

## Biologia molecular/genética

Geluk A, Klein MR, Franken KL, van Meijgaarden KE, Wieles B, Pereira KC, Bühner-Sékula S, Klatser PR, Brennan PJ, Spencer JS, Williams DL, Pessolani MC, Sampaio EP, Ottenhoff TH. Postgenomic approach to identify novel *Mycobacterium leprae* antigens with potential to improve immunodiagnosis of infection. [Infect Immun](#) 2005; 73(9):5636-44.

Early detection of *Mycobacterium leprae* infection is considered an important component of strategies aiming at reducing transmission of infection, but currently available diagnostic tools often lack sufficient sensitivity and specificity to reach this goal. Recent comparative genomics have revealed the presence of 165 *M. leprae* genes with no homologue in *M. tuberculosis*. We selected 17 of these genes for further study. All 17 genes were found to be expressed at the mRNA level in *M. leprae* from infected mice and from a multibacillary leprosy patient. Additional comparative genomic analyses of all currently available mycobacterial genome databases confirmed 12 candidate genes to be unique to *M. leprae*, whereas 5 genes had homologues in mycobacteria other than *M. tuberculosis*. Evaluation of the immunogenicity of all 17 recombinant proteins in PBMC from 127 Brazilians showed that five antigens (ML0576, ML1989, ML1990, ML2283, and ML2567) induced significant gamma interferon levels in paucibacillary leprosy patients, reactional leprosy patients, and exposed healthy controls but not in most multibacillary leprosy patients, tuberculosis patients, or endemic controls. Importantly, among exposed healthy controls 71% had no detectable immunoglobulin M antibodies to the *M. leprae*-specific PGL-I but responded to one or more *M. leprae* antigen(s). Collectively, the *M. leprae* proteins identified are expressed at the transcriptome level and can efficiently activate T cells of *M. leprae*-exposed individuals. These proteins may provide new tools to develop tests for specific diagnosis of *M. leprae* infection and may enhance our understanding of leprosy and its transmission

## Biologia molecular/genética

Ohyama H, Ogata K, Takeuchi K, Namisato M, Fukutomi Y, Nishimura F, Naruishi H, Ohira T, Hashimoto K, Liu T, Suzuki M, Uemura Y, Matsushita S. Polymorphism of the 5' flanking region of the IL-12 receptor beta2 gene partially determines the clinical types of leprosy through impaired transcriptional activity. [J Clin Pathol](#) 2005; 58(7):740-3.

**BACKGROUND:** Individual differences in T cell responsiveness to interleukin 12 (IL-12), resulting from inherited factors, may be responsible for differences in the intensity of cell mediated immune (CMI) responses in patients with leprosy, a disease with a wide clinical spectrum. **AIM:** Polymorphisms in the 5' flanking region of the IL12RB2 gene were analysed to determine potential immunogenetic factors affecting CMI responses, using leprosy as a model. **METHODS:** Polymorphisms in the 5' flanking region of IL12RB2 were examined using direct sequencing techniques, and allele frequencies between patients with lepromatous leprosy and patients with tuberculoid leprosy were compared. The effect of these single nucleotide polymorphisms (SNPs) on IL12RB2 expression was estimated using the dual luciferase reporter gene assay in Jurkat T cells. **RESULTS:** Several SNPs, including -1035A>G, -1023A>G, -650delG, and -465A>G, were detected within the 5' flanking region of IL12RB2. The frequency of haplotype 1 (-1035A, -1023A, -650G, -464A) was high in the general Japanese population, but was significantly lower in lepromatous patients compared with tuberculoid patients and healthy controls. Reporter gene assays using Jurkat T cells revealed that all haplotypes carrying one or more SNP exhibited a lower transcriptional activity compared with haplotype 1. **CONCLUSION:** SNPs within the 5' flanking region of IL12RB2 affect the degree of expression of this gene and may be implicated in individual differences in CMI responsiveness to mycobacterial antigens, leading to lepromatous or tuberculoid leprosy.

## Biologia molecular/genética

Santhosh RS, Pandian SK, Lini N, Shabaana AK, Nagavardhini A, Dharmalingam K. Cloning of *mce1* locus of *Mycobacterium leprae* in *Mycobacterium smegmatis* mc2 155 SMR5 and evaluation of expression of *mce1* genes in *M. smegmatis* and *M. leprae*. [FEMS Immunol Med Microbiol](#) 2005; 45(2):291-302.

Plasmid pSET152 is a broad host range mobilizable vector which integrates into streptomyces chromosome utilizing *att* site and *int* function of slashed circleC31. Transformation of this plasmid into *Mycobacterium smegmatis* mc2 155 SMR5 gave stable transformants carrying the pSET152 as an integrated copy. Integration occurred at the cross over sequence 5'TTG disrupting the *gatA* gene (Glu-tRNA(Gln) amidotransferase subunitA), which is non-essential under conditions used. Recombinant pSET152 plasmids carrying *mce1* locus of *Mycobacterium leprae* were used to construct *M. smegmatis* transformants carrying the *mce1* locus in their chromosome. RT-PCR analysis revealed specific transcripts of *M. leprae mce* in *M. smegmatis*. The transcribed mRNA carried intergenic regions between genes of *mce1* locus indicating that *mce1* locus is an operon. Examination of *M. leprae* specific mRNA from lepromatous leprosy patient's biopsy showed that *mce* locus is transcribed as an operon in the pathogen also.

## Biologia molecular/genética/epidemiologia

Zhang L, Budiawan T, Matsuoka M. Diversity of potential short tandem repeats in *Mycobacterium leprae* and application for molecular typing. [J Clin Microbiol](#) 2005; 43(10):5221-9.

A recent advance in molecular typing for tracing the transmission of leprosy is the discovery of short tandem repeats (STRs) in *Mycobacterium leprae*. To substantiate polymorphic loci from STR as promising candidates for molecular typing tools in leprosy epidemiology, 44 STR loci including 33 microsatellites and 11 minisatellites were investigated among 27 laboratory strains by sequencing PCR products. Not all STRs were necessarily polymorphic. Thirty-two out of the 44 loci were polymorphic. Nine polymorphic loci were suitable for identifying genotypes according to the discriminatory capacity, stability, and reproducibility. All the strains were classified into independent genotypes by the selected nine loci. Three multi-case households were subjected to molecular typing. *M. leprae* obtained from household cases showed identical copy numbers by TTC triplet alone, but the isolates from one family contact case were divided into different genotypes by adding eight other polymorphic loci. The combination of information from multiple loci allows increasing levels of discrimination and it is likely that the generation and documentation of data will result in the choice of a potential molecular typing tool for leprosy epidemiology.

## Cirurgia/ulcera

Gahalaut P, Pinto J, Pai GS, Kamath J, Joshua TV. A novel treatment for plantar ulcers in leprosy: local superficial flaps. [Lepr Rev](#) 2005; 76(3):220-31.

Plantar ulceration is the most common serious disability occurring in patients of leprosy. Growth and emergence of innovative procedures in plastic surgery has greatly revolutionized the treatment of this highly frustrating problem. In the present study, a total of 40 leprosy patients were included. These ulcers were managed using different types of local superficial flaps (advancement, rotation, transposition and first toe web flap). Majority of ulcers healed within 4 weeks and patients were discharged within 6-8 weeks postoperatively. Patients were followed up for a period of 6 months to 3 years. Ulcers recurred in only 25% of all the ulcers operated upon and we observed that management of plantar ulcers by using appropriate local superficial plantar flaps is a viable option and worth trying in view of low incidence of recurrence and relatively shorter duration of hospital stay.

## Cirurgia/ulcera

Malaviya GN. Closure of simple heel ulcers by skin stretching. [Indian J Lepr](#) 2005; 77(3):255-65.

A majority of heel ulcers, at least to begin with, extend to dermis or to the fat pad in its superficial part and an appropriate skin closure can heal these ulcers as most of the padding is in tact. Since the skin is adherent to the deeper structures with fibrous bands it has to be stretched or undermined (by cutting the fibrous bands) to close the wound without tension. 17 feet in 11 patients (10 males; one female) in the 12-54 year age-group were operated upon and followed up. Because skin is adherent to deeper tissues by fibrous septae, stretching of skin was planned to mobilize it for a tension-free closure. Of the 17 feet, 13 could be re-examined after 30 months or more. Most of the minor recurrences were seen in the first 6 months after surgery. Major recurrences were seen in 2 feet (one case). The suture line did not show hyperkeratosis and the scar merged well into the surrounding skin after one year. Available data suggest that simple heel ulcers can be made to heal with a good scar by skin-stretching and suture, and, by radiography of the foot, it is worth separating those cases in which ulcer is not extending deep involving calcaneum. The size of the ulcer in heel is important for the success of the operation. The procedure is not intended for big wounds (>15 mm in width).

## Clinica

Armour KS, Scolyer RA, Barnetson RS. Borderline lepromatous leprosy presenting as a single cutaneous plaque. [Australas J Dermatol](#) 2005; 46(3):181-3.

A 38-year-old Indonesian man presented with a single anaesthetic plaque on his right forearm and no other sensory changes. His clinical presentation was consistent with tuberculoid leprosy, but histopathology of a skin biopsy from the lesion showed borderline lepromatous disease. The patient was treated with multidrug therapy for multibacillary disease. Seven months after initiation of treatment his solitary skin anaesthetic plaque became tumid, and he developed multiple small plaques on his arms, legs and face, without evident neuritis. He was clearly in a reversal reaction (type 1), which slowly resolved with treatment of prednisone.

## Clinica

Gupta R, Singal A, Pandhi D. Genital involvement and type I reaction in childhood leprosy. [Lepr Rev](#) 2005; 6(3):253-7.

We describe the case of a 4-year-old boy, with a positive family history of multibacillary leprosy (borderline-borderline) in his 12-year-old sister. The patient was diagnosed to have borderline lepromatous (BL) leprosy, BI of 4 + and had two erythematous, infiltrated plaques over the scrotum. He developed type reaction, 3 months following initiation of multibacillary multidrug therapy (MB-MDT) and responded favourably to systemic corticosteroids.



## Clinica

Kar BR, Job CK. Reversal reaction and Mitsuda conversion in polar lepromatous leprosy: a case report. [Lepr Rev](#) 2005; 76(3):258-62.

A 22-year-old male polar lepromatous leprosy patient who became Mitsuda positive after 36 months of multidrug therapy (MDT) is reported. Lepromatous leprosy (LL) is a state of specific immunosuppression and is invariably irreversible. The finding of Mitsuda positivity in histopathologically proven polar lepromatous leprosy is extremely uncommon, and conversion of lepromin status following MDT has not so far been reported. This case reports confirms the observations made by Waters et al. regarding lepromin conversion in lepromatous patients.

## Clinica

Sehgal VN. Lucio's phenomenon/erythema necroticans. [Int J Dermatol](#) 2005; 44(7):602-5.

Lucio's phenomenon/erythema necroticans is a peculiar reaction pattern that occurs in untreated pure primitive diffuse lepromatous leprosy (PPDL) and/or relapsing leprosy recognized as spotted leprosy of Lucio. The small number of reported cases in the world literature suggests that it is fairly uncommon. Its clinical features are fairly characteristic and consist of extensive, bizarre, painful ulcerations of the skin, with constitutional symptoms being conspicuous by their absence. The clinical diagnosis is confirmed by microscopic pathology marked by proliferation and mobilization of polyblasts and histiocytes, dilatation, endothelial proliferation, luminal occlusion, and thrombosis of the superficial and mid-dermal blood vessels and demonstration of acid-fast bacilli in the blood vessel walls. Its precise pathogenesis is still unclear, but is believed to occur either through the usual or the alternate pathway of complement activation in the natural history of erythema nodosum leprosum. The clinical and immunological features of reactions in leprosy, including erythema nodosum leprosum, are well known and have been critically evaluated elsewhere.

## Clinica/epidemiologia

Ferreira IN, Alvarez RRA. Hanseníase em menores de quinze anos no município de Paracatu, MG (1994 a 2001) / Leprosy in patients under fifteen years of age in the city of Paracatu-MG (1994 to 2001). [Rev. bras. epidemiol](#) 2005; 8(1):41-49.

O município de Paracatu-MG é considerado prioritário para ações de controle da hanseníase devido às suas taxas de detecção e prevalência desta nosologia, sobretudo em menores de quinze anos. Nos anos de 1998 e 1999, realizou-se um trabalho de esclarecimento sobre sinais e sintomas da doença para a população de cerca de oito mil escolares, o que contribuiu para o incremento da taxa de detecção da doença em menores de quinze anos, sendo o município classificado como hiperendêmico entre os anos de 1997 e 2001. Realizou-se também um trabalho de desenho descritivo de quarenta e cinco pacientes diagnosticados e tratados no município de Paracatu entre 1994 e 2001. Cinquenta e três por cento dos diagnósticos foram em crianças do sexo masculino, 75,5 por cento dos casos situavam entre dez e quatorze anos de idade e a escolaridade da população deste estudo está defasada em relação à idade, sendo que 84 por cento da clientela morava em zona urbana. Todos os inscritos (100 por cento) foram casos novos, 56 por cento de forma multibacilar, forma clínica Dimorfa, e 44 por cento de formas paucibacilares, como a forma clínica indeterminada (30,8 por cento) e a Tuberculóide (13,2 por cento). Todos foram tratados segundo o esquema padrão, com 100 por cento de cura. Vinte e quatro por cento dos doentes apresentaram reações no diagnóstico e durante o tratamento, e 9 por cento apresentaram reações no pós-alta. Vinte e dois por cento dos doentes apresentavam algum grau de incapacidade no diagnóstico e 13 por cento apresentavam algum grau de incapacidade na alta (índice considerado alto). Verificou-se que 62 por cento dos pacientes tinham contatos intradomiciliares portadores de hanseníase, sendo que somente 15,5 por cento destes contatos foram verificadas as duas cicatrizes da vacina BCG. A hanseníase é um sério problema de saúde pública no município estudado, e o trabalho realizado com escolares foi fundamental para o aumento da detecção dos casos.(AU).

## Clinica/epidemiologia/aspectos psicossociais

John AS, Rao OS, Kundu R, Raju MS. Leprosy among adolescents in Kolkata, India. [Indian J Lepr](#) 2005; 77(3):247-53.

Leprosy, manifesting during adolescence when significant physical and emotional changes are taking place, poses further stress and strain both on the individual and on the family. Based on hospital records, focus group discussions and in-depth interviews, data on 258 adolescent leprosy patients seen at a leprosy referral hospital in Kolkata, India, are presented. The male-female sex ratio was 1.93:1, 56.6% were multibacillary patients and 13.2% had grade 2 disability. At the time of final follow up, 10% of PB and 33% of MB patients had already discontinued treatment. The commonest complication was reaction (14.5%). Adolescents were still dependent on their parents for health matters. Data obtained from questionnaires confirmed the role of social stigma in hiding, delay in starting of MDT and defaulting. Frequent hospital admissions resulted in loss of jobs and disruption of studies and caused psychological disturbances. It is critical to identify and treat adolescent leprosy on a priority basis. Health education and counselling programmes must be more focused and acceptable. Further research is necessary.

## Clinica/histopatologia

Wang CY, Huang PH, Cheng YW, Ho JC, Chen WC. Leprosy in the Department of Dermatology, Chang Gung Memorial Hospital at Kaohsiung from 1988 to 2004: a clinical and histopathologic study of 13 cases. *Chang Gung Med J* 2005; 28(10):716-23.

**BACKGROUND:** Leprosy has long been in Taiwan, but it has never been eradicated. Incidental cases are easily overlooked nowadays because most younger dermatologists are unfamiliar with this disease. **METHODS:** We review and analyze 13 cases diagnosed as leprosy at the Department of Dermatology, Chang Gung Memorial Hospital at Kaohsiung from 1988 to 2004, all of which were histopathologically proven. **RESULTS:** The ages of the 13 recruited patients ranged from 31 to 73 (mean, 58.6) years, without a gender preference (male: female, 7:6). Two male patients were under 40 years old; one was a foreign worker from Thailand and the other was a local person in Penghu working as the chief officer on a fishing boat. The most-common clinical subtype was lepromatous leprosy (5/13), followed by borderline lepromatous leprosy, borderline tuberculoid leprosy, and tuberculoid leprosy (each 2/13), and then borderline leprosy and indeterminate leprosy (each 1/13). The initial clinical impression before the histopathological diagnosis included granuloma annulare, generalized eczema, lymphoma, syphilis, papular urticaria, cutaneous tuberculous infection, Sweet's syndrome, erythema annulare centrifugum, and hematoma. Most of these patients only received irregular treatment after the diagnosis was made and were soon lost to follow-up. **CONCLUSIONS:** With increasing numbers of foreign workers and immigrants living in Taiwan in recent years, leprosy seems to have become a challenging diagnosis for younger dermatologists. Dermatologists should keep this ancient disease in mind and not overlook it. Because of the necessity of prolonged medication, complete treatment and long-term follow-up of leprosy cases will remain a major problem in public health.

## Clinica/histopatologia/bactrioscopia

Shetty VP, Wakade AV, Ghate SD, Pai VV, Ganapati RR, Antia NH. Clinical, histopathological and bacteriological study of 52 referral MB cases relapsing after MDT. [Lepr Rev](#) 2005; 76(3):241-52.

Fifty-two BB-LL relapse cases referred to our centre during 1997-2003 were investigated in detail. Twenty-four cases had been treated with extended MB-MDT [until smear negativity (NON-FDT)]. The remaining 28 cases (54%) had received one of the fixed duration regimens (FDT), of whom 11 had 24 months and 6 had 12 months of WHO MB-MDT. Eleven cases had received rifampicin/ofloxacin (RO) treatment. Follow-up slit skin smear reports were available for 41 cases, all but three cases had been smear negative at some point after release from treatment. None of the cases showed any clinical or bacteriological evidence of upgrading, i.e. LL to BT where as downgrading BB to BL occurred in five cases. The duration between cessation of treatment and reappearance of lesions (DCTR) varied from 2 to 15 years. The mean DCTR was longest (9.4 years) for the NON-FDT and 24 months MB-MDT cases. The mean DCTR was significantly lower in the 12 months MB-MDT and RO treated cases (6.8 and 6.2 years, respectively). Four of RO treated cases and four cases with multiple episodes of reaction had DCTR less than 5 years. Inadequate treatment/poor killing of *Mycobacterium leprae* results in early onset relapse, whereas 'persisting' or 'drug resistant mutants' contribute to late onset relapse.

## Clinica/imunologia

Roberts LJ, Huffam SE, Walton SF, Currie BJ. Crusted scabies: clinical and immunological findings in seventy-eight patients and a review of the literature. [J Infect](#) 2005; 50(5):375-81.

**OBJECTIVES:** To describe the clinical and immunological features of crusted scabies in a prospectively ascertained cohort of 78 patients. **METHODS:** All patients requiring inpatient treatment for crusted scabies in the 'top end' of the northern territory of Australia over a 10 year period were prospectively identified. Demographics, risk factors, and immunological parameters were retrospectively compiled from their medical records and pathology databases. **RESULTS:** More than half the patients with crusted scabies had identifiable immunosuppressive risk factors. Eosinophilia and elevated IgE levels occurred in 58% and 96% of patients, respectively, with median IgE levels 17 times the upper limit of normal. Seventeen percent had a history of leprosy but 42% had no identifiable risk factors. There was a decrease in mortality after the introduction of a treatment protocol consisting of multiple doses of ivermectin combined with topical scabicides and keratolytic therapy. **CONCLUSIONS:** Crusted scabies often occurs in patients with identifiable immunosuppressive risk factors. In patients without such risk factors, it is possible that the crusted response to infection results from a tendency to preferentially mount a Th2 response. The treatment regime described was associated with a reduction in mortality. This is the largest reported case series of crusted scabies.

## Clinica/imunologia

Sarazin E, Nacher M, Toure Y, Clyti E, El Guedj M, Aznar C, Vaz T, Sainte-Marie D, Sobesky M, Carme B, Couppié P. [Dermatologic manifestations associated with immune reconstitution syndrome in HIV+ patients starting HAART: a retrospective study in French Guiana] [Bull Soc Pathol Exot](#);98(3):187-92, 2005 Sep.

Immune reconstitution syndrome (IRIS) is an unusual inflammatory reaction to an opportunistic infection in an HIV-positive patient. This syndrome occurs when immunity is restored in the first months of an effective highly active antiretroviral treatment (HAART). First, we described all patients with a cutaneous form of IRIS. Then, between 1992 and 2004 we conducted a retrospective cohort study comparing Herpes Zoster and Herpes Simplex infections among untreated patients, patients treated by HAART for  $\leq$  six months, and patients treated for  $>$  six months. We observed three cases of atypical leprosy and three original observations: two of these were fistulisation of lymph node histoplasmosis and tuberculosis, the third one reports the recurrence of a treated cutaneous leishmaniasis. Multivariate analysis showed that, after controlling for age, sex and CD4 counts, patients receiving HAART for  $\leq$  six months were more likely to develop Herpes Zoster or herpes simplex infections ( $p < 0.005$ ). Herpes Simplex and Herpes Zoster infections are the two most frequent dermatological manifestations in our tropical setting. Although mycobacterial infections are more rarely observed than in visceral IRIS, the increased incidence of leprosy may be quite significant when the availability of HAART spreads to developing countries.

Abscesso/ET



## Clinica/imunopatologia

Montagna NA, de Oliveira ML, Mandarim-de-Lacerda CA, Chimelli L. Leprosy: contribution of mast cells to epineurial collagenization. [Clin Neuropathol](#) 2005; 24(6):284-90.

**BACKGROUND:** Leprosy, a disease caused by *Mycobacterium leprae*, is an important health problem worldwide. It is responsible for an irreversible nerve damage in which fibrosis plays an important role. The existence of an interaction between mast cells and different fibrotic conditions has long been observed. Tryptase, the most abundant protein product of human mast cells, has been shown to be mitogenic for fibroblasts and to increase type I collagen production. **PATIENTS AND METHODS:** In order to explore the possible relationship between tryptase-rich mast cells and nerve fibrosis in leprosy, we studied 24 sural nerve biopsies of patients with leprosy neuropathy. Mast cells stained with mouse antihuman mast cell antitryptase clone AA1 as well as fibrosis, were quantitatively estimated in both epi- and endoneurial compartments. **RESULTS:** There was a remarkable association between collagen increase and tryptase-rich mast cell density in the epineurium but not in the endoneurium of leprosy nerves. **CONCLUSION:** Since the epineurium in leprosy is type I collagen rich, the present findings support a tryptase-rich mast cell contribution to epineurial collagenization in leprosy through their tryptase secretion.

## Clinica/patologia/tratamento

Agrawal A, Pandit L, Dalal M, Shetty JP. Neurological manifestations of Hansen's disease and their management. [Clin Neurol Neurosurg](#) 2005; 107(6):445-54.

Hansen's disease is almost eliminated from developed countries but in developing countries of Africa, Asia and Latin America leprosy is still considered to be a public health problem. *Mycobacterium leprae* have the affinity for peripheral nerves and neuropathy is a cardinal manifestation of the disease. The nerve damage affects sensory, motor, and autonomic fibers resulting in the physical impairments and limitation of physical activities and social participation. Leprosy is a curable disease and treatment provided in the early stages will avert the disabilities. Approach to the neuritic leprosy depends on its clinical characteristics, nerve biopsy, and histological appearance of dermatological and neurological lesions. In this article we review the literature and discuss the pathology, clinical features, diagnosis and management of neurological manifestations of leprosy.

## Clinica/terapêutica

Vaquero N, Soto I. Tratamiento de los estados reaccionales de la lepra / Treatment of leprosy reactions. [Rev. argent. dermatol](#) 2005; 86(2):92-100.

Los estados reaccionales de la lepra son episodios agudos o que se producen en el transcurso de la evolución crónica de la enfermedad, como resultado de la activación brusca de la inmunidad celular (reacción tipo 1), o de una inapropiada estimulación de la inmunidad humoral (reacción tipo 2). Su tratamiento integral comprende, además de la terapia medicamentosa, medidas fisioterápicas adecuadas para evitar futuras secuelas discapacitantes: técnicas sencillas de inmovilización con férulas, ejercicios terapéuticos, parafinoterapia, electroestimulación. En la reacción tipo 1, muy frecuentemente acompañada de neuritis aguda, es de elección la corticoterapia junto al manejo del daño neural. En las reacciones tipo 2, que comprenden una amplia gama de manifestaciones clínicas de distinta severidad tanto en piel como en otros órganos y sistemas, las drogas más eficaces siguen siendo la talidomida, los corticoides y la clofazimina. Recientes publicaciones proponen la utilización de otras drogas como la pentoxifilina, zafirlukaste y tenidap, con escasa experiencia en lepra, en nuestro medio. En los episodios reaccionales crónicos de ambos tipos, y con el objetivo de disminuir la dosis y dependencia a los corticoides, utilizamos habitualmente la clofazimina. En caso de falta de respuesta se recomiendan los inmunosupresores azatioprina y ciclosporina, con resultados variables(AU).

## Clinica/terapêutica/reações adversas

Tiscornia JE, Aletti M, Luna R, Pellerano G, Kien MC, Chouela E. Trasplante renal y lepra / Renal transplantation and leprosy. [Dermatol. argent](#) 2005; 11(1):48-52.

Presentamos un paciente varon de 62 años que diez años despues de ser sometido a un trasplante renal contrajo lepra dimorfa lepromatosa. A los ocho meses de recibir la terapeutica multidroga de la Organizacion Mundial de la Salud desarrollo un cuadro de deterioro agudo de la funcion del riñon trasplantado relacionado con la administracion de rifampicina. El paciente evoluciono en forma favorable con la suspension del farmaco y continuo tratamiento para su enfermedad de Hansen con un esquema alternativo con buena evolucion. Destacamos la dificultad terapeutica del paciente trasplantado con lepra y la necesidad de un estricto control nefrologico durante el tratamiento. El compromiso renal por rifampicina es raro; su incidencia aumenta cuando el farmaco es administrado en forma intermitente (AU).

## Controle

Ishida Y, Hikita K. [JICA Leprosy Control and Basic Health Services Project in Myanmar]. [Nihon Hansenbyo Gakkai Zasshi](#) 2005; 74(3):185-90.

Japan International Cooperation Agency (JICA) implemented a 5-year long bilateral technical cooperation project, [quot ]Leprosy Control and Basic Health Services Project[quot ] in Myanmar. The project was implemented by National Leprosy Control Program, Department of Health with close technical collaboration of JICA experts mainly from International Medical Center of Japan (IMCJ) and National Sanatoriums of leprosy in Japan. It accelerated to achieve the elimination of leprosy at national level, which was declared in January 2003, and at sub-national level onward. It also developed the appropriate technologies for prevention of disability and prevention of worsening of disability (POD/POWD), which were introduced in 9 townships as a pilot service program. The Government stratified the POD/POWD services as a national program since 2005 by taking up the former pilot area to start with. The project also strengthened the function of referral system of leprosy control (Diagnosis and treatment), POD/POWD and physical rehabilitation. Beside leprosy, the project conducted a series of refresher trainings for primary health care givers, Basic Health Service Staff (BHS), of project areas (48 townships) to improve the services on tuberculosis, Malaria, Leprosy, Trachoma and HIV/AIDS for 3 years (2001-2003), which was evaluated in 2004. It contributed to improve the services at township level hospitals in procurement of audio-visual equipments and in conducting microscope training on leprosy, Malaria and tuberculosis at project areas.

## Controle

Pandey A, Patel R. Integration of leprosy control into general health care system: observations from a state with low endemicity. [Indian J Lepr](#) 2005; 77(3):229-38.

The study was undertaken as part of operational research to assess the level of integration of leprosy services into general health care system in 24 low or moderately endemic states/union territories by the Ministry of Health and Family Welfare, Government of India. Himachal Pradesh was one of the nine randomly selected states for the study. Out of the 12 districts in the State, 2 were selected randomly for the study. In each of the selected districts, 8 health facilities (that included a district hospital, an urban hospital/urban health centre, an Employees' State Insurance Hospital, a community health centre and a primary health centre) and 9 sub-centres were surveyed. Selection was done randomly at each stage. Data were collected on training in leprosy of general health care staff, availability of drugs for MDT in the system and maintenance of leprosy records by the staff of the system. The study showed mixed results. About half (53.2%) of the existing medical officers, 83.9% of health supervisors and 96.8% of multi-purpose workers were trained in leprosy. But only 31.3% of medical officers were able to diagnose leprosy and most of them were relying on vertical staff and skin specialists for confirmation. MDT services were provided by 20% of rural and 66.7% of urban health facilities that were acting as treatment centres. None of the health facilities had 3 months' stock of all types of blister packs, as per the guidelines of the Government of India. None of the sub-centres was involved in MDT delivery. However, reporting as per SIS formats was universal. The study emphasized the need for training and better management of MDT drug stock.

## Educação/aspectos sociais

White C. Explaining a complex disease process: talking to patients about Hansen's disease (leprosy) in Brazil. [Med Anthropol Q](#) 2005; 19(3):310-30.

Patient explanatory models of Hansen's disease (leprosy) in Rio de Janeiro, Brazil, tend to be syntheses of folk models of illness and health, biomedical models to which patients are exposed at different stages in the treatment process, and individual patient experiences of illness. The sensitive presentation of biomedical information about Hansen's disease to patients has the potential to increase adherence to treatment programs and increase patient confidence in the biomedical system. Conversely, withholding or poor presentation of biomedical information can create misunderstanding and confusion for patients. In this article, I explore the ways in which people who are affected by Hansen's disease in Rio de Janeiro learn about different aspects of their illness and its treatment from health care professionals.

## Educação/relação médico-paciente

White C. Explaining a complex disease process: talking to patients about Hansen's disease (leprosy) in Brazil. [Med Anthropol Q](#) 2005; 19(3):310-30.

Patient explanatory models of Hansen's disease (leprosy) in Rio de Janeiro, Brazil, tend to be syntheses of folk models of illness and health, biomedical models to which patients are exposed at different stages in the treatment process, and individual patient experiences of illness. The sensitive presentation of biomedical information about Hansen's disease to patients has the potential to increase adherence to treatment programs and increase patient confidence in the biomedical system. Conversely, withholding or poor presentation of biomedical information can create misunderstanding and confusion for patients. In this article, I explore the ways in which people who are affected by Hansen's disease in Rio de Janeiro learn about different aspects of their illness and its treatment from health care professionals.



## Epidemiologia

Kumar A, Yadav VS, Girdhar A, Girdhar BK. Leprosy situation in the slums of Agra City-- epidemiological findings. [Indian J Lepr](#) 2005; 77(3):239-45.

The present article is the result of a study of the leprosy caseload in Agra City and is based on a house-to-house survey conducted during April-July 2003 in 5 areas. During the survey 198,150 persons were examined, and 287 cases were detected, giving a prevalence rate of 14.5/10,000. A majority of them (92%) were new cases, detected and diagnosed for the first time. The patient load was found to be unevenly distributed with comparatively more number of patients in areas such as Jamuna Kinara, Shah Ganj and Lohamandi. Among the 264 newly detected cases, 14.8% were of MB type. Overall deformity of grade  $\geq 2$  was seen in 2.8% of patients--0.4% in PB and significantly high at 18% in MB leprosy. The observations reveal that leprosy is endemic in slum areas of Agra City.

## Epidemiologia

Withington SG, Maksuda AN, Hamid Salim MA, Ahmed JU. Current status of leprosy and leprosy control in Bangladesh: an ongoing collaboration. [Lepr Rev](#) 2005; 76(3):209-19.

Elimination of leprosy as a public health problem, defined by a registered prevalence of less than one case per 10,000 population, was achieved by Bangladesh in 1998, and steady reduction in prevalence is ongoing. It is less certain whether a sustained reduction in case detection is occurring, with little overall change in some longstanding programme areas, though the overall annual new case detection rate has fallen by over one-third between 1996 and 2004, from 9.8 to 6.1 per 100,000. Concerns about 'hidden' cases have been raised in Bangladesh as elsewhere, though the National Leprosy Elimination Campaign of 1999 detected relatively fewer new cases than in other countries, and mainly in low endemic areas. Investigation into the correct diagnosis of leprosy and recording and reporting practices has not suggested high levels of over-diagnosis or 'over-registration'. Both before and since achievement of the elimination target at national level, the collaboration of Non-Governmental Organizations with the national Leprosy Elimination Program has been considerable. NGOs now support ongoing leprosy control efforts in rural and urban populations, moderate to high endemic for leprosy, amounting to 50% of the entire population, and NGO staff look after 75% of all new cases in Bangladesh. This close collaboration has highlighted the potential for large-scale partnership in disease control, and has expanded to extensive partnership in tuberculosis control, which will hopefully enhance cost-effectiveness and quality of both programmes. Further challenges remain in the area of urban leprosy control, where leprosy case finding represents 30% of the whole country, but public health infrastructure and community organization is weakest. Sustaining of leprosy services in the long term is a significant concern, and new modes of collaboration, with a more technical, supportive role for NGOs in some areas is being piloted.

## Epidemiologia/clinica

Gill AL, Bell DR, Gill GV, Wyatt GB, Beeching NJ. Leprosy in Britain: 50 years experience in Liverpool. [QJM](#) 2005; 98(7):505-11.

**BACKGROUND:** Leprosy is a chronic infection that presents with varying dermal and neurological symptoms, and which can lead to extensive disability and morbidity, often with accompanying social stigma. **AIM:** To review the patients presenting to the Liverpool School of Tropical Medicine (LSTM) between 1946 and 2003, looking specifically at country of birth and of infection, details of clinical presentation, diagnosis, management and reactions. **DESIGN:** Retrospective record review. **METHODS:** We retrieved all available clinical records for patients seen between 1946 and 2003 (n = 50), consisting of letters, hospital and LSTM casenotes, and some radiographs and photographs. Any history of tuberculosis or diabetes was recorded. **RESULTS:** Most patients (64%) were born in the Indian subcontinent, and most were thought to have contracted the disease there (62%). Features at presentation included anaesthetic skin lesions in 19 (36%), hypopigmentation in 15 (30%), and peripheral nerve enlargement in 25 (50%). Diagnoses were made by a combination of clinical data and biopsy (60%), and slit skin smears were positive for acid-fast bacilli in 61% of multibacillary patients. Initial presentation was with a leprosy reaction in five cases (10%), and reactions were documented in 42% of all patients. Treatments were varied, progressing from traditional Eastern medicine to the WHO-approved multidrug therapy in use today, with prophylaxis for children and close contacts. **DISCUSSION:** Leprosy remains an important diagnosis to consider in patients with a history of work or travel in the tropics, and is a diagnosis with far-reaching medical, social and emotional consequences.

## Epidemiologia/controlle

Nagao E. [Survey on the present conditions of the residents regarding aging, aftereffects and subsequent complication]. [Nihon Hansenbyo Gakkai Zasshi](#) 2005; 74(3):211-9.

A survey of present conditions of the residents regarding aging, aftereffects and subsequent complication was conducted and its data were analyzed in the National Leprosarium Osima Seisho-en; located on an isolated island of the Seto Inland Sea. The results showed that they have become older with a various type of disease and most of them suffered from aftereffects caused leprosy, although after therapy. This survey also suggests that future problems in the management of our leprosarium will no doubt be to cope with the aging and to reducing our scale.

## Epidemiologia/controlle

Sato K. [Effect of physician shortage on today's Hansen's disease management]. [Nihon Hansenbyo Gakkai Zasshi](#) 2005; 74(3):221-5.

In recent years, the total patient population of Hansen's disease has been rapid declining throughout Japan by as many as 200 - 250 each year. This decline is due to the aging of existing patients, and scarcity of new cases. Less patients are a welcome phenomenon. However, existing treatment facilities are now confronted with prob.

## Epidemiologia/controlle

Withington SG, Maksuda AN, Hamid SMA, Ahmed JU. Current status of leprosy and leprosy control in Bangladesh: an ongoing collaboration. [Lepr Rev](#) 2005; 76(3):209-19.

Elimination of leprosy as a public health problem, defined by a registered prevalence of less than one case per 10,000 population, was achieved by Bangladesh in 1998, and steady reduction in prevalence is ongoing. It is less certain whether a sustained reduction in case detection is occurring, with little overall change in some longstanding programme areas, though the overall annual new case detection rate has fallen by over one-third between 1996 and 2004, from 9.8 to 6.1 per 100,000. Concerns about 'hidden' cases have been raised in Bangladesh as elsewhere, though the National Leprosy Elimination Campaign of 1999 detected relatively fewer new cases than in other countries, and mainly in low endemic areas. Investigation into the correct diagnosis of leprosy and recording and reporting practices has not suggested high levels of over-diagnosis or 'over-registration'. Both before and since achievement of the elimination target at national level, the collaboration of Non-Governmental Organizations with the national Leprosy Elimination Program has been considerable. NGOs now support ongoing leprosy control efforts in rural and urban populations, moderate to high endemic for leprosy, amounting to 50% of the entire population, and NGO staff look after 75% of all new cases in Bangladesh. This close collaboration has highlighted the potential for large-scale partnership in disease control, and has expanded to extensive partnership in tuberculosis control, which will hopefully enhance cost-effectiveness and quality of both programmes. Further challenges remain in the area of urban leprosy control, where leprosy case finding represents 30% of the whole country, but public health infrastructure and community organization is weakest. Sustaining of leprosy services in the long term is a significant concern, and new modes of collaboration, with a more technical, supportive role for NGOs in some areas is being piloted.

lems. The most serious problem is shortage of treating physicians. The causes of the shortage are (1) the aging of the existing patient population that creates mounting need for medical-surgical care and (2) the nation-wide shortage of physician in national sanatoria all over Japan. Let me present a sketch of the current situation at Amamiwakouen Hospital as an illustration. Amamiwakouen is a government-run sanatorium. It is responsible to take care of inpatient as well as out patients. Currently, there are 70 long term inpatients, who are handicapped by Hansen's disease sequela of various degrees. 11 minimally former inpatients are followed at the outpatient clinic. The clinic is also open to all community citizens. The number of annual clinic visitors averages 6,500 - 7,000. They come with wide range of problems requiring a dermatologist. While the total number of full-time staff is 100, only two are licensed physicians at present. This is indeed a disastrous situation. Therefore a number of contract physicians are recruited from nearby medical institutes to meet the demand.

## Epidemiologia/terapêutica

Ishii N, Mori S. [Leprosy situation in Myanmar before and after multidrug therapy]. [Nihon Hansenbyo Gakkai Zasshi](#) 2005; 74(3):177-80.

We introduced history of leprosy in Myanmar based on the book of Myanmar Academy of Medical Science published entitled [quot ]CONQUEST OF SCOURGES IN MYANMAR (Compiled and Edited by Ko Ko, Kyaw and U Thaung) at 2002. [quot ]Leprosy Elimination Programme in Myanmar (Kyaw Lwin and Kyaw Nyunt Stein)[quot ] was appeared at chapter III in it. After dapsone treatment appeared, leprosy control program has started. Health system and service were developed and leprosy control program was also included in them. The integration of the elimination activities into basic health workers, such as midwives and health volunteers, has enabled the participation of a wide range of people in the community. After 1990s, multidrug therapy (MDT) was covered whole area of Myanmar, and task force for leprosy elimination was formed at State/Division, District and Township level. Finally Myanmar achieved the elimination of leprosy in January in 2003.

## Estigma

Chaturvedi SK, Singh G, Gupta N. Stigma experience in skin disorders: an Indian perspective. [Dermatol Clin](#) 2005; 23(4):635-42.

Dermatologic disorders generally have a major impact on patients' daily activities, psychologic and emotional state, and social relationships. The intensity of impact of skin disease on an individual person is extremely variable, however, and depends on natural history of the disorder; the patient's demographic characteristics, personality, character, and value; the patient's life situation; and the attitudes of society. Social stigma toward dermatologic disorders in the Indian society is quite widespread, especially toward leprosy. Dermatologists are expected to consider quality of life issues along with social aspects, nature of disorder, efficacy, and tolerability of various therapeutic options to optimize relief and comfort to their patient.



## Genética/epidemiología/demografía

Bakker MI, May L, Hatta M, Kwenang A, Klatser PR, Oskam L, Houwing-Duistermaat JJ. Genetic, household and spatial clustering of leprosy on an island in Indonesia: a population-based study. [BMC Med Genet](#) 2005; 6:40.

**ABSTRACT :** **BACKGROUND :** It is generally accepted that genetic factors play a role in susceptibility to both leprosy per se and leprosy type, but only few studies have tempted to quantify this. Estimating the contribution of genetic factors to clustering of leprosy within families is difficult since these persons often share the same environment. The first aim of this study was to test which correlation structure (genetic, household or spatial) gives the best explanation for the distribution of leprosy patients and seropositive persons and second to quantify the role of genetic factors in the occurrence of leprosy and seropositivity. **METHODS :** The three correlation structures were proposed for population data (n = 560), collected on a geographically isolated island highly endemic for leprosy, to explain the distribution of leprosy per se, leprosy type and persons harbouring *Mycobacterium leprae*-specific antibodies. Heritability estimates and risk ratios for siblings were calculated to quantify the genetic effect. Leprosy was clinically diagnosed and specific anti-M. *leprae* antibodies were measured using ELISA. **RESULTS :** For leprosy per se in the total population the genetic correlation structure fitted best. In the population with relative stable household status (persons under 21 years and above 39 years) all structures were significant. For multibacillary leprosy (MB) genetic factors seemed more important than for paucibacillary leprosy. Seropositivity could be explained best by the spatial model, but the genetic model was also significant. Heritability was 57% for leprosy per se and 31% for seropositivity. **CONCLUSION :** Genetic factors seem to play an important role in the clustering of patients with a more advanced form of leprosy, and they could explain more than half of the total phenotypic variance.

## Genética/epidemiología

Ranque B, Alcais A, Thuc NV, Woynard S, Thai VH, Huong NT, Ba NN, Khoa PX, Schurr E, Abel L. A recessive major gene controls the Mitsuda reaction in a region endemic for leprosy. [J Infect Dis](#) 2005; 192(8):1475-82.

**BACKGROUND:** Leprosy is a chronic infectious disease caused by *Mycobacterium leprae*. The Mitsuda reaction is a delayed granulomatous skin reaction elicited by intradermal injection of heat-killed *M. leprae*. Interestingly, results of the Mitsuda test are positive in the majority of individuals, even in areas not endemic for *M. leprae*. Like leprosy, the Mitsuda reaction is thought to be genetically controlled, but its mode of inheritance is unknown, although the role of the NRAMP1 gene has previously been reported. **METHODS:** We conducted a segregation analysis of quantitative Mitsuda reactivity in 168 Vietnamese nuclear families ascertained through patients with leprosy. **RESULTS:** We found strong evidence ( $P < 10^{-9}$ ) for a major gene controlling the Mitsuda reaction independently of leprosy clinical status. Subsequent linkage analysis showed that this major gene was distinct from NRAMP1. Under the major-gene model, approximately 12% of individuals are homozygous for the recessive predisposing allele and are predicted to display high levels of Mitsuda reactivity (mean, approximately 10 mm, versus 5 mm in other individuals). **CONCLUSION:** We provide evidence that the Mitsuda reaction is controlled by a major gene. Our study paves the way for the identification of this gene and should provide novel insight into the mechanisms involved in granuloma formation, especially in *M. leprae* infection.

## Hansniase experimental/imunopatologia

López-Hurtado M, Flores-Medina S, Díaz-García FJ, Guerra-Infante FM. Partial characterization of phagocytic activity in neutrophils of the nine-banded armadillo *Dasypus novemcinctus*. [Vet Immunol Immunopathol](#) 2005; 106(3-4):269-75.

Though the armadillo is important as a research model in leprosy studies, the activity of armadillo's neutrophils is an aspect of little research. The aim of this study was carried out to partially characterize the chemotaxis, endocytosis and bacteriocidal ability of the neutrophils found in the nine-banded armadillo (*Dasypus novemcinctus*). Results showed that the chemotactic activity of the neutrophils, evaluated by the movement of the neutrophils through a nitrocellulose membrane (5 microm) in response to a chemo-attractive substance, was greater towards the armadillo serum (5.16+/-1.35 migration index,  $p < 0.05$ ) than towards the formil methionyl leucil phenylalanine (fMLP, 1.43+/-0.18 migration index) or human serum (0.56+/-0.18 migration index). Regarding endocytic capacity of the neutrophils and the monocytes against *Escherichia coli* was evaluated by a flow cytometry and using opsonized and non-opsonized *E. coli*-FITC at the following incubation times: 5, 10, 20, 30 and 60 min. The largest percentage of endocytosis by the neutrophils was 92.32+/-0.12% with opsonized bacteria and 77.73+/-14.33% with non-opsonized bacteria at 10 min incubation time, while the largest percentage of endocytosis by monocytes was 89.94+/-1.40% with opsonized bacteria and 73.07+/-15.6% with non-opsonized bacteria at 20 min incubation time. Evaluation of the bacteriocidal capacity of neutrophils using the methyl-thiazol-tetrazolium salts (MTT) reduction color-measurement assay showed an 89.0+/-10% mortality rate of non-opsonized *E. coli* and 89.0+10% of opsonized *E. coli*. In conclusion, the armadillo neutrophils show a good phagocytosis and bacteriocidal activity; however, a deficiency in the migration towards the fMLP was observed. This deficiency could be a cause so that the armadillo neutrophils do not respond quickly to invading microorganism.

## Hanseníase experimental/epidemiologia

Truman R. Leprosy in wild armadillos. [Lepr Rev](#) 2005; 76(3):198-208.

Wild nine-banded armadillos (*Dasypus novemcinctus*) in the south central United States are highly endemic natural hosts of *Mycobacterium leprae*. Surveys conducted over the last 30 years on more than 5000 animals confirm that the infection is present among armadillos in Arkansas, Louisiana, Mississippi and Texas. Highest prevalence rates are found among the animals in low-lying alluvial and coastal areas, primarily in Louisiana and Texas. Both animal density and local factors may contribute to the detectability of armadillo leprosy in those regions. Little evidence for *M. leprae* infection is found among armadillos elsewhere in the US range, and only a few reports relate finding the infection among animals in Central or South America. However, the issue has received only scant attention in other countries. Armadillos only recently expanded their range into the US, and leprosy was present in Texas and Louisiana prior to the arrival of armadillos. The ecological relationship between humans and armadillos with *M. leprae* in this region remains unclear. However, infected armadillos constitute a large reservoir of *M. leprae* and they may be a source of infection for some humans in this country, and perhaps in other locations across the animal's range.

## História/paleopatologia

Baldsen JL. Testing conditional independence in diagnostic palaeoepidemiology. [Am J Phys Anthropol](#) 2005; 128(3):586-92.

Leprosy was a well-known and dreaded disease in the Middle Ages. A substantial fraction of the adult population carried leprosy-related lesions. Previous research analyzed the occurrence and implications of seven such lesions in samples of medieval skeletons. These analyses were carried out under the assumption of conditional independence among lesion scores. The present paper examines this assumption by developing a test based on the odds ratios and applying the test to three rural medieval samples from Europe: Tirup from the 12th-14th century AD in Jutland, Denmark; Refshale from the 12th-14th century AD on the island of Lolland, Denmark; and Lauchheim from AD 460-680 in southern Germany. Signs of nonzero prevalence of leprosy at death were found in all three samples: Tirup, 25.5% (95% CI, 17.2-34.6%); Refshale, 39.1% (95% CI, 25.5-54.7%); and Lauchheim, 16.2% (95% CI, 10.0-22.9%). It is shown that when leprosy is the prime factor creating variation in the lesion scores in and between samples, the assumption of conditional independence cannot be rejected.

## Imunologia

Ellertsen LK, Wiker HG, Egeberg NT, Hetland G. Allergic sensitisation in tuberculosis and leprosy patients. [Int Arch Allergy Immunol](#) 2005; 138(3):217-24.

**BACKGROUND:** A negative association has been observed between infections and allergy in several studies. The aim of the present study was to examine whether tuberculosis and leprosy patients have more or fewer allergies than healthy individuals. **METHOD:** Sera from tuberculosis patients, leprosy patients and healthy controls were analysed by ELISA and Pharmacia Unicap for serological markers for allergy and mycobacterial infection. The serological markers for allergy were total IgE, specific IgE using Phadiatop and specific IgE to the dust mite allergen *Dermatophagoides pteronyssinus* 1 (Der p 1). Serological markers for mycobacterial infections included specific IgG to a mixture of bacille Calmette-Guérin culture filtrate antigens, to purified mannose-capped lipoarabinomannan (manLAM) and to purified secreted antigen 85B. **RESULTS:** Both tuberculosis and leprosy patients had significantly higher levels of total IgE than controls. Furthermore, a significantly higher level of specific IgE (Phadiatop) was also found in the tuberculosis patients compared with controls. A similar result, but not statistically significant, was observed for the leprosy group. Specific IgG to antigen 85B and to manLAM was found to be significantly higher in both tuberculosis and leprosy patients compared with controls. In addition, leprosy patients had significantly more IgG to the BCG culture filtrate antigen than controls. **CONCLUSIONS:** The results indicate that patients with mycobacterial infections have allergic sensitisation more frequently compared with healthy controls. This is seemingly in contrast with the notion that there is a negative association between allergy and infection ('hygiene hypothesis'). However, since only one in ten of those infected with *Mycobacterium tuberculosis* will develop the disease, patients with active mycobacterial disease represent a selected group. A similar relationship applies for leprosy. It is conceivable that those predisposed to allergy are less resistant to mycobacterial infections.

quais, após avaliação desse teste, foram submetidos a novo teste de Mitsuda. Outros 28 Mitsuda-negativos receberam a inoculação de placebo e, posteriormente, foram avaliados por meio de novo teste de Mitsuda. **RESULTADOS:** Nos pacientes inoculados com a mitsudina experimental houve respostas favoráveis: em 25 deles reações macroscópicas positivas, em quatro das quais, com granuloma tuberculóide. Avaliados por meio de novo teste de Mitsuda, quatro deles responderam com típicas reações Mitsuda-positivas, com granuloma tuberculóide. Nos pacientes testados com placebo, as respostas foram negativas; a um novo teste de Mitsuda, houve uma resposta positiva. **CONCLUSÕES:** Em hansenianos Mitsuda-negativos, testados com mitsudina experimental, foram constatadas 14,29 por cento de respostas favoráveis, com reações de Mitsuda-símbles provocadas por essa mitsudina; testados os pacientes, novamente, com o antígeno de Mitsuda, foram constatadas 14,81 por cento de respostas favoráveis, com reações positivas. (AU).

## Imunologia

Miranda RN, Pereira LC, Tarlé SF, Mello SL de, Mesquita L A F, Dechandt IT. Desenvolvimento de preparado antigênico Mitsuda-símile e sua avaliação em pacientes multibacilares Mitsuda-negativos / Development of a Mitsuda-like antigen and its evaluation in multibacillary, Mitsuda-negative leprosy patients [An. bras. dermatol](#) 2005; 80(4):355-362.

**FUNDAMENTOS:** A hanseníase, causada pelo *Mycobacterium leprae*, manifesta-se por forma clínica denominada paucibacilar, benigna, Mitsuda-positiva, imunocompetente, e por outra forma, denominada multibacilar, grave, Mitsuda-negativa, imunodeficiente. Doentes multibacilares, eliminadores de bacilos, são considerados os mantenedores da endemia hanseniana. **OBJETIVOS:** Os autores testaram cultura de micobactérias, obtida em laboratório, em pacientes Mitsuda-negativos, em busca de possível viragem imunológica. **MÉTODOS:** Com a cultura de micobactérias, foi preparado antígeno mitsudina-símile, que foi testado em 28 hansenianos Mitsuda-negativos, os

## Imunología/clínica

Rada E, Aranzazu, Nacarid, Convit J. Ciertos aspectos inmunológicos en los estados reaccionales en la enfermedad de Hansen: revisión / Some immunological aspects in the reaccional states of Hansen disease: review, [Invest. clín](#) 2005; 46(4):381-389.

El problema clínico crucial en la lepra son los episodios de inflamación aguda que conllevan a daño de los nervios. Aun cuando el *Mycobacterium leprae* ha sido eliminado mediante el uso de antibióticos, la muerte de la bacteria no es una solución completa al daño ocasionado en los nervios. Dos de los fenómenos inmunopatológicos más frecuentes son: Reacciones tipo I conocidas como reacciones de reversión (RR) y las Reacciones tipo II, como eritema nodoso leproso (ENL). Estas reacciones tipo II se han definido como: una complicación inmunológica en los pacientes multibacilares. Ambos tipos de reacciones están acompañadas por el incremento de citocinas pro-inflamatorias principalmente TNF- $\alpha$ , IL-1, IL-2, IL-4, IL-6, IL-8, INF- $\gamma$ , IL-10, IL-12, entre otras. En un análisis retrospectivo realizado en una población de 150 pacientes del Servicio Central de Dermatología del Instituto de Biomedicina sometidos a terapia multidroga (PQT) y PQT + inmunoterapia, ambos grupos presentaron fenómenos reaccionales tipo II, sólo el grupo que adicionalmente recibió inmunoterapia presentó además reacciones del tipo I. El grupo de pacientes que presentaron ENL estuvo asociado con presencia de gran cantidad de bacilos en las lesiones(AU).



## Imunopatologia

Jardim MR, Antunes SL, Simons B, Wildenbeest JG, Nery JA, Illarramendi X, Moraes MO, Martinez AN, Oskam L, Faber WR, Sarno EN, Sampaio EP, Bühner-Sékula S. Role of PGL-I antibody detection in the diagnosis of pure neural leprosy. [Lepr Rev](#) 2005; 76(3):232-40.

Pure neural leprosy (PNL) is difficult to diagnose because skin lesions and acid-fast bacilli (AFB) in slit smears are absent. At present, the gold standard for PNL diagnosis is the histopathological examination of a peripheral nerve biopsy. Even so, detection of bacteria is difficult and histological findings may be non-specific. Furthermore, nerve biopsy is an invasive procedure that is only possible in specialized centres. Therefore, there is a need for additional diagnostic methods that may help to confirm the clinical diagnosis of PNL. In the present study, an additional laboratory test, the ELISA for anti-phenolic glycolipid I (PGL-I) IgM antibodies, was performed on 103 individuals with clinical and neurophysiological signs of peripheral neuropathy, of which 67 were diagnosed as PNL patients and 36 remained as 'not diagnosed as PNL', as well as on a control group of 34 patients with other neurological diseases. An antibody response was present in 14/67 (21%) of the patients diagnosed as PNL as compared with 3/34 (9%) of controls. Anti-PGL-I positivity was observed in 5/8 (63%) of the AFB positive cases. Patients whose diagnosis was confirmed solely by *Mycobacterium leprae* PCR on the nerve sample had 4/25 (16%) seropositivity. In addition, anti-PGL-I antibodies were detected in 9/40 (23%) of the PNL patients who were PCR negative for *M. leprae* DNA. Moreover, two patients who showed clinical and electrophysiological manifestations suggestive of PNL were diagnosed with the help of their positive test results in the anti-PGL-I ELISA. In conclusion, detection of antibodies against PGL-I in patients with peripheral neuropathy is useful as an additional laboratory test to help PNL diagnosis.

## Imunoterapia

Kalianina OV, Iushchenko AA. [Development of antileprosy vaccines]. [Zh Mikrobiol Epidemiol Immunobiol](#) 2005; (2):93-100.

The absence of an effective antileprosy vaccine, capable of preventing the spread of leprosy hinders its control in endemic countries. Developing such a vaccine is highly difficult due to the absence of reproducible methods for the in vitro cultivation of *Mycobacterium leprae*. The results of field trials of earlier proposed vaccines (BCG and BCG in combination with killed *M. leprae*) are indicative of their insufficient efficacy. The article presents a review of literature, including historical information, current problems and the main approaches to the development of vaccine against leprosy.

## Infecção experimental/epidemiologia

Truman R. Leprosy in wild armadillos. [Lepr Rev](#) 2005; 76(3):198-208.

Wild nine-banded armadillos (*Dasypus novemcinctus*) in the south central United States are highly endemic natural hosts of *Mycobacterium leprae*. Surveys conducted over the last 30 years on more than 5000 animals confirm that the infection is present among armadillos in Arkansas, Louisiana, Mississippi and Texas. Highest prevalence rates are found among the animals in low-lying alluvial and coastal areas, primarily in Louisiana and Texas. Both animal density and local factors may contribute to the detectability of armadillo leprosy in those regions. Little evidence for *M. leprae* infection is found among armadillos elsewhere in the US range, and only a few reports relate finding the infection among animals in Central or South America. However, the issue has received only scant attention in other countries. Armadillos only recently expanded their range into the US, and leprosy was present in Texas and Louisiana prior to the arrival of armadillos. The ecological relationship between humans and armadillos with *M. leprae* in this region remains unclear. However, infected armadillos constitute a large reservoir of *M. leprae* and they may be a source of infection for some humans in this country, and perhaps in other locations across the animal's range.

## Oftalmologia/cirurgia

Mpyet C, Dineen BP, Solomon AW. Cataract surgical coverage and barriers to uptake of cataract surgery in leprosy villages of north eastern Nigeria. [Br J Ophthalmol](#) 2005; 89(8):936-8.

**AIMS:** To determine the coverage, outcome, and barriers to uptake of cataract surgery in leprosy villages of north eastern Nigeria. **METHODS:** People 30 years and above resident in eight leprosy villages were examined. Cataract blind people were questioned about the reasons they had not been treated. Subjects who had received an operation for cataract were examined to determine the outcome and, where applicable, the causes of poor outcome. **RESULTS:** 480 people were examined. Cataract was the commonest cause of blindness. The cataract surgical coverage (people) was 39.2% for orthodox surgery and 29.7% for couching. After surgery, visual acuity  $>$  or  $=3/60$  had been restored to 82.1% of eyes that had had orthodox surgery, but only 58.6% of eyes that had been couched. Cost was the commonest reason given for not seeking treatment for cataract. **CONCLUSIONS:** Cataract is the major cause of blindness in this population but cataract surgical needs are currently not being met. There is a need for better collaboration between leprosy control and ophthalmic services, improved education of people affected by leprosy, a commitment to improving orthodox cataract surgery outcomes, and consideration of a possible role for traditional healers as sources of referral for orthodox surgical services.

## Patologia

Goto M, Aung T, Kitajima S. [Pathological diagnosis of leprosy in developing countries]. [Nihon Hansenbyo Gakkai Zasshi](#) 2005; 74(3):191-8.

In the developing countries where leprosy is prevalent, diagnosis of leprosy is made from clinical signs and symptoms. However, when difficult and doubtful cases increase after the advance of leprosy control programs, definitive diagnosis of leprosy by histopathology become necessary. This report describes our experience of technical support to re-establish histopathology service and introduction of immunohistochemistry in the leprosy referral center of Myanmar, and we discuss the ideal way of international technical support. This activity was performed as a part of leprosy control and basic health services project of Japan International Cooperation Agency (JICA) since 2000 to 2005.

## Reabilitação/prevenção de incapacidades

Yamaguchi T. [Background of development and effectiveness of myanmar sandals (the activity of Leprosy Control and Basic Health Services Project in Myanmar)]. [Nihon Hansenbyo Gakkai Zasshi](#) 2005; 74(3):199-203.

[quot ]Leprosy control and Basic health service Project[quot ] was terminated at March 2005 within the scope of the period. I was assigned to develop the Plantar protect footwear for neuropathic feet, which called [quot ]Myanmar Sandals[quot ] in common. These sandals are not made by new technologies but made by basic knowledge. I would like to report about this activity as which is a part of distinguished strategy of ODA (Official Development Assistance) for developing country, but not as the technical report of these sandals. There is only one National Leprosy Hospital in Myanmar. At the time this project started, there were only two footwear technicians for the people who had disabilities by after effect of Hansen's disease in this country. And, it would appear that the number of the people is over 50,000. Furthermore, the budget of national hospital is not enough to refill necessary consumable supplies and materials. Although, I should instruct new technique which like making in Japan in ordinary circumstances, I could not think that such technical transfer by using costly imported materials would bring beneficial effect and be continued. We were bound to be anxious about such situations when we made the plan. As a result of examining a plan based on these situations, we reached the conclusion that development of the simplified ready-made footwear was pressing need.

## Reabilitação/treinamento

Nagato I. [Training of the rehabilitation staffs through taking measures against leprosy in Union of Myanmar]. [Nihon Hansenbyo Gakkai Zasshi](#) 2005; 74(3):205-9.

I participated in [quot ]Leprosy Control and Basic Health Service Project in Myanmar[quot ] by JICA from 2002 to 2004. I went to Myanmar three times as a short-term expert of physiotherapy. I carried out evaluation training for physio staffs in national Yenanthar leprosy hospital. They learned how to evaluate activity of daily living. And they were able to make modified spoons and the canes. Later, they looked for the contents to evaluate by themselves. And they evaluated and decided by themselves what they should do. They felt the necessity for toilet chairs, modified beds and etc. They formed the plan and manufactured them. They were able to perform by themselves. It is thought that evaluation was fixed to staffs. This knowledge will surely be helpful to patients. I expect that this knowledge will be put to evaluations and exercises of many diseases. The physio staffs of this hospital will surely perform. Cooperation of the shoemaker and nursing staffs is very secure. I hope that it may become the model of saying [working in cooperation with other occupational descriptions] from now on.

## Terapêutica

Vijayaraghavan R, Suribabu CS, Sekar B, Oommen PK, Kavithalakshmi SN, Madhusudhanan N, Panneerselvam C. Protective role of vitamin E on the oxidative stress in Hansen's disease (Leprosy) patients. [Eur J Clin Nutr](#) 2005; 59(10):1121-8.

**BACKGROUND:** A constellation of reactive oxygen species (ROS) capable of damaging cellular constituents generated in excess during the chronic, inflammatory, neurodegenerative disease process of leprosy. The consequences of this leads to enhanced oxidative stress and lower antioxidant status. Enzymatic antioxidants provide first line defense against ROS. We have measured the levels of oxidative stress indices like lipid peroxidation (LPO), protein carbonyls together with enzymatic antioxidants in the blood samples of control and leprosy patients. Nutritional rehabilitation by way of exogenous supplementation of functionally efficient antioxidants like vitamin E reactivates the enzymatic antioxidant system and guards against the insult caused by ROS during the pathogenesis of the disease and antileprosy chemotherapy. **DESIGN:** Untreated leprosy patients were selected on the basis of clinical examination and skin smear. All diagnosed untreated leprosy patients received multi drug therapy (MDT) consisting of rifampicin, dapsone and clofazimine as recommended by World Health Organization. A small number of untreated cases were selected for co-supplementation of vitamin E along with MDT. Oxidative stress indices, enzymatic and nonenzymatic antioxidant status were assayed in untreated, MDT treated and those supplemented vitamin E along with MDT. **STATISTICAL METHODS:** We have compared the significance in the mean $\pm$ s.d. values of the oxidative stress indices and the levels of antioxidants using one way analysis of variance (ANOVA) between control, untreated, MDT treated and those supplemented vitamin E with MDT and the results were significant at  $P < 0.05$ . Statistical analysis of the results suggests that oral administration of vitamin E lowers oxidative stress and augments antioxidant status in affected individuals. **Results:** Enhanced oxidative stress as evidenced by increased LPO and protein carbonyl in leprosy cases lowers the antioxidant status. Treatment with MDT has a limited impact on increased oxidative stress and decreased antioxidant status. Coadministration of vitamin E along with MDT decreases oxidative stress and activate the antioxidant status. **DISCUSSION:** The excess production of ROS as seen in leprosy cases could lead to degeneration of tissues and derangement of internal organs. The possible reason for the decreased antioxidant status in leprosy cases may be increased production of ROS, deranged liver function, and the free radical producing ability of drugs used in MDT of leprosy. Intervention with antioxidant supplementation like vitamin E prevents oxidative stress mediated through ROS and activates the net antioxidant status during the chronic course of the disease and antileprosy chemotherapy.



## Terapêutica/clinica

Vara N, Marfatiya Y. A study on the impact of FD-MDT on 200 leprosy patients. [Indian J Lepr.](#) 2005; 77(3):217-27.

A study was carried out from June 1999 to June 2001 to assess the impact of fixed duration multidrug therapy (FD-MDT) in newly detected cases of leprosy in terms of clinical and neurological improvement and changes in the bacillary index of skin smear for AFB. 200 new leprosy cases (both PB & MB) were started on FD-MDT. Of these 200 cases, 16 were of pure neuritic leprosy. After treatment, out of 184 cases with typical skin lesions of leprosy, all 26 PB cases showed inactivity of skin lesions, and, of the remaining 158 MB cases, 40.5% showed inactivity and 59.5% showed complete resolution of skin lesions. Out of 68 skin smear-positive cases, 42 cases with a BI of  $\leq 3$  became smear-negative, while others showed gradual fall in the BI. Such heavily bacilliferous cases were continued with treatment for 1 more year to prevent relapse. As FD-MDT alone does not cure established sensory and motor impairment, it did not show any change in 19% of the patients presented with permanent sensory motor disturbance. FD-MDT prevents progression of sensory/motor disturbance.

## Terapêutica/reações adversas

Alves-Rodrigues EM, Ribeiro LC, Silva MD, Takiuchi A, Rabel-Filho OC, Martini-Filho D, Fontes CJ. Renal hypersensitivity vasculitis associated with dapsone. [Am J Kidney Dis](#) 2005; 46(4):e51-3.

We describe clinical and pathological features of kidney and skin involvement in a patient with hypersensitivity vasculitis associated with dapsone. Although visceral damage occurs rarely, similar skin and kidney histopathologic and immunohistochemical findings indicate that this organ is a target for type IV cell-mediated dapsone reaction. To our knowledge, this is the first reported case of renal hypersensitivity vasculitis associated with dapsone.

## Terapêutica/reações adversas

Kaur J, Khandpur S, Seith A, Khanna N. Dapsone-induced eosinophilic pneumonitis in a leprosy patient. [Indian J Lepr](#) 2005; 7(3):267-71.

A leprosy patient with no prior history of respiratory complaints, developed symptoms of dry cough, fever and dyspnea after six weeks of therapy. Peripheral eosinophilia and radiological evidence of pulmonary interstitial infiltrates pointed towards the possibility of drug-induced eosinophilic pneumonitis. The results of relevant tests for other possible pathologies were normal. The resolution of symptoms without any intervention other than withdrawal of the drug and subsequent re-challenge proved dapsone to be the cause.

## Terminologia

Opromolla PA, Martelli ACC. A terminologia relativa à Hanseníase / Terminology related to Hansen's disease. [An. bras. dermatol](#) 2005; 80(3):293-294.

A padronização internacional de doenças é um processo complexo que necessita de uma equipe especializada. Esta comunicação visa a esclarecer e sugerir correções de um provável equívoco na tradução, para o português da CID-10, do código A30, no qual os termos "borderline" e "dimorfo" são utilizados como subcategorias distintas e não como sinônimos, assim como substituir a designação "lepromatosa" por "virchoviana" pois, no Brasil, o vocábulo "lepra" foi abolido dos textos oficiais, por uma lei federal em 1995.