in the near future we may use multiple targets to predict infection and leprosy development.

**Schuring RP, Hamann L, Faber WR, Pahan D, Richards JH, Schumann RR, et al. Polymorphism N248S in the human Toll-like receptor 1 gene is related to leprosy and leprosy reactions. J Infect Dis. 2009 Jun 15; 199(12):1816-9.**

We investigated the association between a polymorphism of a key innate immunity receptor, Toll-like receptor 1 (TLR1) N248S, and susceptibility to leprosy and its clinical presentation. TLR1 N248S has been shown elsewhere to diminish TLR1 signaling and subsequent leprosy disease. The homozygous genotype SS was more frequent ( $P=0.012$ ) and the heterozygous SN genotype was less frequent ( $P=0.015$ ) in patients with leprosy than in control subjects. Additional observed differences in allelic frequency in patients who experienced reversal reactions and/or erythema nodosum leprosum reactions indicates that altered TLR1 function, or at least a TLR1 N248S-linked trait, may affect the progression from infection to disease as well as the disease course and the risk of debilitating reactional episodes in this population.

**Lini N, Shankernarayan NP, Dharmalingam K. Quantitative real-time PCR analysis of Mycobacterium leprae DNA and mRNA in human biopsy material from leprosy and reactional cases. J Med Microbiol. 2009 Jun; 58(Pt 6):753-9.**

*Mycobacterium leprae*, the causative agent of leprosy, is uncultivable in defined media. Development of new diagnostic tools which do not depend on growth of bacteria is needed for the early detection of *M. leprae* and for monitoring the effectiveness of chemotherapy. We used a real-time PCR-based assay to quantify the copy number of bacterial DNA and hsp18 mRNA from 47 leprosy patients using paraffin-embedded biopsy samples. The assay used was specific, sensitive and reproducible. The applicability of this approach in monitoring the chemotherapy of leprosy was examined. A reduction in DNA and mRNA during chemotherapy was observed and hsp18 mRNA could not be detected in patients who underwent 2 years of multidrug therapy (MDT). However, a considerable amount of *M. leprae* DNA could be detected even after 2 years of MDT. A significant amount of hsp18 mRNA was found in reactional cases as well. This raises important questions regarding the role of bacterial antigens in leprosy reactions and the rationale of omitting antibiotics in the treatment of reactional cases. Results in this study show that real-time PCR could be a better tool for the careful monitoring of bacillary DNA and mRNA in lesions, which will help to improve diagnosis, disease progression and the treatment regimen.

**de Messias-Reason I, Kreamsner PG, Kun JF. Functional haplotypes that produce normal ficolin-2 levels protect against clinical leprosy. J Infect Dis. 2009 Mar 15; 199(6):801-4.**

Host factors have been shown to play a significant role in the susceptibility to and clinical outcome of leprosy. Here, we analyze polymorphisms of the gene encoding ficolin-2 (FCN2), which is a soluble pattern-recognition molecule. A total of 158 patients with leprosy and 210 healthy control subjects from Brazil were investigated. Polymorphisms in the promoter and exon 8 of FCN2 were assessed by DNA sequencing. The distribution of

functional FCN2 haplotypes among patients was significantly different from that among the control subjects ( $P = .004$ ). These results unveil an immunogenetic role for ficolin-2 in the host response against *M. leprae*.

**Torres-Avila JF, Colorado CL, Gamboa LA, Araujo MJ, León-Franco CI, Guerrero-Guerrero MI. Genotyping Colombian *Mycobacterium leprae* for determining disease transmission patterns. Rev Salud Publica (Bogotá). 2009 Jan-Feb;11(1):3-13.**

**OBJECTIVE:** Assessing VNTR (variable-number tandem repeat) variability of *Mycobacterium leprae* from Colombian patients with and without prior treatment to identify potential sources of infection and to understand the patterns of disease transmission. **METHODOLOGY:** This was a descriptive cross-sectional study where a convenience sample of biopsies was taken from 161 multibacillary leprosy patients; diagnosis and monitoring of the disease had been requested for these patients. DNA was extracted from *M. leprae* and standardised using the PCR technique for *M. leprae* VNTR, genotypes were established and different clusters grouped by unweighted pair group method with arithmetic mean (UPGMA). **RESULTS:** 22 different VNTR genotypes were found from 161 samples, of which 100 samples (62.1%) had a single u-VNTR genotype and the remaining genotypes were VNTR 17 (5.6%), VNTR 20 (4.3%), VNTR 18 (4.3%), VNTR 14 (4.3%) and VNTR 13 (3.7%), namely those forming groups or clusters. **CONCLUSION:** This study showed that clones can be detected with varying degrees of virulence / aggressiveness by cluster analysis, implying the need for more monitoring programme activities which will result in a real decline in microorganism transmission.

**Alban SM, Sella SR, Miranda RN, Mira MT, Soccol VT. PCR-restriction fragment length polymorphism analysis as a tool for *Mycobacterium* species identification in lepromas for lepromin production. Lepr Rev. 2009 Jun; 80(2):129-42.**

**OBJECTIVES:** The aim of the present work was to standardise a PCR-Restriction Fragment Length Polymor-

phism analysis (PRA) as a tool to detect the mycobacteriologic composition of lepromas from leprosy patients used in the production of lepromin to improve the quality of the Mitsuda test. **DESIGN:** PCR-Restriction Fragment Length Polymorphism analysis using hsp65 and rpoB genes were applied to 11 reference strains of mycobacteria, including *M. leprae*, and the obtained PRA profiles were compared to mycobacteria in clinical specimens. **RESULTS:** Out of the biopsies studied, 52.2% had DNA fragment amplified for both genes (hsp65 and rpoB) for *M. leprae*. However, other *Mycobacterium* species were observed in samples of lepromatous leprosy patients. Here we discussed the importance of mycobacteria identification in the antigen of Mitsuda production to be used in the evaluation of leprosy. **CONCLUSIONS:** Our results suggest that the use of the molecular approach for sample selection can contribute to an improvement in the quality of produced lepromin.

**Akama T, Suzuki K, Tanigawa K, Kawashima A, Wu H, Nakamura K, et al. Detection of RNA expression on whole genome analysis of *Mycobacterium leprae* by tiling array. Nihon Hansenbyo Gakkai Zasshi. 2009 Feb; 78(1): 49-54.**

Completion of *Mycobacterium leprae* genome sequence revealed that there are many pseudogenes and non-coding regions, but rather small numbers of protein-coding genes. Although it was thought that pseudogenes and non-coding regions were silent and junk, our previous studies indicated that RNA expression was detected from these regions. To elucidate comprehensive RNA expression pattern on *M. leprae* whole genome, tiling array was designed and total RNA of *M. leprae* Thai-53 strain was analyzed. As a result, highly expressed regions were detected among not only the gene regions but also pseudogenes and non-coding regions. Since some of the RNA expression levels were modulated by MDT, evaluation of RNA expression pattern might be a good indicator for the treatment of leprosy.

Suzuki K, Nakamura K, Tanigawa K, Kawashima A, Wu H, Akama T, et al. **Comprehensive analysis of RNA expression of *Mycobacterium leprae* and clinical and biological significance.** *Nihon Hansenbyo Gakkai Zasshi.* 2009 Feb; 78(1): 61-5.

Completion of *Mycobacterium leprae* genome sequence revealed that there are many pseudogenes and non-coding regions, but rather small numbers of protein-coding genes. This result indicates that *M. leprae* is a very unique organism, and this future is important to understand the biological nature and/or pathogenicity of *M. leprae*, which remain unclear. We attempted to find the biological nature of *M. leprae* by detecting the gene and pseudogene regions transcribed at high level. We detected the genomic regions including pseudogenes and demonstrated that six out of twelve high expression regions were pseudogenes. In addition, its transcription level was changed when *M. leprae* infects macrophage. RNA was detected from genes, pseudogenes and non-coding regions. The expression levels of these regions were different among patients and a part of them is disappeared just after treatment. These results suggested that RNA derived from pseudogene and non-coding region have some function concerning the infection and/or intracellular parasitism and that the analysis of pseudogene and non-coding region expression pattern of *M. leprae* is available as a criterion for therapeutic effect and disease type of leprosy, and a prognostic marker.

#### HANSENÍASE EXPERIMENTAL

Lamagna B, Paciello O, Ragozzino M, Papparella S, Montagnaro S, Lamagna F. **Isolated lepromatous conjunctivo-corneal granuloma in a cat from Italy.** *Vet Ophthalmol.* 2009 Mar-Apr; 12(2): 97-101.

**OBJECTIVE:** To describe a case of a conjunctivo-corneal mass in a cat associated with acid-fast bacilli. **METHODS:** A 2-year-old female black European Short-Hair cat, living outdoors in a suburban environment in Italy, was referred for evaluation of a nodular, vascularized mass of 2 weeks duration. The mass involved the dorsal bulbar conjunctiva at the temporal canthus of OS and invaded the sclera and cornea. Routine ophthalmic and systemic

examination, serologic testing, cytology and histology of the mass were performed. *Mycobacterium* specific polymerase chain reaction (PCR) of variable regions 1, 2 and 3 of the 16S ribosomal RNA (rRNA) gene was also performed. **RESULTS:** Neutrophils, lymphocytes, macrophages and giant cells with intracytoplasmic acid-fast bacilli were seen on cytological examination. The histological examination confirmed the presence of a granulomatous lesion with acid-fast bacilli within macrophages. Bacteriological culture of the material from the lesion was negative for *Mycobacterium* spp. *Mycobacterium* 16S rRNA gene specific PCR was positive. A diagnosis of feline leprosy was made. The owners refused any treatment, and 1 year later the lesion was still present. **CONCLUSIONS:** Veterinary ophthalmologists should be aware of conjunctivo-corneal leproma as an unusual symptom of leprosy.

Hagge DA, Saunders BM, Ebenezer GJ, Ray NA, Marks VT, Britton WJ, et al. **Lymphotoxin-alpha and TNF have essential but independent roles in the evolution of the granulomatous response in experimental leprosy.** *Am J Pathol.* 2009 Apr; 174(4): 1379-89.

Recent studies identified an association between genetic variants in the lymphotoxin-alpha (LTalpha) gene and leprosy. To study the influence of LTalpha on the control of experimental leprosy, both low- and high-dose *Mycobacterium leprae* foot pad (FP) infections were evaluated in LTalpha-deficient chimeric (cLTalpha(-/-)) and control chimeric (cB6) mice. Cellular responses to low-dose infection in cLTalpha(-/-) mice were dramatically different, with reduced accumulation of CD4(+) and CD8(+) lymphocytes and macrophages and failure to form granulomas. Growth of *M. leprae* was contained for 6 months, but augmented late in infection. In contrast, tumor necrosis factor knockout and tumor necrosis factor receptor 1 knockout FPs exhibited extensive inflammatory infiltration with an increase in *M. leprae* growth throughout infection. Following high-dose infection, cB6 FP induration peaked at 4 weeks and was maintained for 12 weeks. Induration was not sustained in cLTalpha(-/-) FPs that contained few lymphocytes and no granulomas. There was a reduction in the expression levels of inflammatory cytokines, chemokines,



and chemokine receptors, including nitric oxide synthase 2, vascular cell adhesion molecule, and intercellular cell adhesion molecule. Furthermore, cLTalpha(-/-) popliteal lymph nodes contained a higher proportion of naïve CD44(lo)CD62L(hi) T cells than cB6 mice, suggestive of reduced T cell activation. Therefore, both LTalpha and tumor necrosis factor are essential for the regulation of the granuloma, but they have distinctive roles in the recruitment of lymphocytes and maintenance of the granulomatous response during chronic *M. leprae* infection.

**Gidoh M. Structure and anti-*M. leprae* activity relationships of new quinolones.** *Nihon Hansenbyo Gakkai Zasshi.* 2009 Feb; 78(1): 17-23.

Due to the emergence of drug resistant *M. leprae*, there is a need to look for new drugs for the treatment of leprosy. We evaluated the effectiveness of new quinolones in vitro as well as in vivo. The in vitro and in vivo results suggested that a cyclopropyl group at the 1-position, COOH at the 3-position, OH at the 4-position, NH<sub>2</sub> or OH-substitutions at the 5-position, F at the 6-position, 5- and 6-membered rings at the 7-position, halogen (F or Cl) or OCH<sub>3</sub> at the 8-position of the quinolone core structure remarkably enhance anti-*M. leprae* activities of the drug.

**Fukutomi Y, Maeda Y, Matsuoka M, Makino M. Temperature dependency for survival of *Mycobacterium leprae* in macrophages.** *Nihon Hansenbyo Gakkai Zasshi.* 2009 Feb; 78(1): 7-16.

Hansen's disease is caused by an infection with an intracellular pathogen, *Mycobacterium leprae*, which mainly inhabits macrophages and Schwann cells. However, little is known about the survival or growth mechanisms of the bacilli in mouse and human macrophages. In the present study, by using radiorespirometry analysis for the evaluation of the viability of *M. leprae*, we observed that in vitro incubation of *M. leprae*-infected macrophages at 35 degrees C was more growth permissive than at 37 degrees C, and supplementation with the immunosuppressive cytokine IL-10 supported the survival of the

bacilli in the macrophages for 3 weeks, whereas viability of the bacilli was gradually lost if cultured without IL-10. In human macrophages, *M. leprae* retained its viability when cultured at 35 degrees C for at least 4 weeks without IL-10. However, the viability of *M. leprae* was almost lost within 2 weeks if cultured at 37 degrees C. These data suggest that temperature is a crucial factor for the survival of *M. leprae* in host cells.

**Loughry WJ, Truman RW, McDonough CM, Tilak MK, Garnier S, Delsuc F. Is leprosy spreading among nine-banded armadillos in the southeastern United States?** *J Wildl Dis.* 2009 Jan; 45(1): 144-52.

In the United States, nine-banded armadillo (*Dasypus novemcinctus*) populations are derived from two sources: (1) a continuous range expansion from Mexico led to western populations, some of which, particularly along the western Gulf Coast and west side of the Mississippi River delta, exhibit persistently high rates of leprosy infection, and (2) a small group of animals released from captivity in Florida gave rise to eastern populations that were all considered leprosy free. Given that western and eastern populations have now merged, an important question becomes, to what extent is leprosy spreading into formerly uninfected populations? To answer this question, we sampled 500 animals from populations in Mississippi, Alabama, and Georgia. Analyses of nuclear microsatellite DNA markers confirmed the historic link between source populations from Texas and Florida, but did not permit resolution of the extent to which these intermediate populations represented eastern versus western gene pools. Prevalence of leprosy was determined by screening blood samples for the presence of antibodies against *Mycobacterium leprae* and via polymerase chain reaction amplification of armadillo tissues to detect *M. leprae* DNA. The proportion of infected individuals within each population varied from 0% to 10%. Although rare, a number of positive individuals were identified in eastern sites previously considered uninfected. This indicates leprosy may be spreading eastward and calls into question hypotheses proposing leprosy infection is confined because of ecologic constraints to areas west of the Mississippi River.

**Domurado D, Hernandez-Valdepeña I, Domurado M, Coudane J, Braud C, Baussard JF, et al. Nanoaggregates of a random amphiphilic polyanion to carry water-insoluble clofazimine in neutral aqueous media. Eur J Pharm Sci. 2009 Feb 15; 36(2-3): 345-51.**

Clofazimine, an antibiotic drug active against mycobacteria and used for the treatment of leprosy, is a very weak base insoluble in neutral aqueous media. It may cause rather severe secondary effects. Basically, these two shortcomings can be minimized by combination with a drug carrier. The potential of a polymeric carrier composed of nanosized aggregates formed by hydrophobized poly (methyl vinyl ether-alt-maleic acid) to solubilize clofazimine in neutral aqueous media and to administer it to mice was investigated. This amphiphilic polyanion was synthesized by partial esterification of commercial poly (methyl vinyl ether-alt-maleic anhydride) by dodecanol. An aggregate-forming analog bearing mannose residues aimed at targeting mannose receptors born by macrophages was also synthesized and characterized. In the presence of the aggregates, rather large amounts of clofazimine were compatibilized with neutral aqueous media. Comparison with a water-insoluble neutral dye, namely yellow OB, showed that the apparent solubilization of clofazimine was due to a synergistic combination of electrostatic and hydrophobic interactions and not only to the latter as in the case of yellow OB. Despite its favorable in vitro characteristics, clofazimine entrapped within the lipophilic pockets born by the amphiphilic aggregates exhibited no antibiotic activity after administration to mice infected with *Mycobacterium bovis* BCG.

**Rosa PS, Pinke CAE, Pedrini SCB, Silva EA. The effect of iron supplementation in the diet of *Dasybus novemcinctus* (Linnaeus, 1758) armadillos in captivity. Braz. j. boil. Feb. 2009; 69(1):117-22.**

Armadillos of the species *Dasybus novemcinctus* have been used as an experimental model of leprosy. Besides non-human primates, they are the only species naturally infected with *Mycobacterium leprae* and when experimentally inoculated, reproduce the lepromatous form of the disease producing large quantities of bacilli. This

species has been maintained in captivity by numerous researchers and specific housing and feeding requirements have been developed to guarantee their survival during long experimental periods. In the "Lauro de Souza Lima" Institute, armadillos receive dog food, ground beef, boiled eggs and vitamin C. However, despite the balanced diet, anemia has been observed in some captive animals, especially in armadillos inoculated with *M. leprae* in advanced stages of infection. Thus, the objective of the present study was to evaluate the effect of iron sulfate supplementation in the feed provided for armadillos, both inoculated and non-inoculated with *M. leprae*, by means of the evaluation of their hematological profile. Fourteen armadillos received 10 mg/animal of iron sulfate (Hematofer®) diluted in sterile water mixed with their daily feed for 50 days. Hemograms and serum iron dosages for each armadillo were performed before and after supplementation. The hematocrit values increased significantly after iron supplementation, both in armadillos inoculated and non-inoculated with *M. leprae*. It is possible that the amount of iron in the feed is insufficient for the formation of hemoglobin, leading to microcytic anemia. Dietary supplementation with iron sulfate reversed this state, showing the importance of understanding the metabolism of exotic species for their maintenance in captivity, and thus ensuring their well-being.

## **HISTÓRIA**

**Terencio Las AJ. Centenary of the Fontilles Sanatorium. Actas Dermosifiliogr. 2009 Jun; 100(5):362-73.**

In recognition of the centenary of the Fontilles Sanatorium, we present some details of its history. The article discusses the foundation of the sanatorium by some of the numerous lepers with no health coverage in the region of Valencia, and Alicante in particular. After a difficult period between 1909 and 1932, the sanatorium was seized by the Republican government. After the civil war, it was returned to the board of trustees, who entrusted administrative tasks to the Compañía de Jesús while health care was overseen by the National Health Board. This coexistence was uneasy, and the board of trustees took over again in 1943. We comment on the transition

from a sanatorium and colony into a hospital providing health care, research and training, and treatment with sulfones and subsequently other effective drugs. Also discussed are its role in the elimination of leprosy from Spain, admission to the International Federation of Anti-leprosy Associations in 1969, and its projects in endemic countries, with the ultimate goal of achieving a world free of leprosy.

**Leandro JA. A hanseníase no Maranhão na década de 1930: rumo à Colônia do Bonfim. Hist. ciênc. saúde-Manguinhos abr.-jun.2009; 16(2): 433-47.**

Destacam-se alguns aspectos da hanseníase e da política de saúde para os hansenianos do Maranhão, na década de 1930. O equacionamento da doença no estado seguiu o compasso imposto pelas políticas nacionais de saúde centralizadoras, desenvolvidas no período varguista: mais vigilância sanitária sobre os portadores da moléstia e a construção de colônia de isolamento compulsório para doentes contagiantes caracterizaram sobremaneira a década no que tange à profilaxia da então chamada lepra. Achilles Lisboa foi o médico que melhor traduziu esse período, e seus discursos são aqui destacados, pois contribuíram para moldar com agressividade as políticas públicas de exclusão direcionadas aos hansenianos maranhenses.

**Castro SMS, Watanabe HAW. Isolamento compulsório de portadores de hanseníase: memória de idosos. Hist. ciênc. saúde-Manguinhos abr.-jun. 2009; 16(2): 449-87.**

De 1924 a 1962 o Brasil utilizou a internação compulsória de pacientes de hanseníase como controle da doença na comunidade. Com o final dessa política, muitos pacientes continuaram a viver nessas unidades. O Asilo Pirapitingui, hoje Hospital Dr. Francisco Ribeiro Arantes, é a única retaguarda asilar para internação de portadores de hanseníase por indicação social. Obtivemos o relato da história de vida de oito de seus remanescentes, que foram gravados e transcritos. A análise temática desses relatos permitiu a identificação das seguintes catego-

rias: hanseníase; internação; vida cotidiana; a instituição; condições atuais de saúde; e permanência na instituição após a extinção da internação compulsória.

**Mellagi AG, Monteiro YN. O imaginário religioso de pacientes de hanseníase: um estudo comparativo entre ex-internos dos asilos de São Paulo e atuais portadores de hanseníase. Hist. ciênc. saúde-Manguinhos abr.-jun. 2009; 16(2):489-504.**

Analisa a religiosidade de pacientes portadores de hanseníase que viveram dois períodos distintos da história do tratamento dos doentes: o do internamento em asilos e o da prática atual. Dez entrevistas semiestruturadas focalizaram saúde, religião e hanseníase, abordando os meios de enfrentamento religioso nos dois grupos. No grupo de ex-internos, constatou-se a presença da religião institucionalizada, que atendia aos propósitos de vigilância e da terapêutica isolacionista. Os atuais portadores de hanseníase ainda sentem o peso do estigma da 'lepra' em determinadas situações. Foram aplicados também cinco questionários a profissionais de saúde do DHDS, que apresentam suas considerações sobre a religião do paciente e o tratamento.

**Rivero RE, Martínez, ZB; Corcho DB, Fernandez TT, Sinchay, AGP. La lepra, un problema de salud global. Rev. cuba. med. gen. Integr ene.-mar. 2009; 25(1).**

Le lepra constituye una enfermedad conocida desde el año 2000 a.n.e., que causó verdaderos estragos a poblaciones enteras y azotó ininterrumpidamente a todos los continentes. Ha sido considerada una enfermedad mutilante, incurable, repulsiva y estigmatizante, lo que ha generado un trato inhumano hacia las personas que la padecen, constituyendo aún hoy un problema de salud importante para algunos países. En el presente artículo se describen algunos apuntes sobre la evolución histórica de la lepra en Cuba y a nivel mundial.

**Sangi KCC, Miranda LF, Spindola T, Leão AMM. Hanseníase e estado reacional: história de vida de pessoas acometidas. Rev. enferm. UERJ abr.-jun. 2009; 17(2):209-14.**

Trata-se de um estudo de natureza qualitativa com emprego do método de história de vida que objetivou descrever a interferência do estado reacional na história de vida das pessoas acometidas pela hanseníase. Foi realizada em 2006, numa unidade básica de saúde, no município do Rio de Janeiro. Foram entrevistados 13 clientes com estado reacional em tratamento com poliquimioterapia ou pós-alta, que responderam a uma entrevista aberta, respeitando-se os aspectos éticos. A análise dos relatos evidenciou que existe interferência do diagnóstico tardio e tratamento inadequado na ocorrência do estado reacional e desenvolvimento de sequelas. O atendimento da equipe multiprofissional é observado como necessário para o efetivo tratamento e reabilitação da saúde, destacando-se a presença do enfermeiro.

**Rodríguez G, Pinto R, López F, Gómez Y. Eritema nudoso leproso persistente y enteropatía letal por clofazimina. Biomédica (Bogotá) mar. 2009; 29(1): 18-24.**

Introducción. La enteropatía por clofazimina es una complicación grave de este fármaco, cuando se usa a dosis altas para la reacción leprosa tipo 2 y otras enfermedades. Objetivo. Presentar una mujer de 31 años con síntomas de lepra, incluidos episodios de eritema nudoso leproso, agravados durante el embarazo, sin diagnóstico médico preciso. Relatar la evolución de su enteropatía letal por clofazimina. Materiales y métodos. Entrevista con la paciente y sus familiares, revisión de la historia clínica y de la literatura pertinente. Resultados. La paciente presentó lesiones cutáneas anestésicas y varios episodios de eritema nudoso, agravados durante sus embarazos. Luego de epistaxis repetidas y perforación del tabique nasal, se diagnosticó lepra lepromatosa, 12 años después de numerosas consultas médicas. Su esposo y su hija de 12 años presentaron signos de lepra para la cual se trataron. La paciente tuvo episodios de reacción tipo 2 durante la poliquimioterapia, para los cuales recibió 400 mg diarios de clofazimina. A los dos meses de

este tratamiento comenzó a presentar dolor abdominal persistente durante más de un año, muy serio y episódicamente exacerbado, manejado con analgésicos y antiespasmódicos, incluida la morfina. Tuvo, además, diarrea, estreñimiento, náuseas, pérdida de peso y adenopatías mesentéricas. Falleció sin diagnóstico de su afección intestinal. No se hizo autopsia. Conclusiones. La clínica final de la paciente sugiere que se trata de un caso de enteropatía letal por clofazimina, una complicación que no se había reconocido previamente en nuestros pacientes. Es necesario aumentar el conocimiento de la lepra entre los médicos.

**Cruz A. The Hospital-Colônia Rovisco Pais: the last Portuguese leprosarium and the contingent universes of experience and memory. Hist Cienc Saude Mangueiras. 2009 Apr-Jun;16(2):407-31.**

The Hospital-Colônia Rovisco Pais was inaugurated in Portugal in the 1940s for the treatment, study and prophylaxis of leprosy based on the compulsive internment model, whose configuration reflects the total institution concept proposed by Goffman. It concerns an important hygiene project of the Estado Novo. Its educative paradigm combined elements inspired in European social medicine and the ideology of the paternalistic Portuguese dictatorial regime. The Hospital Colony here will be thought of as a disciplinary dispositive, developing considerations regarding the confrontation between disciplinary power and experience. Memory emerges as a contingent instrument to access the practices and interstitial meanings woven into the Hospital Colony's daily life, seeking to find out about the experience of its former patients as political subjects.

#### **IMUNOLOGIA**

**Iyer A, Eijk M, Silva E, Hatta M, Faber W, Aerts JM, et al. Increased chitotriosidase activity in serum of leprosy patients: association with bacillary leprosy. Clin Immunol. 2009 Jun; 131(3): 501-9.**

Human phagocyte-specific chitotriosidase is associated with several diseases involving macrophage activation.

Since macrophage activation plays an important role in the control of *Mycobacterium leprae* infection, we studied the association of chitotriosidase with leprosy both in serum and in situ in lesional skin biopsies from patients. Serum samples from 78 Indonesian leprosy patients (39 non-reactional and 39 reactional leprosy patients) and 36 healthy controls (HC) from the same endemic region were investigated. The patients were classified as multibacillary (MB, n=69) or paucibacillary (PB, n=9) based on the bacterial index in slit-skin smears. Thirty-six of the reactional patients had erythema nodosum leprosum (ENL), while only 3 had reversal reaction (RR). Follow-up serum samples after corticosteroid treatment were also obtained from 17 patients with ENL and one with RR. Multibacillary (MB) patients showed increased chitotriosidase activity in serum as compared to paucibacillary (PB) patients and healthy controls. Although no significant difference was observed between reactional and the corresponding non-reactional groups, ENL showed significantly higher chitotriosidase activity as compared to HC. Furthermore, corticosteroid treatment resulted in significant decline of enzyme activity in ENL sera. Chitotriosidase activity correlated with levels of neopterin, another macrophage activation marker, but not with IL-6, IFN-gamma, TNF-alpha and IL-10. Immunohistochemical staining of 6 MB (LL=5, BL=1) lesional skin sections from stored material showed positive staining for chitotriosidase within lipid-laden macrophages suggesting that macrophages are the source of the enzyme detected in serum. Thus, serum chitotriosidase activity is potentially useful in distinguishing MB from PB leprosy and in monitoring response to therapy in ENL.

**Pessach I, Walter J, Notarangelo LD. Recent advances in primary immunodeficiencies: identification of novel genetic defects and unanticipated phenotypes. *Pediatr Res.* 2009 May; 65(5 Pt 2): 3R-12R.**

Primary immunodeficiencies (PIDs) have traditionally been defined according to their immunologic phenotype. Far from being concluded, the search for human genes that, when mutated, cause PID is actively being pursued. During the last year, four novel genetic defects that cause severe combined immunodeficiency and

severe congenital neutropenia have been identified. At the same time, the immunologic definition of primary immunodeficiencies has been expanded by the recognition that genetic defects affecting innate immunity may result in selective predisposition to certain infections, such as mycobacterial disease, herpes simplex encephalitis, and invasive pneumococcal infections. Studies of genetically determined susceptibility to infections have recently shown that immunologic defects may also account for novel infectious phenotypes, such as malaria or leprosy. Finally, a growing body of evidence indicates that primary immunodeficiencies may present with a noninfectious clinical phenotype that may be restricted to single organs, as in the case of atypical hemolytic uremic syndrome or pulmonary alveolar proteinosis. Overall, these achievements highlight the importance of human models, which often differ from the corresponding animal models.

**Geluk A, Spencer JS, Bobosha K, Pessolani MC, Pereira GM, Banu S. From genome-based in silico predictions to ex vivo verification of leprosy diagnosis. *Clin Vaccine Immunol.* 2009 Mar;16(3): 352-9.**

The detection of hundreds of thousands of new cases of leprosy every year suggests that transmission of *Mycobacterium leprae* infection still continues. Unfortunately, tools for identification of asymptomatic disease and/or early-stage *M. leprae* infection (likely sources of transmission) are lacking. The recent identification of *M. leprae*-unique genes has allowed the analysis of human T-cell responses to novel *M. leprae* antigens. Antigens with the most-promising diagnostic potential were tested for their ability to induce cytokine secretion by using peripheral blood mononuclear cells from leprosy patients and controls in five different areas where leprosy is endemic; 246 individuals from Brazil, Nepal, Bangladesh, Pakistan, and Ethiopia were analyzed for gamma interferon responses to five recombinant proteins (ML1989, ML1990, ML2283, ML2346, and ML2567) and 22 synthetic peptides. Of these, the *M. leprae*-unique protein ML1989 was the most frequently recognized and ML2283 the most specific for *M. leprae* infection/exposure, as only a limited number of tuberculosis patients responded to

this antigen. However, all proteins were recognized by a significant number of controls in areas of endemicity. T-cell responses correlated with in vitro response to *M. leprae*, suggesting that healthy controls in areas where leprosy is endemic are exposed to *M. leprae*. Importantly, 50% of the healthy household contacts and 59% of the controls in areas of endemicity had no detectable immunoglobulin M antibodies to *M. leprae*-specific PGL-I but responded in T-cell assays to  $\geq 1$  *M. leprae* protein. T-cell responses specific for leprosy patients and healthy household contacts were observed for ML2283- and ML0126-derived peptides, indicating that *M. leprae* peptides hold potential as diagnostic tools. Future work should concentrate on the development of a sensitive and field-friendly assay and identification of additional peptides and proteins that can induce *M. leprae*-specific T-cell responses.

**Makino M, Maeda Y, Kai M, Tamura T, Mukai T. GM-CSF-mediated T-cell activation by macrophages infected with recombinant BCG that secretes major membrane protein-II of Mycobacterium leprae. FEMS Immunol Med Microbiol. 2009 Jan;55(1): 39-46.**

The potential of *Mycobacterium bovis* Bacillus Calmette-Guerin (BCG) needs to be augmented to efficiently activate CD4(+) T cells through macrophages. *Mycobacterium leprae*-derived recombinant major membrane protein (MMP)-II induced GM-CSF production from macrophages. A recombinant BCG-SM that secretes MMP-II more efficiently produced GM-CSF and activated interferon (IFN)-gamma-producing CD4(+) T cells than did vector control BCG when infected with macrophages. The T-cell activation by BCG-SM was dependent on the GM-CSF production by macrophages. Interleukin (IL)-10 production by macrophages stimulated with *M. leprae* was inhibited in a GM-CSF-dependent manner when the precursor monocytes were infected with BCG-SM. BCG inducing GM-CSF production was effective in macrophage-mediated T-cell activation partially through IL-10 inhibition.

**Parkash O. Classification of leprosy into multibacillary and paucibacillary groups: an analysis. FEMS Immunol Med Microbiol. 2009 Jan; 55(1): 1-5.**

Classification of leprosy patients into multibacillary and paucibacillary determines the duration of their treatment. Misclassification leads to increased risk of relapse due to insufficient treatment if a multibacillary patient is classified as paucibacillary. This also prolongs the time the patient is infective. Over the years, the criteria used for classification (for treatment purpose) of leprosy patients have changed significantly from bacterial index measuring approach through number of skin lesions. The reliability of both of these criteria has been questioned. Several studies have shown that the presence of antibodies to the *Mycobacterium leprae*-specific antigens correlates with the bacterial load of a leprosy patient. Further, there are reports where results of serology and bacteriological approaches have been found to agree substantially. Thus, serology seems to be a worthwhile convenient alternative tool for classification of leprosy into multibacillary or paucibacillary. Nevertheless, in view of the limitations of various classification criteria, follow-up studies are called for to understand the efficiency of various approaches in preventing relapse after treatment. The method ensuring the lowest rate of relapse could be adopted for future use in classifying these patients.

**Chow D, Okinaka L, Souza S, Shikuma C, Tice A. Hansen's disease with HIV: a case of immune reconstitution disease. Hawaii Med J. 2009 Mar; 68(2):27-9.**

Immune reconstitution inflammatory syndrome (IRIS) is an acute symptomatic expression of a latent infection during the recovery of the immune system usually as a response to antiretroviral therapy (ART). Opportunistic infections can trigger IRIS. Hansen's disease is an infection caused by *Mycobacterium leprae* (*M. leprae*). There have been a limited number of case reports reporting the presentation of the co-infection of HIV and *M. leprae*. We report an unique case of IRIS in a patient co-infected with HIV and *M. leprae* presenting as an exacerbation of his Hansen's Disease where the patient's skin lesions progressed from borderline tuberculoid to lepromatous leprosy following ART administration.

Stefani MM, Guerra JG, Sousa AL, Costa MB, Oliveira ML, Martelli CT, et al. Potential plasma markers of Type 1 and Type 2 leprosy reactions: a preliminary report. *BMC Infect Dis.* 2009 May 27; 9:75.

**BACKGROUND:** The clinical management of leprosy Type 1 (T1R) and Type 2 (T2R) reactions pose challenges mainly because they can cause severe nerve injury and disability. No laboratory test or marker is available for the diagnosis or prognosis of leprosy reactions. This study simultaneously screened plasma factors to identify circulating biomarkers associated with leprosy T1R and T2R among patients recruited in Goiania, Central Brazil. **METHODS:** A nested case-control study evaluated T1R (n = 10) and TR2 (n = 10) compared to leprosy patients without reactions (n = 29), matched by sex and age-group (+/- 5 years) and histopathological classification. Multiplex bead based technique provided profiles of 27 plasma factors including 16 pro inflammatory cytokines: tumor necrosis factor-alpha (TNF-alpha), Interferon-gamma (IFN-gamma), interleukin (IL)- IL12p70, IL2, IL17, IL1 beta, IL6, IL15, IL5, IL8, macrophage inflammatory protein (MIP)-1 alpha (MIP1alpha), 1 beta (MIP1beta), regulated upon activation normal T-cell expressed and secreted (RANTES), monocyte chemoattractant protein 1 (MCP1), CC-chemokine 11 (CCL11/Eotaxin), CXC-chemokine 10 (CXCL10/IP10); 4 anti inflammatory interleukins: IL4, IL10, IL13, IL1Ralpha and 7 growth factors: IL7, IL9, granulocyte-colony stimulating factor (G-CSF), granulocyte macrophage-colony stimulating factor (GM-CSF), platelet-derived growth factor BB (PDGF BB), basic fibroblast growth factor (bFGF), vascular endothelial growth factor (VEGF). **RESULTS:** Elevations of plasma CXCL10 (P = 0.004) and IL6 (p = 0.013) were observed in T1R patients compared to controls without reaction. IL6 (p = 0.05), IL7 (p = 0.039), and PDGF-BB (p = 0.041) were elevated in T2R. RANTES and GMCSF were excluded due to values above and below detection limit respectively in all samples. **CONCLUSION:** Potential biomarkers of T1R identified were CXCL10 and IL6 whereas IL7, PDGF-BB and IL6, may be laboratory markers of TR2. Additional studies on these biomarkers may help understand the immunopathologic mechanisms of leprosy reactions and indicate their usefulness for the diagnosis and for the clinical management of these events.

Wallin LZ; Beckhauser AP, Haider O, Araujo F, Silva MB, Skare TL. Mal de Hansen, anticorpos antifosfolípidos e obstrução das artérias fibulares. *Rev. bras. Reumatol mar.-abr.* 2009; 49(2).

Pacientes com Mal de Hansen (MH) podem se apresentar com quadro clínico e laboratorial sugestivo de doenças reumáticas, o que exige um exercício cuidadoso de diagnósticos diferenciais. Descreve-se aqui o caso de uma jovem com MH que se apresentou com lesões cutâneas sugestivas de vasculite, obstrução de vasos fibulares, FAN e anticorpos antifosfolípidos positivos sem muitos estigmas da doença cutânea, ilustrando essa dificuldade.

#### MICOBACTÉRIAS

Lima CS, Marques MA, Debie AS, Almeida EC, Silva CA, Brennan PJ, et al. Heparin-binding hemagglutinin (HBHA) of *Mycobacterium leprae* is expressed during infection and enhances bacterial adherence to epithelial cells. *FEMS Microbiol Lett.* 2009 Mar; 292(2): 162-9.

A heparin-binding hemagglutinin (HBHA) expressed on the surface of *Mycobacterium tuberculosis* is an antigenic protein that has been implicated in bacterial adherence to epithelial cells and systemic dissemination. In this study, the potential role of the *Mycobacterium leprae* HBHA (ML-HBHA) homologue in leprosy was investigated. Initially, the in vivo expression of HBHA and its association with the *M. leprae* cell envelope was confirmed by immunoblotting and proteomic analysis. *Mycobacterium leprae* recombinant HBHA (rML-HBHA) bound to a heparin-Sepharose column, and its capacity to act as an adhesin was demonstrated in experiments showing that the exogenous addition of the protein to latex beads or to *M. leprae* cells promotes a dramatic increase in association with epithelial cells. Finally, serum anti-HBHA immunoglobulin G levels were investigated in individuals infected with *M. leprae*. Altogether, our data indicate that HBHA is recognized during the course of bacterial infection in humans and may play a role in leprosy pathogenesis.

Jadaun GP, Das R, Upadhyay P, Chauhan DS, Sharma VD, Katoch VM. Role of embCAB gene mutations in ethambutol resistance in *Mycobacterium tuberculosis* isolates from India. *Int J Antimicrob Agents*. 2009 May; 33(5): 483-6.

In the present study, ethambutol (EMB) resistance-associated mutations were characterised in the embCAB genes of clinical isolates of *Mycobacterium tuberculosis* (MTB) collected in India. Thirty MTB isolates were tested for their susceptibility to first-line antitubercular drugs using the Löwenstein-Jensen proportion method, and EMB minimum inhibitory concentrations of MTB isolates were determined by the resazurin microtitre assay. Sequencing of various regions of the embCAB genes was performed to identify EMB resistance-associated mutations. Mutations of embB306 were detected in 15 of 23 EMB-resistant MTB isolates. Three EMB-resistant isolates had mutations at codon 270 of the embC gene, two of which also harboured embB306 mutations. No mutation was identified in the embA gene. All seven EMB-sensitive MTB isolates had the wild-type embCAB sequence. In summary, embB306 mutations were associated with EMB resistance, and mutation at codon 270 of the embC gene may contribute to high-level EMB resistance in some MTB isolates.

Gupta A, Geetha N, Mani J, Upadhyay P, Katoch VM, Natrajan M, et al. Immunogenicity and protective efficacy of "*Mycobacterium w*" against *Mycobacterium tuberculosis* in mice immunized with live versus heat-killed *M. w* by the aerosol or parenteral route. *Infect Immun*. 2009 Jan; 77(1): 223-31.

As the disease caused by *Mycobacterium tuberculosis* continues to be a burden, there is a concerted effort to find new vaccines to combat this problem. One of the important vaccine strategies is whole bacterial vaccines. This approach relies on multiple antigens and built-in adjuvanticity. Other mycobacterial strains which share cross-reactive antigens with *M. tuberculosis* have been considered as alternatives to *M. bovis* for vaccine use. One such strain, "*Mycobacterium w*", had been evaluated for its immunomodulatory properties in leprosy. A

vaccine against leprosy based on killed *M. w* is approved for human use, where it has resulted in clinical improvement, accelerated bacterial clearance, and increased immune responses to *Mycobacterium leprae* antigens. *M. w* shares antigens not only with *M. leprae* but also with *M. tuberculosis*, and initial studies have shown that vaccination with killed *M. w* induces protection against tuberculosis in *Mycobacterium bovis* BCG responder, as well as BCG nonresponder, strains of mice. Hence, we further studied the protective potential of *M. w* and the underlying immune responses in the mouse model of tuberculosis. We analyzed the protective efficacy of *M. w* immunization in both live and killed forms through the parenteral route and by aerosol immunization, compared with that of BCG. Our findings provide evidence that *M. w* has potential protective efficacy against *M. tuberculosis*. *M. w* activates macrophage activity, as well as lymphocytes. *M. w* immunization by both the parenteral route and aerosol administration gives higher protection than BCG given by the parenteral route in the mouse model of tuberculosis.

Durnez L, Stragier P, Roebben K, Ablordey A, Leirs H, Portaels F. A comparison of DNA extraction procedures for the detection of *Mycobacterium ulcerans*, the causative agent of Buruli ulcer, in clinical and environmental specimens. *J Microbiol Methods*. 2009 Feb; 76(2): 152-8.

*Mycobacterium ulcerans* is the causative agent of Buruli ulcer, the third most common mycobacterial disease in humans after tuberculosis and leprosy. Although the disease is associated with aquatic ecosystems, cultivation of the bacillus from the environment is difficult to achieve. Therefore, at the moment, research is based on the detection by PCR of the insertion sequence IS2404 present in *M. ulcerans* and some closely related mycobacteria. In the present study, we compared four DNA extraction methods for detection of *M. ulcerans* DNA, namely the one tube cell lysis and DNA extraction procedure (OT), the FastPrep procedure (FP), the modified Boom procedure (MB), and the Maxwell 16 Procedure (M16). The methods were performed on serial dilutions of *M. ulcerans*, followed by PCR analysis with different



PCR targets in *M. ulcerans* to determine the detection limit (DL) of each method. The purity of the extracted DNA and the time and effort needed were compared as well. All methods were performed on environmental specimens and the two best methods (MB and M16) were tested on clinical specimens for detection of *M. ulcerans* DNA. When comparing the DLs of the DNA extraction methods, the MB and M16 had a significantly lower DL than the OT and FP. For the different PCR targets, IS2404 showed a significantly lower DL than *mlsA*, *MIRU1*, *MIRU5* and *VNTR6*. The FP and M16 were considerably faster than the MB and OT, while the purity of the DNA extracted with the MB was significantly higher than the DNA extracted with the other methods. The MB performed best on the environmental and clinical specimens. This comparative study shows that the modified Boom procedure, although lengthy, provides a better method of DNA extraction than the other methods tested for detection and identification of *M. ulcerans* in both clinical and environmental specimens.

**Tanigawa K, Suzuki K, Kimura H, Takeshita F, Wu H, Akama T, et al. Tryptophan aspartate-containing coat protein (CORO1A) suppresses Toll-like receptor signalling in Mycobacterium leprae infection. Clin Exp Immunol. 2009 Jun; 156(3):495-501.**

*Mycobacterium leprae* is an intracellular pathogen that survives within the phagosome of host macrophages. Several host factors are involved in producing tolerance, while others are responsible for killing the mycobacterium. Tryptophan aspartate-containing coat protein (TACO; also known as CORO1A or coronin-1) inhibits the phagosome maturation that allows intracellular parasitization. In addition, the Toll-like receptor (TLR) activates the innate immune response. Both CORO1A and TLR-2 co-localize on the phagosomal membrane in the dermal lesions of patients with lepromatous leprosy. Therefore, we hypothesized that CORO1A and TLR-2 might interact functionally. This hypothesis was tested by investigating the effect of CORO1A in TLR-2-mediated signalling and, inversely, the effect of TLR-2-mediated signalling on CORO1A expression. We found that CORO1A suppresses TLR-mediated signal activation in human

macrophages, and that TLR2-mediated activation of the innate immune response resulted in suppression of CORO1A expression. However, *M. leprae* infection inhibited the TLR-2-mediated CORO1A suppression and nuclear factor-kappaB activation. These results suggest that the balance between TLR-2-mediated signalling and CORO1A expression will be key in determining the fate of *M. leprae* following infection.

**Parashar D, Das R, Chauhan DS, Sharma VD, Lavania M, Yadav VS, et al. Identification of environmental mycobacteria isolated from Agra, north India by conventional & molecular approaches. Indian J Med Res. 2009 Apr; 129(4):424-31.**

**BACKGROUND & OBJECTIVE:** Several environmental mycobacteria have been shown to be important human pathogens linked to immunomodulation especially in relation to effect on vaccination. Hence identification of mycobacteria to the species level is not only relevant to patient management but also to understand epidemiology of mycobacterial diseases and effect on vaccination. We undertook this study to assess the usefulness of various conventional and molecular methods in identification of environmental mycobacterial species from Agra, north India. **METHODS:** One hundred nineteen isolates of environmental mycobacteria were grown from 291 (116 soil and 175 water) samples. These isolates were identified by standard biochemical tests, and a simple, rapid and cost-effective in-house developed gene amplification restriction analysis targeting 16S-23S rRNA spacer and flanking region and 16S rRNA sequencing. **RESULTS:** Biochemical tests could clearly identify only 68.1 per cent (81/119) of isolates to species level. An in-house developed gene amplification--restriction analysis method could confirm the identity of 102 of 119 (85.7%) isolates and the remaining 17 isolates (14.3%) were confirmed by 16S rRNA sequencing also. These 119 environmental mycobacterial isolates, included several potentially pathogenic species such as *M. fortuitum*, *M. chelonae*, *M. avium*, *M. marinum*, *M. manitobense*, *M. kansasii* and others belonged to nonpathogenic species, *M. terrae*, *M. smegmatis* and *M. flavescens*. *M. chelonae* was isolated from water samples only whereas *M. fortuitum* was iso-

lated from both water as well as soil samples. **INTERPRETATION & CONCLUSION:** The in-house developed gene amplification restriction analysis method though failed to accurately identify 14.3 per cent of isolates, facilitated rapid differentiation of most of environmental mycobacteria including potential pathogens from this area and thus would have diagnostic potential in cases with NTM infections. This combination strategy using PCR-RFLP and 16S rRNA sequencing may be useful for characterization of mycobacteria from similar environmental settings from other parts of world.

### **NEUROPATIA**

**Siddaraju N, Sistla SC, Singh N, Muniraj F, Chahwala Q, Basu D, et al. Pure neuritic leprosy with nerve abscess presenting as a cystic, soft tissue mass: report of a case diagnosed by fine needle aspiration cytology. Diagn Cytopathol. 2009 May;37(5): 355-8.**

Pure neuritic leprosy (PNL) with nerve abscess manifesting as a huge, cystic, soft tissue mass is highly uncommon. Fine needle aspiration cytology can serve as an important initial diagnostic modality in such an instance. We report a case of 28-year-old male, who presented with a huge swelling in the lower, medial aspect of the right upper arm. The clinical diagnosis was schwannoma. Fine needle aspiration (FNA) yielded 80 ml of sticky, turbid, pale brown fluid. Cytologic examination revealed abundant, caseous, necrotic material and many degenerated neutrophils in a thin proteinaceous background. Stain for acid fast bacilli (AFB) was negative. Based on an AFB negative, caseous, necrotic material obtained from the soft tissue mass located in the ulnar nerve region, a cytodiagnosis of tuberculoid PNL with nerve abscess was given, and this was confirmed by the subsequent histopathologic examination. Our case emphasizes the major role of minimally traumatic, FNA technique in the diagnosis of rare cases of clinically unsuspected neuritic leprosy. (c) 2009 Wiley-Liss, Inc.

### **ODONTOLOGIA**

**Souza VA, Emmerich A, Coutinho EM, Freitas MG, Silva EH, Merçon FG, et al. Dental and oral condition in leprosy patients from Serra, Brazil. Lepr Rev. 2009 Jun; 80(2):156-63.**

**OBJECTIVES:** To describe dental and periodontal diseases and oral lesions in newly diagnosed leprosy patients. **DESIGN:** Cohort study with 99 leprosy patients carried out at the Leprosy Control Programme Outpatient Clinic, Serra-ES, Brazil. A questionnaire about demographic and clinical data was used. Clinical oral examination was performed through the decayed, missing and filled teeth index (DMFT index), the use and need of prosthesis, periodontal disease and the presence of mucous membrane oral lesions. Skin and oral mucous biopsies were also undertaken. **RESULTS:** Decayed teeth were present in 73% of the patients, at least one lost tooth was present in 71.4%, the mean of the number of lost teeth among the patients in this survey was 88; and 60.3% of the patients did not have their teeth filled. Periodontal disease was present in 80.8%, and gingival bleeding in 92% of the patients. DMFT index average was 14.4. Nine out of the 63 patients presented with oral clinical lesions, however, most of them presented with unspecific chronic inflammation and typical epithelial hyperplasia. **CONCLUSIONS:** These newly diagnosed leprosy patients were similar in respect of oral health to the normal Brazilian population. Serious dental loss and edentulism were observed, as were a high DMFT index and frequency of periodontal diseases. These data highlight a lack of oral health prevention and treatment and poor access even when available.

### **OFTALMOLOGIA**

**Khandpur S, Robertson SJ, Rao PS. Ocular morbidity in leprosy patients with lagophthalmos. Indian J Lepr. 2009 Jan-Mar; 81(1): 1-4.**

Lagophthalmos is a well known complication in leprosy due to the involvement of seventh cranial nerve resulting in incomplete closure of the eyelids. The real magnitude of ocular morbidity as a consequence of lagophthalmos is unknown, as several ocular complications can occur

independently due to involvement of the fifth (trigeminal) nerve or due to secondary infection. Therefore, a study was designed to carefully examine the eyes of 100 consecutive leprosy patients with lagophthalmos seeking treatment at a leprosy referral centre in Delhi. Among the eyes examined, 145 had lagophthalmos. The symptomatology and anterior-posterior chamber morbidity in eyes with lagophthalmos were significantly higher as compared to unaffected eyes. Significantly, higher morbidity was seen regardless of sex or type of leprosy or deformity. Capacity building of the health professionals regarding ocular morbidity and increased emphasis on the importance of self care among patients can significantly reduce ocular morbidity.

#### REAÇÕES ADVERSAS À PQT

**Manifold R, Marshman G. Leprosy: not always an easy diagnosis and often a management challenge. *Australas J Dermatol.* 2009 Feb; 50(1):36-40.**

Leprosy is rare in Australia, particularly in the southern states. We report two cases of leprosy in southern Australia that presented to the dermatology outpatients' department within a 4-month period. The presentation of the first case was complex, making the correct diagnosis difficult. Both cases involved immigrants from South-East Asia, were classified as multi-bacillary leprosy as defined by the World Health Organization, and were commenced on the recommended multiple drug therapy. The ensuing clinical course was complicated, with both cases developing Type 1 leprosy reactions. The first case also developed the rare but serious dapsone-induced delayed hypersensitivity reaction.

**Silva IMCB, Oliveira CAP, Guedes WRC, Oliveira BB, Oliveira DAP, Guedes Filho G. Agranulocytosis induced by multidrug therapy in leprosy treatment: a case report. *Braz. j. infect. Dis apr.* 2009; 13(2):158-60.**

Multidrug therapy (WHO/MDT) in multibacillary leprosy consists of treatment with rifampicin, dapsone and clofazimine. However, adverse effects can cause the patient to abandon treatment. We report on a patient

who presented agranulocytosis and hemolytic anemia associated with this treatment regime. We also examined the importance of laboratory exams for diagnosis and follow-up of the patient, and for early detection of adverse effects, with a view to improving adherence to treatment and contributing to the eradication of Hansen's disease as a public health issue.

**Silva IM, Oliveira CA, Guedes WR, Oliveira BB, Oliveira DA, Guedes Filho G. Agranulocytosis induced by multidrug therapy in leprosy treatment: a case report. *Braz J Infect Dis.* 2009 Apr;13(2):158-60.**

Multidrug therapy (WHO/MDT) in multibacillary leprosy consists of treatment with rifampicin, dapsone and clofazimine. However, adverse effects can cause the patient to abandon treatment. We report on a patient who presented agranulocytosis and hemolytic anemia associated with this treatment regime. We also examined the importance of laboratory exams for diagnosis and follow-up of the patient, and for early detection of adverse effects, with a view to improving adherence to treatment and contributing to the eradication of Hansen's disease as a public health issue.

**Rodríguez G, Pinto R, López F, Gómez Y. Persistent type 2 lepra reaction (erythema nodosum) and clofazimine-induced lethal enteropathy. *Biomedica* 2009 Mar; 29(1):18-24.**

**INTRODUCTION:** Clofazimine enteropathy is a serious complication of clofazimine when used at high doses for treatment of type 2 lepra or erythema nodosum leprosum. **Objective.** A woman is presented who had a delayed diagnosis of leprosy, persistent type 2 lepra reaction and lethal clofazimine enteropathy. **MATERIALS AND METHODS:** A 31-year-old woman presented leprosy symptoms over a 16-year period without medical diagnosis of her disease. During this period, type 2 lepra episodes occurred, but were not accurately diagnosed. These episodes became more severe during her second pregnancy. The patient and her family were interviewed, and her clinical history reviewed. **RESULTS:** After twelve

years of medical consults, lepromatous leprosy was diagnosed, based on perforation of her nasal septum, with a bacterial index of 5. Her husband and a 12-year-old daughter have leprosy symptoms. During multidrug therapy, she presented with repeated type 2 lepra reaction episodes for which she received daily clofazimine 400 mg doses. Two months after this treatment, severe and frequent episodes of intense abdominal pain began to occur. These persisted for more than a year and were managed with in-hospital administration of several classes of painkillers and antispasmodic medication, including morphine. She also presented with sporadic diarrhea, constipation, nausea, weight loss and mesenteric adenopathies. She died finally due to this intestinal condition. No autopsy was performed. **CONCLUSIONS:** The patient's clinical presentation suggested a clofazimine-induced lethal enteropathy, a complication not previously seen in Colombia. This connection was not recognized by the medical officers that treated the patient.

### **RECIDIVA / REATIVAÇÃO**

**Kaimal S, Thappa DM. Relapse in leprosy. Indian J Dermatol Venereol Leprol. 2009 Mar-Apr; 75(2): 126-35.**

Leprosy is unique in terms of the nature of the causative organism (*Mycobacterium leprae*), the chronicity of the disease, its prolonged treatment and the definitions of "cure" and "relapse." The principal mode of assessing the efficacy of therapeutic regimens in leprosy is the "relapse rate." There are wide variations in estimates of relapse rates after the World Health Organization (WHO) multidrug therapy in different regions. The important predisposing factors for relapse include the presence of "persister" bacilli, monotherapy, inadequate/irregular therapy, presence of multiple skin lesions/thickened nerves and lepromin negativity. The conventional methods of confirming activity or relapse in an infectious disease (demonstration and/or culture of the etiologic agent) have limited utility in leprosy because of the difficulty in demonstrating bacilli in paucibacillary (PB) cases and absence of a method of in vitro cultivation of *M. leprae*. Bacteriological parameters are useful in multibacillary (MB) leprosy, whereas in PB leprosy, the criteria for relapse depend primarily on clinical features. Although there are

no widely available serologic tests for leprosy other than in a research setting, various immunological tests may be useful for monitoring patients on chemotherapy as well as for confirming suspected cases of relapse. The main differential diagnoses for relapse are reversal reactions, erythema nodosum leprosum and reactivation/resistance/reinfection. The most reliable criteria for making an accurate diagnosis of relapse include clinical, bacteriological and therapeutic criteria. Additional ones that may be used, depending on the setting, are histopathological and serologic criteria. Relapsed cases of leprosy should be identified and put back on chemotherapy as soon as possible to prevent further disability and transmission of infection. Factors that should be considered in choosing an appropriate regimen are the type of leprosy (PB or MB), previous treatment and drug resistance. Occasionally, clinicians may need to use their judgement to modify the standard WHO treatment regimens according to the scenario in each patient.

**Lopes RV, Ohashi CB, Cavaleiro LH, Cruz RBP, Veiga RR, Miranda FR, et al. Development of leprosy in a patient with ankylosing spondylitis during the infliximab treatment: reactivation of a latent infection? Clin Rheumatol. 2009 May; 28(5): 615-7.**

The use of tumor necrosis factor alpha as a treatment for chronic inflammatory conditions has been shown to be associated with an increased risk of developing infections, especially *Mycobacterium tuberculosis*, atypical mycobacteria, and other microorganisms. We report the case of a 58-year-old man with ankylosing spondylitis, receiving infliximab treatment, who presented with multiple plaques on the face, chest, and extremities, a thickened, tender ulnar nerve, and severe neuritis of the feet. The results of a biopsy of these lesions revealed histopathological features of lepromatous Hansen disease. The use of anti-tumor necrosis factor biologic agent on this patient may have resulted in either a new infection or reactivation of a latent infection of *Mycobacterium leprae*.

**Hulmani M, Marne RB, Dandakeri S. A case of lepromatous leprosy with multiple relapses. Lepr Rev. 2009 Jun; 80(2):210-4.**

We report a case of multiple relapses in a lepromatous leprosy patient after treatment with World Health Organisation (WHO) recommended multibacillary multi-drug therapy (MBMDT). The patient responded well to reintroduction of MDT after each relapse.

**Kiran KU, Krishna MKV, Meher V, Rao PN. Relapse of leprosy presenting as nodular lymph node swelling. Indian J Dermatol Venereol Leprol. 2009 Mar-Apr; 75(2): 177-9.**

Lymphadenopathy is known to be associated with lepromatous leprosy and has also been observed as a feature of type-2 lepra reaction. However, nodular lymph node enlargement is not commonly reported in leprosy patients or as a feature of relapse. We herewith are presenting a case of bacteriological relapse in a patient of lepromatous leprosy treated 22 years before till smear negativity with WHO multidrug therapy (MDT) multibacillary type (MB). She presented with prominent nodular swelling of the cervical group of lymph nodes along with generalized lymphadenopathy, which was mistakenly treated as tubercular lymphadenopathy. A diagnosis of late bacteriological relapse of lepromatous leprosy presenting with prominent lymphadenopathy and ENL was made after relevant investigations. The patient was started on treatment with WHO MDT MB (daily dapsone and clofazimine and monthly rifampicin) and thalidomide (200 mg/day). Nerve pain regressed within 2 weeks of therapy. The lymph nodal swelling regressed within 3 months of starting treatment.

#### **REUMATOLOGIA**

**Pereira HL, Ribeiro SL, Pennini SN, Sato EI. Leprosy-related joint involvement. Clin Rheumatol. 2009 Jan; 28(1): 79-84.**

We estimate the prevalence and evaluate the clinical characteristics of leprosy related arthritis. One thousand, two hundred fifty-seven leprosy patients were attended

at "Alfredo da Matta" outpatient clinic in the state of Amazonas, Brazil from July to October 2004. Among them, 115 patients were identified with articular pain and were referred for evaluation with rheumatologist. Blood samples were collected and radiological evaluation of the involved joints was performed. All patients with arthritis who continued to be followed up were reevaluated. One hundred fifteen leprosy patients (9.1%) were identified with articular involvement. The articular complaints were attributed to a defined rheumatic disease in 36 cases and excluded from further analysis. Twenty-four patients had arthralgia, and 55 (37 males and 18 females) had leprosy-related arthritis. The prevalence of arthritis was similar in both genders, and all patients with leprosy-related arthritis had lepromatous or borderline type. Most of patients had polyarticular and symmetrical arthritis and had completed the multidrug therapy and was under reaction treatment. The mean duration of articular symptoms at the time of study was 1.06 years (ranging from 5 days to 14 years). Ninety-one percent of patients with leprosy-related arthritis presented erythema nodosum leprosum or reversal reactions. Only five patients with arthritis had never presented reactions. Fifty percent of patients became asymptomatic during the mean 24 months of follow-up. Leprosy-related arthritis has a lower prevalence than previously reported. Most cases of leprosy-related arthritis were associated with reactional episodes, and in a large number of cases, the arthritis had a chronic course not responsive to the conventional therapy for reactions.

**Sheetal S, Arvind C. Lest we forget Hansen's disease (leprosy): an unusual presentation with an acute onset of inflammatory polyarthritis and the rheumatology experience. Int J Rheum Dis. 2009 Apr;12(1):64-9.**

Several forms of arthritis and rheumatism can sometimes complicate leprosy. However, its presentation as an acute onset arthritis is unusual. We report two adult male naïve patients who presented to our rheumatology outpatient clinic with acute onset inflammatory polyarthritis, skin rash and mild sensory neurodeficit. Borderline lepromatous leprosy (in typlndian J Pharm Sci. 2009 Jan;71(1):106-10.

**SAÚDE PÚBLICA**

**Khatami A, San Sebastian M. Skin disease: a neglected public health problem.**

*Dermatol Clin.* 2009 Apr; 27(2): 99-101.

Skin diseases are among the most common health problems in humans. Considering their significant impact on the individual, the family, the social life of patients, and their heavy economical burden, the public health importance of these diseases is underappreciated. This article discusses the importance of dermatologic public health and makes recommendations for better addressing this neglected topic.

**Shetty VP, Thakar UH, D'souza E, Ghate SD, Arora S, Doshi RP, Wakade AV, Thakur DV. Detection of previously undetected leprosy cases in a defined rural and urban area of Maharashtra, Western India. *Lepr Rev.* 2009 Mar; 80(1):22-33.**

**INTRODUCTION:** Leprosy has been a major public health problem in India for centuries. In India, between 2001 and 2005, the prevalence of leprosy was reduced by 80%. This sharp decline in the prevalence of leprosy alongside the cessation of active surveillance for detection of leprosy cases has raised a sense of alarm in the scientific community. **MATERIALS AND METHODS:** This is a total population survey aiming to estimate the prevalence of undetected active cases of leprosy in the community in defined rural (Panvel Taluka, Raigad District) and urban (M-East Ward, Mumbai) areas by health workers from Kushth Nivaran Samiti (Panvel) and Lok Seva Sangam (Mumbai). Those provisionally diagnosed with leprosy were subjected to an independent verification using clinical, bacteriological and histopathological investigations at the Foundation for Medical Research. **FINDINGS:** A population of 196,694 and 600,247 was covered in defined rural and urban areas respectively. In the rural area on examining 178,646 individuals, 120 provisionally diagnosed leprosy cases were detected, of which 65 were paucibacillary (PB) and 55 were multibacillary (MB) based on the WHO operational classification used by health workers at field level. In the urban area, of the 512,434 individuals who were examined, 134 provision-

ally diagnosed leprosy cases were detected with 92 PB and 42 MB cases. Among the clinically confirmed cases, 35.6% (32/90) and 34.9% (36/109) in rural and urban areas respectively were children. **CONCLUSIONS:** There are large numbers of undetected leprosy cases in the community with a high proportion of MB patients and children among them. This indicates active transmission pointing to the need for a paradigm shift in leprosy care services and control programme.

**Sehgal VN, Srivastava G, Singh N, Prasad PV. Histoid leprosy: the impact of the entity on the postglobal leprosy elimination era. *Int J Dermatol.* 2009 Jun; 48(6):603-10.**

A fresh focus on histoid leprosy is the primary objective of this article, especially in the context of the postglobal leprosy elimination era. The emergence of the entity following dapsone monotherapy is well recognized, in addition to de novo cases. Irregular and inadequate therapies, coupled with resistance to dapsone and/or mutant organisms, are responsible. It was considered to be worthwhile to take stock of the condition through its history, nomenclature, epidemiology, clinical characteristics, diagnosis, and differential diagnosis. The bacteriologic and histopathologic features and immunologic profile are also described

**TERAPÊUTICA**

**Medeiros S, Catorze MG, Vieira MR. Hansen's disease in Portugal: multibacillary patients treated between 1988 and 2003. *J Eur Acad Dermatol Venereol.* 2009 Jan; 23(1): 29-35.**

**BACKGROUND:** There is an estimate low incidence of patients with Hansen's disease in Portugal. Following the 1982 World Health Organization (WHO) recommendations, extended multidrug therapy (MDT) was started for multibacillary (MB) patients. Patients were then treated with rifampicine (RFP), clofazimine (CLF) and dapsone (DDS) for a minimum of 2 years or until smear negativity. The aim of this study was to evaluate MDT efficacy in our patient population. **METHODS:** Retrospective and de-

scriptive study of 102 MB patients who underwent MDT from 1988 to 2003. RESULTS: The number of new MB patients has gradually increased since 1960, the first year of our consultation, due mostly to a rise in imported cases. Overall, 34% of the subjects were immigrants, mainly from former Portuguese Colonies. Forty-six patients had previously received monotherapy with DDS (mean duration of this treatment, 22 years). Relapse after MDT occurred in 9 cases (8.8%), but importantly, all relapsed cases were smear negative at least on one occasion after the end of treatment, suggesting these were true relapses rather than treatment failures. CONCLUSIONS: Despite the 2-year WHO-MDT regimen, patients with MB disease clearly face the possibility of relapse. We propose that any reduction in the duration of therapy such as the recently proposed 6-month standard MDT is likely to increase the relapse rate even further. Important issues for future consideration are the needs to identify those at risk of relapse and in need of alternative antimicrobial treatment with a prolonged clinical follow-up.

**Rao PN, Suneetha S, Pratap DV. Comparative study of uniform-MDT and WHO MDT in Pauci and Multi bacillary leprosy patients over 24 months of observation. *Lepr Rev.* 2009 Jun; 80(2):143-55.**

STUDY DESIGN: An open comparative study between WHO MDT and U-MDT regimen in all types of leprosy over 24 months of observation was carried out at Gandhi Hospital, Secunderabad, India. Periodic assessment of clinical and histopathological parameters at 6 monthly intervals was performed in both groups of patients for grading response to the treatment regimens. PATIENTS AND METHODS: One hundred and twenty-seven newly diagnosed, untreated leprosy patients classified into PB (< or = 5 skin lesions) and MB leprosy (> 5 skin lesions) were alternately allocated into Study (U-MDT for 6 months) and Control groups (WHO MDT) at entry. Out of the 127 patients included, 64 patients (M-44, F-20; PB leprosy 32 & MB leprosy 32) could be followed-up regularly. These 64 patients were clinically assessed and graded into Good, Moderate and Poor response at 6, 12 and 18 months of the study, and 44 of these patients were also assessed at 24 months of the study. Histopathological assess-

ments were also done at the above intervals. RESULTS: PB PATIENTS: The control and study groups comprised of 14 and 18 patients respectively. When clinical grades were compared, the numbers of Moderate and Good responses were 78% and 61% at 6 months, 86% and 94% at 18 months and 82% and 100% at 24 months in the PB Control and Study groups respectively, suggesting better progressive improvement in the Study group compared to Control group, but the differences were not significant (At 6 months  $P = 0.2195$ , at 18 months  $0.7305$ , at 24 months  $P = 0.3500$ ) Histopathological assessment at 12 months, showed higher percentage of Good responses (100%) in the PB-Study group than in the PB-Control group (86%). MB PATIENTS: The MB Control and Study groups comprised of 22 and 10 patients respectively. In clinical improvement grades, Good responses in the Control group was 36%, 45% and 77% at 12, 18 and 24 months of study, whereas the Study group did not have a single Good response at 12 and 18 months with the Poor responses being 50%, 67% and 75% at 12, 18 and 24 months. These differences between the groups were significant at all periods of assessment. (At 12 months  $P = 0.0465$ , at 18 months  $P = 0.0014$ , at 24 months  $P = 0.0064$ ). Histopathological assessment showed higher the percentage of Good responses in Control group (100%) compared to Study group (50%) at 18 months. CONCLUSION: U-MDT of 6 months duration was well tolerated and effective in patients with PB leprosy but was too short a regimen adequately to treat patients with MB leprosy.

**Shen J, Liu M, Zhou M, Wengzhong L. Occurrence and management of leprosy reaction in China in 2005. *Lepr Rev.* 2009 Jun; 80(2):164-9.**

BACKGROUND: Leprosy reactions are a major cause of disability before, during and after anti-bacterial treatment. Prompt diagnosis and correct management of reaction is a crucial matter for improving the quality of leprosy health services. OBJECTIVES: To describe the pattern of leprosy reaction and its management in China during 2005. METHODS: A retrospective survey using a questionnaire was carried out in all the provinces of China at the beginning of 2006. Patients included were those

presenting with leprosy reaction between 1 January and 31 December 2005. RESULTS: 452 questionnaires from 25 provinces were analysed. There were 313 male and 139 female patients who had 159 Type I reactions, 273 Type II reactions and 20 Type I and II mixed reaction. 72.4% of reactions occurred in the first year of MDT and 27.6% of patients during the second year of MDT. The highest frequency of reaction was during the first 6 months of MDT; 57.3% of patients developed new nerve impairment during and after MDT. CONCLUSIONS: New nerve function impairment and disability still occurs among patients during and after MDT. The early detection and management of leprosy reaction remains important.

**Jing Z, Zhang R, Zhou D, Chen J. Twenty five years follow up of MB leprosy patients retreated with a modified MDT regimen after a full course of dapsone mono-therapy. *Lepr Rev.* 2009 Jun; 80(2):170-6.**

BACKGROUND: The relentless emergence of dapsone resistance amongst *M. leprae* threatened leprosy control programmes, and increased the relapse rate of patients cured with dapsone monotherapy. OBJECTIVE: The study aimed to analyse the effect on the relapse rate of dapsone-cured multibacillary (MB) leprosy patients, of re-treatment, using a multidrug therapy (MDT) regimen which differed from the WHO recommended regimen. DESIGN: 794 MB leprosy patients who had been released from treatment after dapsone monotherapy were selected, amongst them 657 were re-treated for 1 year using the modified multidrug therapy regimen (mMDT) including rifampicin, clofazimine and dapsone, and 137 patients were observed as control cases. RESULTS: The regimen was well tolerated with good compliance: 620 patients completed re-treatment with mild side effects and a low incidence of leprosy reactions. There was a statistically significant difference between the relapse rates of re-treated and control groups (chi squared  $f = 57.44$ ,  $P < 0.001$ ). Furthermore, the relapses in the re-treated group were significantly more likely to be later than those in the control group ( $t = 25.62$ ,  $P < 0.001$ ). CONCLUSIONS: Re-treatment with this modified regimen is acceptable and can reduce the risk of early relapse in dapsone-cured patients. The problem of persisters causing late relapse is likely to remain.

**Pardillo FE, Burgos J, Fajardo TT, Dela Crux E, Abalos RM, Paredes RM, Andaya CE, Gelber RH. Rapid killing of *M. leprae* by moxifloxacin in two patients with lepromatous leprosy. *Lepr Rev.* 2009 Jun;80(2):205-9.**

INTRODUCTION: Previously we reported a 2-month clinical trial of moxifloxacin therapy in eight patients with MB leprosy (7 LL and 1 BL), finding both rapid killing of *M. leprae* and clinical improvement, without serious side effects or toxicities. Here we report the outcomes in two patients treated with moxifloxacin. DESIGN: Two previously untreated LL patients were treated with a single 400 mg dose of moxifloxacin, no therapy for 7 days and then daily 400 mg moxifloxacin for 48 days. Clinical response, viability of *M. leprae* in the skin, and side effects/toxicities were carefully monitored. RESULTS: In both patients a single dose of moxifloxacin resulted in significant killing of *M. leprae* ( $P < 0.001\%$ ). In both patients no viable *M. leprae* were found after 15 doses of moxifloxacin. Improvement in skin lesions occurred again remarkably rapidly and no untoward effects were noted. CONCLUSION: Loss of viable *M. leprae* was quite rapid, similar to that found previously only for rifampicin, patients improved rapidly, and moxifloxacin was well tolerated.

### **TRANSMISSÃO**

**Ghorpade A. Post-traumatic inoculation tuberculoid leprosy after injury with a glass bangle. *Lepr Rev.* 2009 Jun; 80(2):215-8.**

A lesion of tuberculoid leprosy in an Indian lady presenting at the site of injury from a broken glass bangle is reported. The diagnosis was by classical clinical features and histopathology. The importance of the skin in leprosy transmission is emphasized.

### **ÚLCERA**

**Huygen K, Adjei O, Affolabi D, Bretzel G, Demangel C, Fleischer B. Buruli ulcer disease: prospects for a vaccine. *Med Microbiol Immunol.* 2009 May;198(2): 69-77.**

Buruli ulcer disease (BUD), caused by *Mycobacterium ulcerans*, is a neglected bacterial infection of the poor



in remote rural areas, mostly affecting children. BUD is a mutilating disease leading to severe disability; it is the third most common mycobacterial infection in immunocompetent people after tuberculosis and leprosy. It is most endemic in West Africa, but cases have been reported from more than 30 countries. Treatment with antibiotics is possible, long-lasting and requires injections; there are cases of treatment failures, and the disease is prone to resistance. A vaccine against *M. ulcerans* would protect persons at risk in highly endemic areas, and could be used as a therapeutic vaccine to shorten the duration of treatment and prevent relapses. There is considerable evidence supporting the notion that generation of a vaccine is feasible. This article reviews the present state of the art with special emphasis on the immunology of the infection and the prospects for development of a vaccine.

**Portaels F, Silva MT, Meyers WM. Buruli ulcer. Clin Dermatol. 2009 May-Jun; 27(3): 291-305.**

Buruli ulcer is an indolent necrotizing disease of the skin, subcutaneous tissue, and bone that is caused by *Mycobacterium ulcerans*. Buruli ulcer is presently the third most common mycobacterial disease of humans, after tuberculosis and leprosy, and the least understood of the three. The disease remained largely ignored by many national public health programs, but more recently, it has been recognized as an emerging health problem, primarily due to its frequent disabling and stigmatizing complications. The contribution discusses various aspects of Buruli ulcer, including its geographic distribution, incidence, and prevalence; mode of transmission, pathogenesis, and immunity; clinical manifestations; laboratory diagnosis; differential clinical diagnosis; and treatment.

**Bhatt YC, Panse NS, Vyas KA, Patel GA. Free tissue transfer for trophic ulcer complicating leprosy. Indian J Plast Surg. 2009 Jan-Jun;42(1):115-7.**

Plantar ulceration is the commonest disability in leprosy and occurs in about 10 to 20% of leprosy patients. Various loco-regional flaps have been described for reconstruction of trophic ulcers; however, very large defects are

not amenable to local flaps and free flaps form one of the important treatment options. We present a case of a post Hansen's trophic ulcer over the forefoot managed using a radial artery forearm free flap. Debridement of the osteomyelitic bone, removal of the bony prominences, coverage by a well-vascularised tissue, end-to-side arterial anastomosis, use of anterior tibial as the recipient vessel and good postoperative compliance in foot care on the part of the patient gave us good results.

**Ebenso J, Muyiwa LT, Ebenso BE. Self care groups and ulcer prevention in Okegbala, Nigeria. Lepr Rev. 2009 Jun; 80(2):187-96.**

**OBJECTIVE:** To assess the impact of the three self-care Groups on ulcer prevalence and readmission rates in Okegbala hospital. **DESIGN:** A retrospective, descriptive study. The evaluation combined four data collection methods namely (i) records survey, (ii) semi-structured interviews of individual members of self-care groups, (iii) group discussions and (iv) key informant interviews. **RESULTS:** Record surveys show that the ulcer prevalence has decreased by almost 75% since the adoption of the self-care group; admissions to hospital for ulcer care have reduced, and the mean interval between admissions has increased by 7 months. Semi structured interviews and group discussions show that all members have a greater sense of control of their ulcers and general health; and that self-care groups have a potential of catalysing community solidarity and development. **CONCLUSIONS:** This small study shows that self-care groups are valuable for reducing ulcers and giving members a greater sense of control of their ulcers and general health resulting in fewer hospital admissions. We recommend a multi-centre, controlled, prospective study incorporating different settings (e.g. urban, rural, near hospitals, within field leprosy programmes) to test these findings. Such a study has the potential of influencing policy and health-service reorientation of ulcer care in future.

