LITERATURA CORRENTE
CURRENT LITERATURE

CLÍNICA

ANTUNES, S.L.G. et al. Distinct patterns of microvasculature in the cutaneous lesions of leprosy. *Int.I. Leprosy*, v.68, n.2, p.143-151, June, 2000.

This work is an investigation on the microvasculature of the cutaneous infiltrates of leprosy with the immunohistochemical staining of endothelial cells in cutaneous biopsies. Anti-Factor VIII-related antigen antibody (anti-FVIII-ra) and Ulex Europaeus-1 lectin (UEA-1) binding were utilized as endothelial cell markers. Thirty-nine patients grouped according to the Ridley-Jopling classification (14 borderline tuberculoid, 18 borderline lepromatous, 6 lepromatous, and 1 indeterminate leprosy) were selected for this study. Two microvascular architectural patterns could be clearly distinguished: lepromatous lesions presented a dense and tortuous mesh of microvessels among the *Mycobacterium leprae* -glutted macrophages; whereas the microvessels in the tuberculoid lesions were restricted to the periphery of the granulomas and were not seen among the central epithelioid cells. We were able to distinguish three basic morphological kinds of infiltrate distribution related to the microvessels: micronodules, cords and macronodules. Intensifications of the FVIII-ra immunoreactivity and UEA1 binding capacity were observed in the endothelial cells of microvessels involved by the inflammatory infiltrate. A distinct cytokine expression profile at the leprosy poles and the role of mast cells in angiogenesis were speculated as factors contributing to these distinct patterns. Growth of the lesion and systemic dissemination of M. *leprae* in the bipolar spectrum of leprosy may hypothetically be influenced by the vascular-infiltrate relationship. The detection of angiogenesis in the cutaneous lesions of leprosy may bring about alternate and/or additional strategies for leprosy treatment.

BROWEN, J.R. et al. Vasculitic neuropathy in a patient with inactive treated lepromatous leprosy.). *Neural. Neurosurg. Psychiatry.*, v.68, n. 4, p.496-500, Apr., 2000.

A 46 year old Asian male with previously treated lepromatous leprosy developed a stepwise multifocal sensory disturbance 25 years later. Neurophysiology demonstrated marked deterioration from previous studies. Sural nerve biopsy disclosed a vasculitic process superimposed on inactive lepromatous leprosy. Immunocytochemical stains for mycobacterial antigen showed deposits within nerve and vessel walls. A delayed vasculitic neuropathy precipitated by persisting mycobacterial antigen is proposed.

CABRINI, J.M.; MACIA, A.; SUDAROVICH, M.; BRESSANELLI, A.; BOTTASSO, O.A. Evolución bacteriológica de la lepra lepromatosa según la presencia de episodios de eritema nudoso leproso. *Fontilles Rev. Leprol.*, v.22, n.5, p.451-462, Mayo-Agosto, 2000.

Erythema nodosum leprosum (ENL) is a common complication of lepromatous leprosy (LL), that appears to be triggered by immune complex deposition in the vascular wall along with the emergence of cell-mediated immune phenomena, some of them specific to M. *leprae.* To find out wether occurrence of ENL reactions could facilitate a better disease outcome, an evaluation was made on the time by which LL patients attained bacteriological negativity (TBN), depending on the appearance of ENL episodes during treatment.

The study consisted of a retrospective analysis of clinical records from 106 patients, mostly sulfone recipients, 27 cases undergoing no ENL episodes and 79 patients who had developed reactions of distinct severity and frequency.

Groups were similar as to age, sex distribution, treatment schedule and degree of involved skin, showing differences in clinical varieties, namely more macular cases in LL without ENL. These patients had a significantly shorter TBN (3.2±0,4 years) than LL with ENL (6.1±0.3, mean ± sem). A further division of the latter group according to the intensity and frequency of ENL episodes revealed no differences in TBN which appeared similar to the one recorded in the entire group. Occurrence of ENL reactions does not seem to accelerate the chemotherapy-mediated bacillary clearing.

CREANGE, A. Neuropathies infectieuses. Rev. Prat., v. 50, n.7, p. 743-748, Apr. 1 2000.

Infective neuropathies constitute a leading cause of

neuropathies in the world. The number of patients with nerve lesions related to leprosy remains high despite decreasing number of new cases requiring multidrug regimens. Peripheral neuropathies associated with HIV infection may be found in up to 50% of patients.

Neuropathies may be related to the inflammatory reaction against viral antigens, immunodepression, opportunistic infections, and iatrogenic complications of antiviral drugs. Hepatitis C virus infection has been found in cryoglobulinemic neuropathies. This virus should be screened for exploration of all neuropathies.

Rare causes of neuropathy, such as poliomyelitis and diphtheria, and treatable neuropathies such as Lyme disease, should not be forgotten.

CROFT, R.P. et al. A clinical prediction rule for nerve-function impairment in leprosy patients. *Lancet*, v. 355, n. 9215, p.1603-1606, May 6, 2000.

BACKGROUND: Nerve-function impairment (NH) commonly occurs during or after chemotherapy in leprosy and is the key pathological process leading to disability and handicap. We describe the development of a simple clinical prediction rule for estimating the risk of NFI occurrence.

METHODS: New leprosy cases who presented to a centre in Bangladesh were recruited and followed up for 2 years in a field setting. We used multivariable regression analysis by Cox's proportional hazards model to identify predictive variables for NFI. Discriminative ability was measured by a concordance statistic. Internal validity was assessed with bootstrap resampling techniques.

FINDINGS: 2510 patients were followed up for 2 years, 166 developed NFI. A simple model was developed with leprosy group (either paucibacillary leprosy (PB) or multibacillary leprosy (MB) and the presence of any nerve-function loss at registration as predictive variables. Patients with PB leprosy and no nerve-function loss had a 1.3% (95% CI 0.8-1.8%) risk of developing NFI within 2 years of registration; patients with PB leprosy and nerve-function loss, or patients with MB leprosy and no nerve-function loss had a 16.0% (12-20%) risk; and patients with MB leprosy with nerve-function loss had a 65% (56-73%) risk.

INTERPRETATION: Our prediction rule can be used to plan surveillance of new leprosy patients. Patients at low risk of NFI may need no follow-up beyond their course of chemotherapy (6 months); patients with intermediate risk need a minimum of 1 year of surveillance; and patients with high risk should have at least 2 years of surveillance for new NFI. Current recommendations for surveillance of patients with leprosy (for the duration of chemotherapy only) exclude an important group of patients who are at risk of developing NFI after completion of treatment.

CROFT, R.P.; NICHOLLS, P.G.; RICHARDUS, J.H.; CAIRNS, W.; SMITH, S. Tratamiento del deterioro agudo de la función neural en la lepra: resultado de un estudio prospectivo de cohorte en Bangladesh. *Fontilles Rev. Leprol.*, v.22, n.5, p.463-480, Mayo-Agosto, 2000.

In this paper, the outcome of 132 patients having acute nerve function impairment (NFI) is reported at 4 and 12 months after the start of prednisolone treatment. In all, 68% of sensory nerves and 67% of motor nerves showed improvement at 12 months, with no statistical difference in responsiveness of various nerves to prednisolone. Duration and severity of impairment were not found significant predictors of treatment outcome. A core of 32% of impaired nerves did not respond to prednisolone, and 12% of impaired nerves had functional deterioration despite treatment. The mean eye-hand-foot (EHF) score improved from 2.02 to 1.33 in the treatment group (median score improved from 2 to 1). Approximately one-third of all patients requiring prednisolone treatment did not receive it, an important reason being that some patients developed new NFI against a background of chronic impairment, and were thus overlooked.

The "unjustly untreated" group of patients had a spontaneous sensory nerve function improvement rate of 62% and motor nerve function improvement rate of 33% at 12 months from onset of NFI. The EHF score showed no statistically significant improvements.

DANIEL, E., et al. Epithelioid granuloma in the iris a lepromatous leprosy patient, an unusual findings. Int. *I. Leprosy*, v. 68, n. 2, p. 152-155, June, 2000.

This case report depicts a case of histopathologically confirmed polar lepromatous (LL) leprosy with a bacterial index of 4+.

He experienced recurrent episodes of erythema nodosum leprosum (ENL) in the first 5 years after diagnosis. Skin smears became negative after 6 years of dapsone monotherapy and have remained negative since that time. At 23 years after diagnosis, the patient had developed cataracts and underwent intracapsular cataract extractions with broad-based iridectomies. In one of the iris specimens, histopathologic examination revealed a focal granuloma composed of epithelioid cells. Subsequently a lepromin skin test showed a positive Mitsuda reaction with a borderline tuberculoid histopathology. This clearly illustrates the immunological upgrading of a polar lepromatous patient perceived first in the iris tissue.

GÓMEZ ECHEVARRÍA, J.R; HERNANDEZ RAMOS, J.M. Lepra tuberculoide. *Fontilles - Rev. Leprol.*, v.22, n.5, p.497-510, Mayo-Agosto, 2000.

Since 1991, the Sanatorium of Fontilles has been involved in public health programs with a special dedication to dermatological pathology and leprosy in the State of Mato Grosso (Brazil). Work has been carried out in the north east area of this Brazilian State (Santa Terezinha, Sao Félix do Araguaia, Porto Alegre do Norte and Alto da Boa Vista) a very endemic area for leprosy in Brazil.

From January 1991 to the present moment 822 individuals were diagnosticated and treated for this disease (585 men and 297 women, 66 patients were children under 14 years).

624 patients were treated according to W.H.O. - Fundação Nacional de Saude recommendations. At this moment 158 patients remain active and on treatment.

The prevalence of the disease in the area is over 45/10.000 population. In this paper the personal experience of the two doctors who carried out the study is explained.

The number of individuals diagnosticated as tuberculoid leprosy was 305 (190 men, 115 females, 12 children less than 14 years old). 232 were treated and discharged as cured with 36 patients still on treatment at this moment.

GÓMEZ ECHEVARRIA, J.R., HERNANDEZ RAMOS, J.M. Lepra indeterminada. *Fontilles - Rev,. Lepro/.*, v.22, n.4, 357-369, Enero-Abril, 2000.

Since 1991 and up to the present the Sanatorium of Fontilles has had health workers colaborating in public health projects with a special dedication to leprosy and dermatological problems in the State of Mato Grosso (Brazil). The projects were carried out in the northeasther part of this Brazilian State (Santa Terezinha, Sao Felix do Araguaia, Porto Alegre do Norte, Luciara y Alto da Boa Vista), region of high endemicity for leprosy.

From January 1991 to the present 882 individual were diagnosed and treated for leprosy 585 men, 297 women and 66 children under 14 years.

724 patients received treated according to WHO-Fundação National de Saude and taken off register; 158 patients remain active and on treatment. The prevalence with for disease in the area is higher than 45/10.000 people. The two doctors who have worked on the field with this project reviewed personal experience with indeterminate leprosy.

The number of patients diagnosed of indeterminate type of leprosy were 141, 93 men (66%) and 48 women (34%), 21 children less than 14 years (15%), 129 cases were treated and taken off register and at present there are 22 cases of this type on treatment.

GRAUWIN, M.Y.; CARTEL, J.L. ; LEPERS, J.P. Comment guérir les ostéites et estéo-arthrites des extrémités des anciens maladies de la lèpre par le sucre cristallisé alimentaire? Acta *Leprol., v.11*, n.4, p.147-152, 1999.

How to treat osteitis and septic arthritis of the extremities in patients with sequellar leprosy using ordinary granulated sugar?

A common problem of osteitis and septic arthritis is the recurrent bone infection after surgical debridement, a problem frequently encountered in patients with sequellar leprosy. In these cases the authors propose the use of an ancient method of post surgical wound care based on the treatment with ordinary granulated sugar. The hyperosmolar climate created this way in the wounds inhibits the bacterial growth, enhances bacterial death and therefore permits the growth of granulation tissue in order to recover the debrided nude bones. At ILAD (Leprosy Institute of Dakar), 36 osteitis and septic arthritis were treated and healed during the last 2 years from March 1995 to March 1997 using this technic. All the wounds healed in the mean-time of 44 days. Only two of them needed a second debridement and healed afterwards. Up to now the method using ordinary sugar was applicated in the treatment of infected wounds, eschars and postsurgical iniections. Our experience shows that it also can be indicated to treat bone infections. This method is easy to apply also under often difficult field conditions and is very cheap.

KAJIHARA, H. et al. Ligth and electron microscopic study of peripheral nerve damage in patients with lepromatous leprosy (LL) and borderline lepromatous leprosy (BL). *Hiroshima I Med Sci.*, v.49, n. 1, p. 83-92, Mar., 2000.

Cutaneous branches of radial nerves in patients with lepromatous leprosy (LL) and borderline lepromatous (BL) were studied by light and electron microscopy. Foamy macrophages were found more or less in the nerve fibers of all leprosy patients and distributed in the epineurial, perineurial and endoneurial areas. In the endoneurium, the foamy macrophages were mainly located in the subperineurial and perivascular spaces. Vacuolated Schwann cells were also found in the nerve fasciculus. In electron microscopy, these foamy macrophages and vacuolated Schwann cells contained numerous small

dense materials, irregular in size and shape, considered to be degenerated and fragmented *Mycobacterium* leprae.

These dense materials were found also in the cytoplasm of vascular endothelial cells. These findings suggest that mycobacteria enter into the endoneurium via the blood vessels. In our present study, on the other hand, it was very difficult to find the intact mycobacteria in the cytoplasm of the foamy macrophages, Schwann cells or endothelial cells, as well as in the Ziehl-Neelsen staining of paraffin sections. The disappearance of intact bacilli in our present study might have been caused by multi drug therapy. The myelinated nerve fibers were degenerated and disappeared in variable degrees. Degenerative changes of the myelin sheath developed from the outer layer to the inner layer with disarrangement of the lamellar structure. These findings were different from myelin destruction of peripheral nerves in Wallerian degeneration. The degenerative changes of the myelin sheath are caused by degeneration and destruction of Schwann cells in leprosy patients. Fibrosis surrounding myelinated and unmyelinated nerve fibers, i.e., periaxonal fibrosis, was found to a greater or lesser extent in the endoneurium. In the present study, it is still unclear whether the periaxonal fibrosis was due to necrosis of the Schwann cells by infection of mycobacteria or to an autoimmune mechanism such as antiperipheral nerve antibody. However, lamellated concentric fibrosis surrounding regenerative myelinated and unmyelinated nerve fibers with the disappearance of mycobacteria suggests that degenerations and regenerations of nerve axons were repeated during clinical cause. These findings indicated that autoimmune mechanisms play an important role in the pathogenesis of periaxonal fibrosis.

LEE, S.H. et al. The changes in hair growth pattern after autologous hair transplantation. *Dermatol. Surg.,* v.25, n. 8, p.605-609, Aug., 1999.

BACKGROUND: Recently donor dominance has been emphasized in autologous hair transplantation while the influence of the recipient site has been considered negligible. In fact, there have been few studies that show this.

OBJECTIVE: This study was performed to examine the influence of the recipient site on transplanted hairs. A clinical study of 19 leprosy patients was performed. These patients had received single hair transplantation due to madarosis and were admitted to The Leprosy Mission, Jesus Hospital, Taegu, Korea, or had visited its outpatient clinic.

METHODS: In this study, the rate of growth, thickness of shaft, and graying rate between the transplanted eyebrow hair in the recipient site and scalp hair near the donor site were compared to observe the changes in the growth pattern of the hairs after transplantation.

RESULTS: For most of the patients, the growth rate and graying rate of transplanted hairs were lower than those of hairs in the donor site.

CONCLUSION: It seems that the recipient site may have an influence on the transplanted hairs. Further studies are needed, including clinical, histopathological, and molecular biological methods.

LIWEN, D. et al. Techniques for covering soft tissue defects resulting from plantar ulcers in leprosy: part Ill use of plantar skin or musculocutaneous flaps and anterior leg flap. *Indian J. Leprosy*, v. 71 n.4, p.423-436, Oct-Dec., 1999.

Anatomical studies suggest that five types of plantar flaps namely, the lateral and medial plantar flaps, the Abductor hallucis-, the Flexor digitorum brevis- , and the Abductor digiti minimi-myocutaneous flaps, can be incised from the central section of the sole. The advantages of a plantar flap are recognizable neurovascular bundles of the sole, wide calibre of constantly located blood vessels, identical histological structure of the donor and the recipient sites, hidden donor site and absence of functional deficit. We have used the plantar flaps in seven cases. There has been no recurrence of ulceration in any of them during the follow-up period of 12 to 108 months.

An anterior leg flap based on the cutaneous branches of the anterior tibial artery, with firmly anchored vessels, a long pedicle with wide vessels may be used not only as a free flap graft for reconstruction of moderate degree distant defects but also as a retrograde island flap graft for the reconstruction of adjacent tissue defect. We have used the retrograde island flap graft based on the anterior tibial artery in five cases of plantar ulceration with satisfactory results. There was no recurrence of ulceration during the follow-up period of 48 to 72 months.

LIWEN, D. et al. Techniques for covering soft tissue defects resulting from plantar ulcers in leprosy: part IV use of medial leg flap and medial knee flap. *Indian J. Leprosy*, v.71, n.4, p.437-450, Oct-Dec., 1999.

The medial leg flap, based on the cutaneous branches of the posterior tibial artery is raised from the middle and lower regions of the medial aspect of the leg. It has a long pedicle, and it can be used as a free flap to reconstruct the distant soft tissue defects and also as an island flap.

We have used this retrograde island flap for surfacing

ulcerated areas in six leprosy patients. The flap survived in all cases. At 24 to 60 months follow-up examination, ulceration had not recurred in any of them.

The medial knee flap consisting of the skin and subcutaneous tissue of the lower part of the medial side of the thigh and the upper part of the leg, is suitable for covering soft tissue cushion defects of the extremities because of the constant vessels, long pedicle, wide diameter, well-recognizable sensory nerves and less subcutaneous fat. We have used the medial knee flap for the resurfacing sizeable raw areas due to ulceration in three leprosy patients. The flap survived in all cases and there was no recurrence of ulceration during the 70-148 months follow-up period.

MAHAISAVARIYA, P. et al. Mast cells in leprosy and leprosy reaction. Int. *I. DermatoL.,* v.39, n.4, p.274-277, Apr., 2000

BACKGROUND: Mast cells can be visualized in routine, acid-fast-staining, paraffin tissue section as metachromatic staining cells, and can be activated to release inflammatory mediators which play a role in the cell-mediated immune response.

METHODS: Skin biopsy tissues were taken from the most active skin lesion of each leprosy patient at the time of diagnosis (nonreactional group) and at the time of reaction (reactional group) during the years 1994-1997 in the leprosy clinic at the Department of Dermatology, Faculty of Medicine, Siriraj Hospital, Mahidol University, Thailand. Mast cells were identified by metachromatic staining (purple) in Fite's stain sections and reported as the average number of cells per high power field in three compartments: at the center and periphery of the granuloma and in the interstitium. The data were analyzed in three groups: nonreactional group, type I, and type II leprosy reactions. The mast cell count of each group and each compartment of the section, expressed as the mean +/- standard error, was compared.

RESULTS: A total of 95 persons were included in the study, but 108 tissue sections were obtained due to nine cases having more than one section. Of these patients, 63 cases (66.32%) had no reaction, 19 cases (20%) had type I reaction, and 13 cases had type II reaction. There was no difference in age and sex among these groups. The mast cell count in the interstitium was higher than that within the granuloma, both at the center and at the periphery, in every type, and the count in this area reduced significantly in leprosy reactions, both type I and type II, compared with the nonreactional group.

CONCLUSIONS: The change in the average mast cell number in nonreactional leprosy and leprosy reactions may indicate the important role of mast cells in dynamic changes in the cell-mediated immune response in leprosy and leprosy reactions.

MORRISON, A. A woman with leprosy is in double jeopardy. *Leprosy Rev.,* 71, n. 2, p.128-143, June, 2000.

The double jeopardy associated with female leprosy patients is the central theme underpinning this essay. It constitutes a combination of biological factors unique to women and culturally defined bias, resulting in more stigmatization and isolation for women. Having examined the female immunological response and biological roles, the essay continues by focusing on the gender-culture perspective of leprosy. It draws upon an historical analysis of the experiences of Indian and African women to illustrate the ways in which gender roles impact upon health education and the utilization of health care services. Concluding comments suggest strategies that might improve female leprosy patient status, and views towards future research.

NUNEZ MARTÍ, J.M. Caries dental en pacientes con enfermedad de Hansen. *Fontiles Rev. Leprol.,* v. 22, n.4, p.371-376, Enero-Abril, 2000.

Dental caries is a disease with a slow evolution, usually months and even years are needed for the production of cavitation. Dental caries do not have the same effect on all teeth and dental superficie. They develop preferentially in areas most affected by plaque and of most difficult access. The factors that influence the production of cariogenic bacterial plaque are proliferation of certain types of flora, sugars with permeability and consequently acid PH production. All these conditions for the formation of dental caries are favored in Hansen's disease patients due to discapacities that hinder a normal oral higiene together with their multidrug therapy that reduces considerably their lingyal saliva PH. Therefore, in this type of patient we find basically three different types of caries.

1. Proximal superficial caries under or on areas of contact.
2. Radicular caries, located on the amelocementarial joint when the dental necks are exposed to the oral environment.
3. Caries on free superficie, that are the less frequent.

Considering these three types of lesions, an early diagnosis and early treatment of damaged tissue are fundamental before a mayor complication originates a loss of the dental piece.

WILDER-SMITH, E.P.; WILDER-SMITH, A.J., NIRKKO, A.C. Skin and muscle vasomotor reflexes in detecting autonomic dysfunction in leprosy. *Muscle Nerve*, v.23, n.7, p, 1105-1112, Jul., 2000.

There are few tests to assess the function of small unmyelinated nerve fibers. One established test is the skin vasomotor reflex (SVMR), which uses laser doppler flow velocimetry The SVMR has the disadvantages of being susceptible to interference (from change of temperature and alerting stimuli) and of requiring expensive equipment. An ultrasound doppler method, which is less expensive, can be used to detect muscle vasomotor reflex (MVMR) activity. We sought to compare the efficacy of these two methods in detecting dysfunction of small unmyelinated nerve fibers in patients with leprosy. SVMR was shown to be less sensitive ($P < 0.01$) and specific ($P < 0.001$) than MVMR. The favorable results of MVMR may be attributed to its lesser susceptibility to interfering sympathetic vasoconstriction from alerting stimuli. MVMR also reflects larger areas of blood vessel innervation than the laser doppler method. In leprosy, nerve damage is typically patchy and may be missed by the smaller sampling of the laser method.

YOUNG, R.J., GILSON, R.T., ELSTON, D.M. Generalized annular borderline tuberculoid leprosy and update in managment of Hansen's disease. Cutis, v.65, n.4, p.203-206, Apr., 2000.

We describe a patient with widespread borderline tuberculoid leprosy and significant peripheral nerve involvement. Despite the presence of widespread lesions, Fite stains and polymerase chain reaction studies were initially negative.

We discuss the diagnosis and treatment of leprosy including recent changes in treatment regimens and duration.

CONTROLE

BAGADE, P.L., BALIRAM, B. Community participation in case detection of leprosy, in Nagpur District of Maharashtra. *Indian J. Leprosy*, v.71, n4, p.465-469, Oct-Dec., 1999.

Involving special community groups for new case detection is of great importance for achieving the target of elimination of leprosy. During 1998-99, thirty village level Mahila mandais (women's groups), 6950 teachers and students and 34 548 heads of families were co-opted to participate in case detection. They examined 56 113 persons including 378 959 school students and 184 940 family members. Of the examined population, 275 were suspected to be cases of leprosy by mahila mandais, 411 by teachers and students and 747 by heads of families. Subsequent examination of the suspected cases by trained medical officers and paramedical workers confirmed 203 of them to be cases of leprosy. This exercise showed that when proper attempts were made to involve the community, case detection activity became easier, besides helping to disseminate knowledge about leprosy in the community.

CROUZAT, M. Bilan de la lèpre en Nouvelle-Calédonie. Evolution de 1983 à 1998. Acta *Leprol.*, v.11, n.4, p.139-144, 1999.

The authors report the results of a retrospective study on the evolution of leprosy in New-Caledonia, French Island in Oceania, between 1983, time of the onset of polychemotherapy (PCT), and 1998. Since 1996, the prevalence is and remains less than 1/10 000. The annual rate detection failed from 15,6 in 1983 to 2,48/100 000 in 1998. Less than 10 new cases are detected annually since 1994. During this period, the number of new patients less than 15-years old decreased and the percentage of multibacillary patients increased, assessing a priori the improvement of the endemicity. One case of relapse was detected in a MB patients treated for 2 years among the 231 new patients.

De CARSALADE, G.Y; ACHIRAFI, A.; FLAGEUL, B. La maladie de Hansen dans collectivité territoriale de Mayotte (Océan Indien): etude rétrospective de 1990 à 1998. *Acta Leprol.*, v.11, n.4, p.133-137, 1999.

Mayotte French island of the Comoro Islands in the Indian Ocean, is located in a leprosy endemic area including the other islands of the archipelago and Madagascar island. As the last Hansen's disease epidemiological study in the island have been reported in 1982, we achieved a new valuation by a retrospective study on the 1990-1998 period. Our investigation showed that the disease was still endemic with a prevalence of 32/100 000 population in 1998 and an high annual new case detection rate (14 to 31/100 000 population). The profile of the newly detected cases was the same that reported at the world level (predominance of males, less than 45-years old adults and paucibacillary forms) with two exceptions: the high percentage of children below 15 years of age (28,2%) and of family cases (25,3%). Moreover, 12,6% of the new cases exhibited disabilities grade 2 at the time of the diagnosis. These features emphasize the need for an enhanced leprosy control in this island which has a well-developed medical assistance.

ESCALADA, R.M. et al. Acción de una O.N.G, en la campana contra la lepra en la Republica Argentina: la Asociación Alemana de Asistencia al Enfermo de Lepra (DAHW). *Fontilles - Rev.* Leprol., v.22, n.4, p.345-355, Enero-Abril, 2000.

The German Leprosy Relief Association (GLRA) was founded in 1957. Since 1959, it is working in the Republic of Argentina. In the beginning of its activities, the organization provided with humanitarian and social help for leprosy patients and with economic support for some centres engaged in leprosy work. Currently, GLRA promotes leprosy control in all endemic regions. It equally supports training of medical and paramedical staff in diagnosis and therapy of the disease, in case-finding and case-holding. Furthermore, GLRA is strengthening the Prevention of Disabilities and the rehabilitation of former leprosy patients as well as the combination of leprosy and tuberculosis control.
Despite the low prevalence of registered leprosy patients in the Republic of Argentina (0,72/10.000), endemic areas like Formosa with a prevalence of 3,92/10.000 continue to exist. The case detection rate remains stable with 555 new cases per year on a average. In this context, the WHO concept (to achieve <<the elimination of leprosy as a Public Health problem» by reducing the registered prevalence below 1/10.000) is questioned.

GIL SUAREZ, R.E., LOMBARDI, C. Leprosy elimination at sub-national level. *Leprosy* Rev, v.71, n.2, p.206-211, June, 2000.

New strategies for the countries that have already achieved the elimination goal, which includes the great majority of the endemic countries, are needed. There is current concern in these countries about the reduction in the political-technical commitment when the goal is achieved and the possibility of the re-mergence of the disease. A review of the literature on the leprosy post-elimination strategy is done. The proposal to estimate the true prevalence using hidden prevalence based on late diagnosis of the new cases is made. Suggestions are explored for strategies of the work after elimination at national level is attained such as the stratification at the first sub-national level, using estimated true prevalence. It is considered necessary to define strategies for the post-elimination phase with the aim of continuing to the long-term objective of the interruption of transmission and the consequent leprosy eradication.

GIRDHAR, B.K.; GIRDHAR, A.; KUMAR, A. Recidivas en pacientes de lepra multibacilares: resultado de la duración del tratamiento. Fontilles - Rev. *Leprol.*, v.22, n.5, p.481-495, Mayo-Agosto, 2000

Two groups of MB leprosy patients, one treated to the point of smear negativity (TSN) and the other given therapy for fixed duration (24 doses of WHO MB regimen) (FDT), were compared for relapse rates during treatment and in the posttreatment period. During the follow-up of 980.2 person years in 260 patients treated with FDT, 20 relapses (2.04/100 patient years) were observed. In the other group of 301 patients, who received therapy till smear negativity, 12 relapses in 1085.46 person years (1.10/100 patients years) occurred. Comparison of survival rates (without relapse) has shown that although there is no difference up to 4 years, the risk of relapse was significantly higher on longer follow-up in the FDT group. In addition, when patients were compared on the basis of initial bacterial load, it was found that the relapse rates in patients with BI >_ 4 was significantly higher ($P < 0.001$) in the FDT group as compared to those receiving treatment till the point of smear negativity (4.29 versus 1.27/100 patient years). All the relapsed patients responded to retreatment with the same drug combination, indicating that the exacerbation in their condition was because of insufficient treatment. It is suggested that to prevent or reduce relapses, treatment where feasible would be continued till smear negativity, at least in patients with high BI.

GOLE, D, et al. "Outside project area leprosy cases in a ward of Mumbai. *Indian J. Leprosy*, v.71, n.4, p.471-475. Oct-Dec., 1999.

Analysis of newly registered smear-positive cases in a ward of the metropolitan city of Mumbai, which has a railway terminus during 1990-97 revealed that 72% of the patients came from outside the project area, most of them arising from the States of Uttar Pradesh, Bihar and Orissa.

They had unstable and temporary residences in the area and were employed in low income hard labour jobs. Nevertheless, it was found that their treatment completion rate was high. Using different approaches, eg. through the community leaders of footpath dwellers and railway platform dwellers, and those of different state language groups' colonies, the new entrants were examined periodically and simultaneously proper rapport was maintained with the medical practitioners of the ward for more referrals to leprosy clinic. Such special approach may have to be developed to tackle such situation in other metropolis in the country.

MITCHELL, P.D., MITCHELL, T.N. The age-dependent deterioration in light touch sensation on the plantar aspect of the foot in a rural community in India: implications when screening for sensory impairment. *Leprosy* Rev., v.71, n.2, p.169-178, June, 2000.

Regular testing for impaired sensation is important in the management of diseases that can cause progressive *nerve* damage, such *as* leprosy. It has been shown that light touch sensibility decreases with age in the hands of healthy individuals, but little research has been undertaken to assess possible changes in the feet in developing countries. This information is needed to allow an appropriate level of sensation to be chosen when screening for nerve damage in the foot. To clarify this, a cross-sectional study on male adults was carried out in the rural town of Salur, Andhra Pradesh, India. A range of Semmes-Weinstein monofilaments were employed at 12 locations on the foot to determine sensation to light touch stimuli in individuals from each decade of adult life. It was found that in this population, sensibility threshold in the foot increases with age and this was noted in both soft and callous skin. This shows the increase was due to neurological factors, not merely due to an increase in callous deposition with advancing age. In the majonty of individuals in their fifties and sixties, the callous skin at the forefoot and heel was unable to detect the 5.07 monofilament (equivalent to 8-12g), previously recommended as a method to screen for plantar neuropathy. All areas of all feet were able to detect the 5.46 filament (approximately 30g). The size of this study (54 individuals) prevents the determination of definitive normal ranges for each decade of life in this population. However, it does demonstrate the degree to which sensation deteriorates with age and could be used as an approximate guide when interpreting the results of sensory testing in similar rural areas of the developing world.

NÚÑEZ MARTÍ, J.M. Calidad odontológica en pacientes con Hansen. Fontilles - *Rev. Leprol.*, v.22, n.5, p.511-518, Mayo-Agosto, 2000.

W.H.O. insists that an effective health program should be based on the complete comprehension of the role of all the diferent factors involved in the development and maintenance of a particular way of life; health and other factors that can have influence in changing certain ways of living into other more healthier forms. A similar approach is applied to the needs of valuable information in relation to the environment and health.

The importance of prevention and health is emphasize in this paper and a health quality control program in odontology for the patients of Hansen's disease of the Sanatorium of Fontilles has been elaborated.

In this article the procedure is explained together with a detailed analysis of the problem, whose final aim is to conscience the patient to adopt daily methods for maintening a proper and healthy life style generally deteriorated in these patients due to disease.

SAYLAN, T. et aI. A scholarship project for the children of leprosy patients in Turkey. Leprosy Rev., v.71, n.2, p. 212-216, June, 2000.

Most of the leprosy patients in Turkey live in the rural areas of Eastern and South-Eastern Anatolia. Those living in the suburbs of the big cities of the Western parts of the country have come there by immigration. Nearly all patients are very poor; they have no land, or only a small amount of soil for cultivation. The incidence of deformities in our patients is high, excluding them from regular employment and a source of income. In Turkey, it is obligatory to attend primary school, but after that education has to be paid for, and the poor families of leprosy patients find it difficult to continue the education of their childreh. As the 'Society for the Struggle Against Leprosy', based in the Istanbul Leprosy Hospital at Bakirköy, we have developed a project to enable patients to continue sending their children to school, whilst at the same time asking the mothers to seek advice and guidance on family planning. The outset objective of this project was to enable children and young people, who otherwise have almost no chance of continuing education, to pursue education at secondary, high school and university levels. It was envisaged that in the long term educated children would be able to find a job and provide effective care and support for parents and other members of the family. This paper describes the administrative and other measures adopted and the results of the project from 1995 to 1998, during which a total of 545 children have been supported at an overall cost of US$ 107,378. The scholarship project has so far been remarkably successful in Turkey and it is hoped that it may provide a model for similar approaches in other countries. An unexpected and extremely encouraging finding has been that females now exceed males in this project and are increasing at all levels, including university entrance.

VISSCHEDIJK, J. et al. *Mycobacterium* leprae-millennium resistant! Leprosy control on the threshold of a new era (See comments). *Trop. Med.* Mt. *Health*, v.5, n.6, p.388-399, Jun., 2000.

Over the past decades, the conditions of leprosy control implementation have changed dramatically. Introduction of multidrug therapy, together with the global effort of the World Health Organization to eliminate leprosy as a public health problem, had a tremendous impact on leprosy control, particularly by decreasing the registered prevalence of the disease. At the beginning of the new millennium, leprosy control programmes face several new challenges. These relate not only to changes in the prevalence of the disease, but also to changes in the context of leprosy control, such as those created by health sector reforms and other disease control programmes. This review discusses current knowledge on the epidemiology of *Mycobacterium leprae* and some important aspects of leprosy control. It is argued that our understanding is still insufficient and that, so far, no consistent evidence exists that the transmission of leprosy has been substantially reduced. Sustainable leprosy control, rather than elimination, should be our goal for the foreseeable future, which also includes care for patients on treatment and for those released from treatment. This, however, requires new strategies.

DIAGNÓSTICO

HAIMANOT, R.T.; MELAKU, Z. Leprosy. *Curr. Opin. Neurol.*, v.13, n.3, p.317-322, Jun., 2000.

Leprosy is a unique infectious disease with a prolonged incubation period and a predilection for skin and nerves. The involvement of nerves by the primary infection as well as the immunologically mediated reversal reactions result in impairment of nerve function and severe disabilities. The introduction of the World Health Organization Multi Drug Therapy over the last two decades has produced dramatic changes in the management and control programmes of leprosy. A recent important contribution to the understanding of leprosy pathogenesis has been the elucidation of the molecular basis for the entry of Mycobacterium leprae into the Schwann cell and the peripheral nerve. Leprosy still remains the commonest cause of peripheral neuropathy in developing countries.

HOFFNER, R. J. ; ESEKOGWU, V. ; MALLON, WK. Leprosy in the emergency department. Acad. *Emerg. Med*, v.7, n.4, p.372-376, Apr., 2000.

OBJECTIVES: Los Angeles County-University of Southern Califomia Medical Center, like many large urban hospitals, has a large immigrant population from regions of the world where leprosy is endemic. Emergency physicians (EPS) in these settings can expect to encounter leprosy patients. This study reviewed the emergency department (ED) course of patients with confirmed leprosy in an attempt to describe the most common presenting patterns so that future cases can be more easily recognized.

METHODS: This was a retrospective chart review of all patients followed in the Hansen's disease clinic. Demographics, leprosy type, clinical presentations to the ED, and medications were recorded.

RESULTS: Of the total number of patients (415), most were of Mexican (52%), Filipino (15%), Vietnamese (14%), and Chinese (5%) origin. Leprosy was classified as lepromatous (56%), borderline (40%), and tuberculoid (4%). There were a total of 118 ED visits by 74 patients. The mean age was 46 years, with 51% male and 49% female. Dermatologic (68%), neurologic (23%), and ophthalmologic (9%) complaints were the most common reasons for ED presentation related to leprosy. The EP did not elicit a history of leprosy in 34% of those patients followed in the leprosy clinic. The ED diagnosis of leprosy was made in 3 of 15 (20%) undiagnosed cases. Of the 63 patients prescribed medications in the leprosy clinic at the time of their ED visits, 22 (35%) ED charts did not report leprosy drugs.

CONCLUSION: Patients with leprosy present to U.S. EDs, and new cases can be identified. Early recognition is important given leprosy's devastating consequences, major drug side effects of medications used for treatment, and improved prognosis with multidrug therapy. A history of leprosy and associated medications are often not documented in the ED chart, which may reflect a continued fear of stigmatization among these patients.

KHAW, G.E. Neural leprosy - a case report. *Med. J. Malaysia*, v.53, n.l, p.114-116, Mar., 1998.

Neural leprosy is rare. This is a report of a 63-year-old Indian man who had long standing multiple peripheral neuropathy. The slit skin smear for acid-fast bacilli of *Mycobacterium leprae* was positive. The skin and nerve biopsies were normal. He was treated with rifampicin, dapsone and dofazimine.

MARTINOLI, C. et al. US and MR imaging of peripheral nerves in leprosy. *Skeletal Radiol.*, v.29, n.3, p.142-150, Mar., 2000.

OBJECTIVE: To analyze peripheral nerves with ultrasonography (US) and magnetic resonance imaging (MR) in leprosy and assess the role of imaging in leprosy patients.

DESIGN AND PATIENTS: Fifty-eight nerves with abnormal clinical features or electromyograms were examined in 23 leprosy patients by means of gray-scale US, Doppler US and MR imaging. Image analysis included: measurement of nerve cross-sectional area; assessment of nerve structure and MR signal intensities; identification of nerve compression within osteofibrous tunnels; detection of endoneural color flow signals and Gd-DTPA enhancement. Correlations were made with clinical findings and a control group of 20 subjects. Fourteen nerves in active reversal reaction were followed up after therapy.

RESULTS: Leprosy nerves were classified into three groups based on imaging appearance: group I consisted of 17 normal-appearing nerves; group II, of 30 enlarged nerves with fascicular abnormalities; group III, of 11 nerves with absent fascicular structure. Group II nerves were from patients subjected to reversal reactions; 75% of patients with group III nerves had a history of erythema nodosum leprosum. Nerve compression in osteofibrous tunnels was identified in 33% of group II and 18% of group III nerves. Doppler US and MR imaging were 74% and 92% sensitive in identifying active reactions, based on detection of endoneural color flow signals, long T2 and Gd enhancement In 64% of cases, follow-up studies showed decreased color flow and Gd uptake after steroids and decompressive surgery.

CONCLUSIONS: US and MR imaging are able to detect nerves abnormalities in leprosy. Active reversal reactions are indicated by endoneural color flow signals as well as by an increased T2 signal and Gd enhancement. These signs would suggest rapid progression of nerve damage and a poor prognosis unless antireactional treatment is started.

RAMESH, V., BEENA, K.R., MUKHERJEE, A. Sporotrichoid presentations in leprosy. *Clin. Exp. Dermatol.*, v.25, *n.3, p.227-230*, May, 2000.

Two adult patients of leprosy, one woman and one man, presented with a clinical picture simulating sporotrichosis. The skin and regional nerve trunk was affected in one, and in the other the disease was confined to the nerve. Both had features of an upgrading reaction following anti-leprosy therapy; this was seen as erosion and scarring of the plaque, and acute onset of abscesses along the easily palpable and thickened nerve that ruptured through the skin. The diagnosis was supported by histopathology. In the light of other infections that give rise to a sporotrichoid pattern of infection it is concluded that leprosy should also be included in this category so that early diagnosis and use of corticosteroids can be implemented quickly to prevent nerve destruction.

SAUNDERSON, P., GROENEN, G. Qué signos físicos son más útiles para el diagnóstico de la lepra? Propuesta basada en la experiencia del proyecto AMFES, Alert Etiopía. *Fontilles - Rev. Leprol.*, v.22, n.4, p.383-395, Enero-Abril, 2000.

As integration of leprosy control programmes proceeds, general health staff will have responsability for the diagnosis of most new cases of leprosy. The training required by these workers has not yet been set out in detail. In this paper the criteria for making the diagnosis of leprosy in the AMFES cohort of 594 new cases are examined. Since this study does not include details of suspects in whom leprosy was excluded on clinical grounds, true sensitivity and specificity values cannot be calculated, but the positive predictive value of the diagnostic criteria can be measured. Sensory loss in a typical skin patch is the most important sign of early leprosy, but was not present in 132 (49%) of the 268 cases with a positive skin smear. Thickening of the ulnar nerve is a valuable sign of leprosy in Ethiopia. It can be taught to health workers, who can practise by examining their own ulnar nerves. It is more likely to be present than nerve function impairment and is particularly important when skin smears are difficult to do or are unreliable. We recommend that five basic signs are used, the presence of any two being diagnostic of leprosy:

- Skin lesion(s) consistent with leprosy.
- Loss of sensation in such a lesion.
- Thickening of either ulnar nerve.
- Loss of sensation in the palm of the hand or the sole of the foot.
- The presence of acid-fast bacilli in skin smears.

Exact policies for the diagnosis of leprosy should be worked out and validated for each national programme.

EPIDEMIOLOGIA

BRUCE, S. et al. Armadillo exposure and Hansen's disease: an epidemiologic survey in southern Texas. *J. Am. Acad. Dermatol.*, v.43, n.2, pt 1, p.223-228, Aug., 2000.

BACKGROUND: Naturally occurring leprosy has been demonstrated in wild nine-banded armadillos (Dasypus novemcinctus). This suggests a possible mode of transmission of human leprosy in regions where armadillo contact is prevalent.

OBJECTIVE: Our purpose was to study the possible relationship between armadillo exposure and Hansen's disease.

METHOD: One hundred one patients (67 men, 34 women) with established Hansen's disease seen in the Hansen's Disease Clinic in Houston, Texas, were questioned about their exposure to armadillos. These patients were divided into two groups: Asian (n=32) and non-Asian (n=69). RESULTS: Seventy-one percent of the non-Asian patients surveyed reported either direct or indirect armadillo exposure. None of the Asian patients reported armadillo exposure (P <.001). Of the non-Asian patients, 75.4% had lepromatous disease versus 50.0% of the Asian patients (P <.001). The average age at diagnosis for the non-Asian group with Hansen's disease in this study was 51 versus 38 years for the Asian group (P <.001).

CONCLUSION: Although it is yet to be determined whether direct transmission from the armadillo to human occurs it is likely based on the high incidence of armadillo exposure in non-Asian patients with Hansen's disease in our study population that this animal acts as a reservoir for human disease. However, the Asian patients reporting no known armadillo exposure likely obtained the disease from person-to-person contact in their respective countries of origin where Hansen's disease has a much higher prevalence.

CHEN, X. S. et al. Leprosy in China: delay in the detection of cases. *Ann. Trop. Med. Parasitol.*, v.94, n.2, p.181-188, Mar., 2000

In a national survey in China, 27,928 cases of leprosy detected by the health authorities between 1984 and 1998 were investigated. The delay between onset of symptoms (estimated from each case's recall) and confirmed diagnosis was < or = 2 years for 55.1% of the new patients but > 10 years for 7.0%, with a median value, overall,• of 22.0 months. The median delay was longer: (1) for the multibacillary cases than the paucibacillary; (2) among farmers than among factory workers; (3) among some nationalities than among others (being longest among the Tu and shortest among the Wei); and (4) for some methods of case-detection than for others. Over the study period, the mean delay decreased with time. The delay was greatest in the areas where leprosy was endemic and/or where access to health services was poor. The later the cases were detected the more likely they were to show disability. Leprosy cases are still going undetected in China, although, over the last 14 years, case-finding has significantly improved.
Age, occupation, nationality, leprosy type and detection method all appear to affect the delay.

PEREIRA, E. dos S. et al. Campana para la eliminación de la lepra Amazonas-Brasil, 1997. *Fontilles - Rev. Leprol.*, v.22, n.4, p.377-382, Enero-Abril, 2000.

A leprosy elimination campaign (LEC) was carried out in 15 endemic areas of Amazonas State, Brazil, in 1997. The LEC concentrated effort to detect leprosy cases during a multi-vaccination national campaign for serious public health problems other than leprosy, such as polio, diphtheria, hepatitis, measles, etc. The national campaign involved intensive population mobilization, giving a valuable opportunity to examine people for leprosy. The LEC personnel included 2.964 individuals (municipal and state health workers and community volunteers), distributed in 688 health units and 53 reference health centers. As a result of the LEC, 74.814 person-to-person communications in the community were given; 10.297 clinical skin examinations were detected on the day of the campaign in urban areas of the municipalities. This total was low, compared to results in other states of Brazil, possibly due to the development of health education activities and regular community services in the state of Amazonas since 1987 and to the early implementation of WHO multiple drug therapy (MDT) from 1982 onwards. Despite the fact that the LEC was carried out only in the urban areas of the municipalities, the finding of no cases of leprosy in 7 out of 15 of them was surprising and may indicate that the prevalence of hidden cases of leprosy is not all that high, at least in these areas of the Amazonas State.

GENÉTICA

MATSUOKA, M. et al. *Mycobacterium* leprae typing by genomic diversity and global distribution of genotypes. *Int. J. Lerposy*, v.68, n.2, p.121-128, June, 2000.

The genetic diversity and related global distribution of 51 Mycobacterium leprae isolates were studied. Isolates

were obtained from leprosy patients from 12 geographically distinct regions of the world and two were obtained from nonhuman sources. Polymerase chain reaction (PCR) followed by DNA sequencing was performed targeting the *rpoT* gene of M. *leprae.* Isolates were classified into two groups based on the number of tandem repeats composed of 6 base pairs in the *rpoT* gene. Isolates from Japan (except Okinawa) and Korea belonged to one group, while those from Southeast Asian countries, Brazil, Haiti and Okinawa in Japan belonged to a second genotype. M. *leprae* obtained from two nonhuman sources (an armadillo and a mangabey monkey) revealed the latter genotype. These results demonstrate the genetic diversity of M. *leprae* and the related genotype-specific distribution in the world.

HISTÓRIA

BRISOU, B. Paul-Louis Simond et la Guyane. *Bull. Soc. Pathol. Exot.,* v.92, n.5, pt.2, p.379-380, Dec., 1999.

On the occasion of the hundredth anniversary of P.-L. Simond's discovery of the flea as vector of plague, the author recounts several episodes of the history of French Guyana where P.-L. Simond had his first position, starting with the official establishment of France in Cayenne in July 1898. During his stay in Guyana (1882-1886), P.-L. Simond directed the leper hospital in Acarouany, near Saint-Laurent du Maroni; it was there that he found the subject for his doctoral dissertation in medicine which he defended after completing his studies at the navy medical school of Bordeaux and which was entitled: "Leprosy and its means of spread in French Guyana".

HAAS, C. J. et al. Detection of leprosy in ancient human skeletal remains by molecular identification of *Mycobacterium leprae. Am. J. Clin. Pathol.,* v.114, n. 3, p.428-436, Sep., 2000.

We isolated ancient DNA from skeletal remains obtained from a South German ossuary (approximately 1400-1800 AD) and from a 10th century Hungarian cemetery partially indicating macromorphologic evidence of leprosy. In samples taken of 2 skulls from Germany and of 1 hard palate from Hungary, *Mycobacterium leprae*-specific fragments of RLEPI and RLEP3 were amplified using polymerase chain reaction (PCR), thereby confirming their specificity by sequencing. In another case, PCR with primers targeting 156110 of Mycobacterium *tuberculosis* gave positive results only for a mandibular specimen. No signal for any mycobacterial DNA was observed in samples from 2 Hungarian foot bones. In ancient material, osseous involvement of M leprae may be detected and distinguished from other mycobacterial infections by specific PCR. In the small bones of leprous hands and feet, not enough M leprae DNA seems to be present for detection. This supports the view that rhinomaxillary leprous alterations result from direct bacterial involvement, while osseous mutilations of hands and feet result from a nervous involvement and/or secondary infections due to small lacerations of the overlying soft tissues.

MORENO-TORAL, E.; LOPEZ-DIAZ, M. T. Disertaciones sobre la lepra en la Sevilla de finales del Siglo de las Luces. Rev. *Neurol.,* v.30, n.9, p.890-896, May 1-15, 2000.

INTRODUCTION: Leprosy is a well-known disease from ancient history. Society reacts violently due to the fear of infection, and the fact that it causes appalling physical mutilation. It is produced by *Mycobacterium leprae,* which only affects the nervous system of human beings.

DEVELOPMENT: The norms and examinations that for many years were practiced upon those suspected of being infected by the leprosy organism are based almost always in a series of requirements that were in keeping with cases of verification, thus named the 'declaration of leprosy. Doctors in the 18th Century, conscious of the consequences of the disease, established a diagnostic procedure for leprosy. But as a result of the medical limitations of the time, and the innate risk of examination of the sufferer in the early phases and their changing symptoms, they adopted a cautious stance and on occasion were overly prudent. These problems remained • established in different dissertations presented in the Royal Society of Medicine and other Sciences of Seville during the last third of the 18th Century. A total of eight dissertations related to this disease are analyzed. Two presented by Doctor Bonifacio Ximenez de Lorite in 1765 and 1788 are noteworthy due to the contents and quality.

IMUNOLOGIA

ADAMS, L.B.; JOB, C. K.; KRAHENBUHL, J. L. Role of inducible nitric oxide synthase in resistence to *Mycobacterium leprae* in mice. *Infect. Immun.,* v.68, n.9 p.5462-5465, Sep., 2000.

The manifestation of leprosy in humans is largely determined by host immunity to *Mycobacterium* leprae and is a model for immunoregulation in a human disease. However, animal models available for exploration of the leprosy spectrum are inadequate. This study explored M. *leprae* infection in mice deficient in inducible nitric oxide

synthase, and this report describes elements resembling borderline tuberculoid leprosy in humans.

BOUCHER, P.; MILLAN, J.; PARENT, M., MOULIA-PELA, J P. Essai comparé randomisé du traitement médical et médico-chirurgical des névrites hanséniennes. Acta *Leprol., v.11*, n.l, p.171-177, 1999.

The aim of the study was to compare the results of the medical treatment alone and of the medico-surgical treatment on leprous neuritis. The patients were followed-up during 2 years, with regular neurological évaluations. The statistical study was performed using the Tukey test.

Ninety-three nerves (ulnar, median, common peroneal and posterior tibial) with a deficit of less than 6 months duration have been studied in 31 leprosy patients. All the patients were treated by steroids but in some of them a nerve surgical decompression was performed.

An improvement of the sensitive and motor deficit was observed in both groups. No significant statistical differences appeared between the 2 groups according to the nerve involved, the duration of the deficit, the form of leprosy and the type of antibacillary treatment. However, the medico-surgical treatment had a significant better result on pain and on major but incomplete nervous involvement.

This study included a limited number of nerves, thus, it would be useful to perform others randomized assays to better define the indications of surgical decompression in the management of leprous neuritis.

PANUNTO-CASTELO, A. et al. The Rubino test for leprosy is a beta2-glycoprotein 1-dependent antiphospholipid reaction. *Immunology*, v.101, n.l, p.147-153, Sep., 2000.

We describe the isolation and identifiçation of three components required for the Rubino reaction (RR), which is the rapid sedimentation of formalinized sheep redblood cells (SRBC) initiated by serum from leprosy patients with defective *Mycobacterium* Ieprae-specific cell immunity. The Rubino reaction factor (RRF) required for this phenomenon, previously identified as an immunoglobulin M (IgM), was purified from leprosy patient serum by adsorption to formalinized SRBC. Purified RRF IgM, when added to formalinized SRBC, did not produce a positive RR. However, when the contact was carried out in the presence of normal human serum (NHS), cells rapidly sedimented. The purified cofactor from NHS contained two components of 70 000 and 50 000 molecular weight (MW), as determined by sodium dodecyl sulphate-polyacrylamide gel electrophoresis (SDS-PAGE). The latter was recognized by the RRF IgM on immunoblot and its N terminal sequence indicated that it was beta2-glycoprotein 1 (beta2-GP1), an anionic phospholipid-binding protein. Methanol-treated formalinized SRBC did not support the RR. Thinlayer chromatography of an extract of membranes indicated that the SRBC ligand was a cell-surface phospholipid. Cardiolipin inhibited the RR. These data demonstrate that the RR involves a trimolecular interaction in which IgM, beta2-GP1 and an SRBC phospholipid participate. By analogy with the antiphospholipid antibodies (anti-PL) that occur in autoimmune processes, serum samples from 29 systemic lupus erythematosus patients with high levels of anticardiolipin antibodies were submitted to the RR. A positive RR was obtained for 45% (13 of 29 patients). These results modify the paradigm of the absolute specificity of the RR for leprosy and demonstrate that RRF [gm is a beta2-GP1-dependent anti-PL.

SHARMA, P et al. Reactional states and neuritis in multibacillary leprosy patients following MDT with/without immunotherapy with *Mycobacterium* w anti-leprosy vaccine. *Leprosy Rev.*, v.71, n.2, p,193-205, June, 2000.

A vaccine based on autoclaved *Mycobacterium* w was administered, in addition to standard multidrug therapy (MDT), to 157 untreated bacteriologically positive, lepromin negative multibacillary leprosy patients, supported by a well matched control group of 147 patients with similar type of disease, who received a placebo injection in addition to MDT. The MDT was given for a minimum period of 2 years and continued until skin smear negativity, while the vaccine/placebo was given at 3-monthly intervals up to a maximum of eight doses. The incidence of type 2 reaction and neuritis during treatment and follow-up showed no statistically significant difference in the vaccine and placebo groups. The incidence of type 1 reaction (mild in most cases), however, was higher in the vaccine group (P = 0.041, relative risk ratio 1.79), considering LL, BL and BB leprosy types together, and considerably higher (P = 0.009) in LL type, probably because of confounding due to higher number of patients with previous history of reaction in this group. The occurrence of reactions and neuritis in terms of single or multiple episodes was similar in the vaccine and placebo groups. The association of neuritis and reactions, as well as their timing of occurrence (during MDT or follow-up), was also similar in the two groups, with more than 90% of accurrences taking place during MDT. The incidence of reversal reaction was significantly higher among the males in the vaccine group (34.5% versus 8.3%, P=0.019). Patients with high initial BI (4.1-6.0) showed higher incidence of reactions (70.3%) as compared to those with

medium (2.1-4.0) and low (0.3-2.0) BI where the reactions were observed with a frequency of 56,1% and 38.8%, respectively. However, unlike reactions, neuritis incidence did not seem to be affected by initial BI to the same extent in the vaccine group, with frequencies of 35.3%, 36.3% and 25.9% in the three mentioned BI ranges. Overall, the vaccine did not precipitate reactional states and neuritis over and above that observed with MDT alone.

SHARMA, P. et al. Induction of lepromin positivity and immunoprophylaxis in household contacts of multibacillary leprosy patients: a pilot study with a candidate vaccine, Mycobacterium w. *Int. J. Leprosy,* v.68, n.2, p.136-142, June, 2000.

We screened 487 household contacts of multibacillary (MB) patients for evidence of disease and their lepromin status. From the 444 results available, 302 (68.02%) were lepromin positive and 142 (31.98%) were lepromin negative on initial testing. The initial lepromin status as assessed in the group of 54 contacts having disease at the outset showed 24 out of 46 (52.2%) to be lepromin positive and 22 of 46 (47.8%) to be lepromin negative. In the same group, among 24 lepromin positives, 22 (91.7%) had paucibacillary (PB) and 2 (8.3%) had multibacillary (MB) disease; among the lepromin negatives, 12 (54.5%) had PB and 10 (45.5%) had MB disease. Out of 72 initially lepromin-negative contacts administered Mycobacterium w vaccine and followed up, the cumulative percentages show that 53 (73.6%) converted to positivity after a single dose, 10 (87.5%) after a second dose and 67 (93.1%) after the third dose. The incidence of new cases with leprosy was 8 out of 231 (3.46%) among leprominpositive contacts and 5 out of 93 (5.38%) among lepromin-negative contacts administered *Mycobacterium* w vaccine. Among 231 lepromin-positive contacts, the new cases occurred in those with a 1+ and 2+ lepromin response only, and no case occurred among 51 contacts with a 3+ lepromin response. The incidence among lepromin-positive contacts in this study (3.46%) was similar to the observations in two other studies: 3.2% by Dharrnendra, et al. and 6.9% by Chaudhary, et al. However, the incidence among lepromin-negative contacts administered Mycobacterium w vaccine was significantly lower than that observed among lepromin-negative contacts not administered any vaccination in the other two studies (14.1% by Dharmendra, et al. and 29.0% by Chaudhary, et al.). To conclude, although a study of small sample size, the preliminary evaluation indicates that administration of Mycobacterium w vaccine seems to have the potential to reduce the incidence of leprosy among household contacts of leprosy patients. More explicit results about the vaccine will be available from the ongoing field trials in Kanpur Dehat in the near future.

WALSH, D. S. et al. Cutaneous delayed-type hyspersensitivity responsiveness in lepromatous and borderline lepromatous leprosy patients as determined by MULTITEST CMI. *Southeast Asian J. Trop. Public* Helath, v.30, n.3, p.518-526, Sep., 1999.

To assess cell mediated immune (CMI) function in patients with lepromatous and borderline lepromatous leprosy (LL and BL), 35 patients were examined with the MULTITEST CMI system to evaluate cutaneous delayed-type hypersensitivity (DTH) responsiveness to 7 recall antigens. Reactions were assessed quantitatively and qualitatively. In addition, patients were classified as "responsive" (> or = 2 positive reactions), "hypo-responsive" (1 positive reaction), or anergic. Only hyporesponsive and anergic patients were re-tested. In 23 patients tested before treatment started (Group 1), 9 were responsive, 4 hypo-responsive, and 10 anergic. Upon re-testing, 10 of the 14 hyporesponsive-anergic subjects showed improvement. In 12 patients assessed after therapy initiation (Group 2), 9 were responsive and 3 others became responsive upon re-testing. Quantitative assessment indicated variable deficiencies in cutaneous DTH reactivity that, in many cases, improved with therapy. Correlations between reactivity and disease severity (LL versus BL) or duration of disease were not observed. The MULTITEST CMI system provided a convenient, safe, and reproducible method to assess cutaneous DTH responsiveness in LL and BL patients. Our findings indicated that most LL and BL patients are able to generate detectable but generally fewer and less robust cutaneous DTH responses to recall antigens, many improving with therapy. However, a semi-quantitative classification whereby patients that reacted to 2 or more antigens were considered "responsive" showed little difference between patients and controls. Overall, the data support the contention that deficits in cutaneous DTH responsiveness probably neither predispose nor necessarily accompany lepromatous disease, a practical consideration as efforts to develop a leprosy vaccine continue.

MICROBIOLOGIA

SCOLLARD, D. M. Association of Mycobacterium leprae with human endothelial cells *in vitro. Lab. Invest.*, v.80, n.5, p.663-669, May, 2000.

Endothelial cell infection by *Mycobacterium* leprae has long been described histologically in all types of leprosy and in some of the acute reactions occurring in this disease. Recent evidence from experimental lepromatous neuritis indicates that M. *leprae* colonizes endothelial cells of epineural blood vessels even in sites of minimal infection, suggesting that interaction between these cells and M. leprae may play an important role in the selective localization of this organism to peripheral nerve. To begin to study the mechanisms involved, we have examined the interaction between M. *leprae* and human umbilical vein endothelial cells (HUVEC) in vitro using light microscopy, scanning and transmission electron microscopy, and confocal laser scanning microscopy. When M. *leprae* were added to confluent monolayers of HUVEC, uptake increased slowly to a maximum at 24 hours. Maximal percentages of infected cells were similar at ratios of organisms:cell over a range of 25:1 to 100:1. The bacilli appeared to lie within membrane-bound vacuoles at all time points. The kinetics of association of *M. leprae* with HUVEC are much slower than has previously been observed with macrophages, possibly due to differences in the binding of M. leprae. Compared with other pathogens that infect endothelial cells, M. *leprae* also appear to be ingested more slowly, and to a more limited degree. The receptors involved in M. *leprae* binding to endothelial cells and the impact of intracellular infection by M. leprae on these cells remain to be determined.

SPIERINGS, E. et al. Novel mechanisms in the immunopathogenesis of leprosy nerve damage: the role of Schwann cells, T cell and *Mycobacterium leprae. Immunol. Cell. Biol.*, v.78, n.4, p.349-355, Aug., 2000.

The major complication of reversal (or type 1) reactions in leprosy is peripheral nerve damage. The pathogenesis of nerve damage remains largely unresolved. In situ analyses suggest an important role for type 1 T cells. *Mycobacterium leprae* is known to have a remarkable tropism for Schwann cells that surround peripheral axons. Reversal reactions in leprosy are often accompanied by severe and irreversible nerve destruction and are associated with increased cellular immune reactivity against M. leprae. Thus, a likely immunopathogenic mechanism of Schwann cell and nerve damage in leprosy is that infected Schwann cells process and present antigens of M. *Leprae* to antigen-specific, inflammatory type 1 T cells and that these T cells subsequently damage and lyse infected Schwann cells. Previous studies using rodent CD8+ T cells and Schwann cells have revealed evidence for the existence of such a mechanism. Recently, a similar role has been suggested for human CD4+ T cells. These cells may be more important in causing leprosy nerve damage in vivo, given the predilection of M. leprae for Schwann cells and the dominant role of CD4+ serine esterase+ Thl cells in leprosy lesions. Antagonism of molecular interactions between M. *leprae*, Schwann cells and inflammatory T cells may therefore provide a rational strategy to prevent Schwann cell and nerve damage in leprosy.

OFTALMOLOGIA

LEWALLEN, S. et al. Progression of eye disease in "cured" leprosy patients: implications for understanding the pathophysiology of ocular disease and for addressing eyecare needs. *Brit. J. Ophthalmol.*, v.84, n.8, p.817-821, Aug., 2000.

BACKGROUND: Ocular damage in leprosy is due either to nerve damage or infiltration by mycobacteria. There is currently little information about the magnitude and nature of incident ocular pathology in cured leprosy patients. This information would increase our understanding of the pathophysiology of ocular involvement in leprosy and help in developing programmes to address the eyecare needs of leprosy patients who have been released from treatment The cumulative incidence of leprosy related ocular pathology and cataract was measured during an 11 year follow up period in cured leprosy patients released from treatment in Korea.

METHODS: In 1988 standardised eye examinations were performed on 501 patients in eight resettlement villages in central South Korea. In May 1999 standardised eye examinations were repeated in this population.

RESULTS: Among the patients in whom there was no sight threatening leprosy related ocular disease (lagophthalmos, posterior synechia, or keratitis) in 1988, 14.7% developed one or more of these conditions. Overall, among those with no vision reducing cataract in 1988, 26.4% had developed a vision reducing lens opacity in at least one eye. Among patients examined in both 1988 and 1999, 14.3% developed visual impairment and 5.7% developed blindness.

CONCLUSION: This study demonstrates that leprosy related ocular pathology progresses in some patients even after they are cured mycobiologically. The progressive leprosy related lesions are the result of chronic

nerve damage; ocular lesions due to infiltration by Mycobacterium leprae did not develop. Based on the factors found to be associated with development of the most visually significant findings (posterior synechia, keratitis, and cataract) certain patients should be targeted at discharge for active follow up eye care. We suggest that patients with lagophthalmos (even in gentle closure), trichiasis, small pupils, and posterior synechiae should be screened regularly for the development of lagophthalmos in forced dosure, keratitis, and cataract.

MAURIN, J.F., et al. La cecite d'origine corneenne en milieu tropical. *Med Trop.(Mars),* v.55, n.4, pt 2, p.445-449, 1995.

Corneal disease is the second most common cause of blindness in tropical countries after cataract. It mainly strikes children who are exposed to numerous infectious agents against which they are unprotected due to the absence of basic health care. In high risk groups, the incidence of childhood corneal-related blindness is more than 20 times higher than in developed countries. There are many causes of corneal-related blindness. Endemic trachoma persists in some areas and inflammatory forms can lead to blindness. Eradication requires instillation of antibiotics in the eye, improvement of sanitary conditions, and campaigns against promiscuity. Xerophthalmia can induce blindness by perforation of the cornea in children with vitamin A deficiency. Measles, herpes simplex keratitis, and corneal ulcer that progresses to bacterial or fungal infections, or to amebic keratitis are also major causes of corneal-related blindness. The incidence of onchocerciasis is decreasing thanks to treatment with ivermectin and programs to control simulium. Neonatal gonococcal ophthalmia and leprosy-associated ocular disease can also lead to blindness. This overview of the various causes illustrates the dose correlation between the level of life and living conditions and the occurrence of corneal-related blindness in tropical areas.

PATOLOGIA

HONG, S. M. et al. Clinicopathologic analysis of 124 biopsy-proven peripheral nerve diseases. *J.* Korean Med. Sci., v.15, n.2, p.211-216, Apr., 2000.

We reviewed clinical, histological and ultrastructural findings of 124 cases of sural nerve biopsy specimens to delineate the trends of peripheral nerve diseases in our institute. Eighty-one were men and 43 were women. We categorized them into five groups: specific diagnosis (66 cases, 53.2%), axonal degeneration type (47 cases, 37.9%), demyelinating type (4 cases, 3.2%), mixed axonal degeneration-demyelinating type (6 cases, 4.8%) and normal (1 case, 0.9%). Cases with specific diagnosis included 21 inflammatory demyelinating polyneuropathy (15 chronic inflammatory demyelinating polyradiculoneuropathy, 6 Guillain-Barre disease), 13 hereditary motor and sensory neuropathy (7 Charcot-Marie-Tooth type **I**, 6 Charcot-Marie-Tooth type II), 10 vasculitis, 6 toxic neuropathy, 4 leprosy, 3 diabetic neuropathy, 2 alcoholic neuropathy, 1 Fabry's disease and other specific diseases (5 cases). In our cases, the proportion of specific diagnoses was higher, while the proportion of demyelinating peripheral neuropathies and normal were lower than those of Westem series. The results of this study indicate that 1) a dose clinicopathologic correlation is important to make a precise diagnosis of peripheral nerve biopsy, 2) Biopsy under strict indication may reduce unnecessary histologic examination, 3) There is no difference in disease pattern of peripheral neuropathy between Western people and Koreans.

MEMPEL, M. et al. Comparison of the T cell patterns in leprous and cutaneous sarcoid granulomas. Presence of Valpha24-invariant natural killer T cells in T- cell-reactive leprosy together with a highly biased T cell receptor Valpha repertoire. *Am. J. Pathol.,* v.157, n.2, p.509-523, Aug., 2000.

The T-cell-reactive (eg, tuberculoid and reversal) forms of leprosy represent a well-defined granulomatous reaction pattern against an invading pathogen. The immune response in cutaneous sarcoidosis is a granulomatous condition that pathologically is very similar to T-cell reactive leprosy. However, it lacks a defined causative agent. In view of the role of NKT cells in murine granulomas induced by mycobacterial cell walls, we have searched for the presence of NKT cells in the cutaneous lesions of both leprosy and sarcoidosis. These cells were present in T-cell-reactive leprosy but were undetectable in cutaneous sarcoidosis. We have also studied the TCR Valpha repertoire in the two diseases. In addition to Valpha24(+) NKT cells, all patients with T-cell-reactive leprosy showed a very restricted T-cell-reactive Valpha repertoire with a strong bias toward the use of the Valpha6 and Valphal4 segments. Valpha6 and Valphal4(+) T cells were polyclonal in terms of CDR3 length and Valpha usage In contrast, most sarcoidosis patients showed a diverse usage of Valpha chains associated with clonal or oligoclonal expansions reminiscent of antigen- driven activation of conventional T cells. Thus the origin and perpetuation of the two kinds of granulomatous lesions appear to depend on altogether distinct T-cell recruiting mechanisms.

SINGH, N.; BIRDI, T. J.; ANTIA, H. H. Differential in vitro modulation of Schwann cell proliferation by *Mycobaterium* leprae and macrophages in the murine strains, Swiss withe and C57BI/6. *J. Peripher. New Syst.*, v.3, n.3, p.207-216, 1998.

The special susceptibility of Schwann cells (SCS) to parasitization by M. leprae and of macrophages to M. leprae-induced defects implicates them in leprous nerve pathogenesis. SC proliferation is an important prerequisite for peripheral nerve regeneration and is regulated by a number of secretory factors. Several of these factors are secreted by SCS themselves as well as by the macrophages which are recruited at the site of lesion to assist in regeneration. SC proliferation, as indicated by 3H-thymidine incorporation, was therefore studied in response to M. *leprae* infection and in the presence of macrophages in order to determine the role of SC in leprous neuropathy. Cells derived from two strains of mice, Swiss White (SW) and C57BI/6 were used, as macrophages from these strains have been shown to differ in their response to M. leprae; such differences are similar to those observed in macrophages from lepromatous and tuberculoid leprosy patients, respectively. Infection with M. *leprae* for a duration of 9 days resulted in reduced proliferation of SCS from SW strain, while SCS from C57BI/6 remained unaffected. However, in the presence of macrophages, SCS from both strains not only showed enhanced proliferation, but SW SCS also overcame the M. leprae-induced suppression of their proliferation. Altered SC proliferation, therefore, can be implicated as a factor in leprous nerve pathogenesis. The strain variation observed in the response of SCS indicate different nerve damage mechanisms in lepromatous and tuberculoid patients.

YAMAUCHI, P. S, et al. A role for CD40-CD40 ligand interactions in the generation of type 1 cytokine responses in human leprosy./ *Immunol.*, v.165, n.3, p.1506-1512, Aug. 1, 2000.

The interaction of CD40 ligand (CD4OL) expressed by activated T cells with CD40 on macrophages has been shown to be a potent stimulus for the production of IL-12, an obligate signal for generation of Th1 cytokine responses. The expression and interaction of CD40 and CD4OL were investigated in human infectious disease using leprosy as a model. CD40 and CD4OL mRNA and surface protein expression were predominant in skin lesions of resistant tuberculoid patients compared with the highly susceptible lepromatous group. IL-12 release from PBMC of tuberculoid patients stimulated with *Mycobacterium leprae* was partially inhibited by mAbs to CD40 or CD4OL, correlating with Ag-induced up-regulation of CD4OL on T cells. Cognate recognition of M. leprae Ag by a T cell clone derived from a tuberculoid lesion in the context of monocyte APC resulted in CD4OL-CD40-dependent production of IL-12. In contrast, M. leprae-induced IL-12 production by PBMC from lepromatous patients was not dependent on CD4OL-CD40 ligation, nor was CD4OL up-regulated by M. *leprae.* Furthermore, IL-10, a cytokine predominant in lepromatous lesions, blocked the IFN-gamma up-regulation of CD40 on monocytes. These data suggest that T cell activation in situ by M. *leprae* in tuberculoid leprosy leads to local up-regulation of CD4OL, which stimulates CD40-dependent induction of IL-12 in monocytes. The CD40-CD4OL interaction, which is not evident in lepromatous leprosy, probably participates in the cell-mediated immune response to microbial pathogens.

PSICOLOGIA

BAUMANN, H. et al. Psychosoziale, okonomische and physische situation ehemaliger leprapatienten in Uganda. *Gesundheitswesen*, v.62, n.6, p.342-346, Jun., 2000.

This study investigates the general living condition, the psychosocial, economical and physical situation of 161 leprosy patients previously treated at the St. Francis Leprosy Hospital at Buluba/Uganda, basing on interviews and clinical examinations. The results point to a negative correlation between general education and specific knowledge of leprosy and highlight a serious psychosocial situation of previously treated leprosy patients. The most important conclusion is that besides leprosy-specific chemotherapy, lifelong extensive general and leprosy-specific health education and posttreatment care can prevent disabilities in leprosy patients.

OLIVEIRA, M. H. de; GOMES, R.; OLIVEIRA, C. M, de. Hanseníase e sexualidade: convivendo com a diferença. Rev. Lat. *Am. Enfermagem,* v.7, n.1, p.85-91, Jan., 1999.

The present article is based on a research that analysed the social effects of leprosy in men and women, identifying the effects in their family life. 10 men and 10 women with leprosy registered in a specific health service were part of this study. The methodology was qualitative, through semi-structured interviews. Data analysis pointed out the fact of the disease perceived as a reason for family disorders and, also, impairing these subjects sexual relationships.

REABILITAÇÃO

SOW, S.O.; TIENDREBEOGO, A.; HAMED OOULD, B.; LIENHART, C.; PONNIGHAUS, J.M. Les infirmités observées chez les nouveaux cas de lèpre dépistés dans le district de Bamako (Mali) en 1994. Acta *Leprol.*, v.11, n.4, p.161-170, 1999.

Our study concerns 244 new cases of leprosy diagnosed in the Bamako district in 1994. 154/244 patients could be contacted and were examined in the Leprosy Department of the Marchoux Institute in Bamako. Results showed that the presence of leprosy induced physical disabilities was associated with male gender (59%), advanced age (68%) and multibacillary disease (68%). Disabilities were also more frequent among patients having a rural or manual occupation at the time of screening or afterwards. There was a significant increase ($p < 0.001$) in the prevalence of disabilities when comparing patients at the time of diagnosis (29%) and thereafter (48%). This means that in 40% of disability cases, lesions developed during or after the treatment. Disabilities were predominantly observed in hands (33%) and feet (29%) with more frequent lesions in lateral popliteal, superior ulnar and posterior tibial nerves. Our results seem to demonstrate the inadequacy of preventive measures and management. This stresses the need for adequate prevention and therapy of leprosy induced disabilities in order to obtain proper eradication of leprosy induced health problems.

TIENDREBEOGO, A.; COULIBALY, I.; SARR, A.M.; SOW, S.O. Nature et sensibilité des bactéries surinfectal les maux perforants plantairesd'origene lépreuse à Institut Marchoux, Bamako, Mali. Acta *Leprol.*, v.11, n.4, p.153-159, 1999.

To determine potential usefulness of antimicrobial agents and to guide their prescription in the treatment of leprosy plantar ulcers, we conducted an in vitro study about germs' nature and sensitivity to antibiotics. We took samples of plantar ulcers secretion from 107 patients at Marchoux Institute. 92,5% of those ulcers were infected. These samples revealed 145 strains of micro-organisms among those, Staphylococcus aureus (70 strains) and genus Pseudomonas (41 strains) were the most frequent. These bacteria were resistant to several antibiotics currently used at Marchoux Institute (tetracyclin, penicillin, cotrimoxazol and erythromicin). Antibiotics, efficient at 80% on tested strains, were expensive for patients. They cannot be recommended for the treatment of local infections. These results outline that the main treatment in plantar ulcers is based upon antiseptic solutions and keeping feet at rest. Antibiotherapy in case of extension of local infection would be based on the results of a previous study of sensitivity.

TERAPÊUTICA

AARESTRUP, F.M., SAMPAIO, E.P.. Experimental *Mycobacterium leprae* infection in BALB/c mice: Effect of BCG administration on TNFa production and granuloma development. *Int. J. Leprosy*, v. 68, n.2, p.156-166, June, 2000.

In the present study, the experimental model of *Mycobacterium leprae* infection in the foot pads of BALB/c mice was used to investigate the effects of BCG administration on tumor necrosis factor-alpha (TNF-a) production and granuloma development. It was observed that mice intravenously infected with BCG 7 months after M. leprae inoculation into the foot pads presented a more effective mycobacteria clearance, revealed by a significant reduction of BCG-colony forming units in the spleen and by the reduction of acid-fast bacilli (AFB) in the foot pads. BCG infection at the peak of M. *leprae* infection also modulated the granulomatous response to M. leprae by converting mononuclear granulomas into an epithelioid-cell granuloma. Furthermore, lower TNF-a serum levels were detected in M. leprae-infected mice when compared to mice infected with M. leprae + BCG. An analysis of the TNF-a gene expression in the spleen by semiquantitative reverse transcription-polymerase chain reactions (RT-PCR) demonstrated that co-infection with BCG induced an earlier expression of TNF-a mRNA than in M. leprae-infected mice. The numbers of TNF-a-positive cells and apoptotic cells were also enhanced in epithelioid versus non-epithelioid granulomas. As a whole, the data suggest that co-infection of M. leprae-infected mice with BCG modulates TNF-a synthesis which, in turn, leads to induction of protective epithelioid granuloma formation in the foot pads and subsequent mycobacterial clearance. Macrophage differentiation into epithelioid cells, in association with the enhancement of TNF-a production at the granuloma site, may represent a triggering signal that induced apoptosis in these cells, leading to mycobacterial elimination. Moreover, the rate of apoptosis in epithelioid granulomas may well be related to the extent of immunopathologically mediated tissue damage

CALABRESE, L.; FLEISCHER, A.B. Thalidomide: current and potential clinical applications. *Am. J. Med*, v.108, n.6, p.487-495, Apr., 2000.

More than three decades after its withdrawal from the world marketplace, thalidomide is attracting growing interest because of its reported immunomodulatory and anti-inflammatory properties. Current evidence indicates that thalidomide reduces the activity of the inflammatory cytokine tumor necrosis factor (TNF)-alpha by accelerating the degradation of its messenger RNA.

Thalidomide also inhibits angiogenesis. Recently, the drug was approved for sale in the United States for the treatment of erythema nodosum leprosum, an inflammatory complication of Hansen's disease. However, it has long been used successfully in several other dermatologic disorders, including aphthous stomatitis, Behcet's syndrome, chronic cutaneous systemic lupus erythematosus, and graft versus-host disease, the apparent shared characteristic of which is immune dysregulation. Many recent studies have evaluated thalidomide in patients with human immunodeficiency virus (HIV) infection; the drug is efficacious against oral aphthous ulcers, HIV-associated wasting syndrome, HIV-related diarrhea, and Kaposi's sarcoma. To prevent teratogenicity, a comprehensive program has been established to control access to the drug, including registration of prescribing physicians, dispensing pharmacies, and patients; mandatory informed consent and education procedures; and limitation of the quantity of drug dispensed. Clinical and, in some patients, electrophysiologic monitoring for peripheral neuropathy is indicated with thalidomide therapy. Other adverse effects include sedation and constipation. With appropriate safeguards, thalidomide may benefit patients with a broad variety of disorders for which existing treatments are inadequate.

CHOGLE, A. et al. Dapsone hypersensitivity syndrome with coexisting acute hepatitis E. *Indian J. Gastroenterol.*, v, 19, n.2, p. 85-86, Apr-Jun, 2000.

A 14-year-old girl presented with fever, generalized lymphadenopathy, skin rash and hepatitis affer starting dapsone. All abnormalities reversed with institution of prednisolone therapy after discontinuation of dapsone. The hepatic involvement was of hepatocellular type; it was associated with IgM anti-HEV antibodies, suggesting coexisting acute hepatitis E. We believe a causal link between the hepatotrophic viruses and dapsone hypersensitivity syndrome could exist.

GIRDHAR, B.K. GIRDHAR, A., KUMAR, A. Relapses in multibacillary leprosy patients: effect of length of therapy. *Leprosy Rev.*, v.71, n.2, p,144-153, June, 2000.

Two groups of MB leprosy patients, one treated to the point of smear negativity (TSN) and the other given therapy for fixed duration (24 doses of WHO MB regimen) (FDT), were compared for relapse rates during treatment and in the post-treatment period. During the follow-up of 980-2 person years in 260 patients treated with FDT, 20 relapses (2-04/100 patient years) were observed. In the other group of 301 patients, who received therapy till smear negativity, 12 relapses in 1085-46 person years (1.10/100 patient years) occurred. Comparison of survival rates (without relapse) has shown that although there is no difference up to 4 years, the risk of relapse was significantly higher on longer follow-up in the FDT group. In addition, when patients were compared on the basis of initial bacterial load, it was found that the relapse rates in patients with BI >_4 was significantly higher ($P<0.01$) in the FDT group as compared to those receiving treatment till the point of smear negativity (4.29 versus 1.27/100 patient years). All the relapsed patients responded to retreatment with the same drug combination, indicating that the exacerbation in their condition was because of insufficient treatment. It is suggested that to prevent or reduce relapses, treatment where feasible would be continued till smear negativity, at least in patients with high BI.

GUPTA, U.D., KATOCH, V.M. Drug resistance in leprosy: lessons from past and future perspective. *Indian J. Leprosy*, v.71, n.4, p.4 51-463, Oct-Dec., 1999.

Some recent studies indicate that the problem of drug resistance in leprosy is very much there but the exact picture is not clear. In the emerging scenario with increasing number of new cases with low bacterial load, the conventional in-vivo and most of current in-vitro methods for deterinination of drug resistance may not help. It is pointed out that newer molecular approaches may be more useful and that it will be important to undertake studies to develop such tools.

JAIN, M. et al. Histological assessment of dermal nerve damage occurring during multidrug therapy, for leprosy. *Int. J. Leprosy*, v. 68, n.2, p,167-71, June, 2000.

This prospective histomorphological assessment of dermal innervation in biopsies taken before and after multidrug therapy (MDT) from 41 leprosy patients: 35

borderline tuberculoid (BT), 3 borderline lepromatous (BL), 3 lepromatous (LL). Biopsies of the same lesions taken before commencement (diagnostic therapy) and at the end of therapy (check biopsy) were compared. Hematoxylin and eosin, immunoperoxidase stain for S-100 protein, and the Holmes' silver impregnation method for nerve cells and fibers were used. Skin biopsies were classified as having detectable or undetectable nerves.

Of 35 patients with BT leprosy, 17 had no detectable nerves in their diagnostic biopsies; in the check biopsies of 13 of these 17, dermal nerves remained undetectable, in 2 they were S-100 positive but were Holmes negative. Identifiable dermal nerves were present in diagnostic biopsies from 18 pattients; in the check biopsies 5 of these 18 had no detectable nerves while in the remaining 13 nerve branches could be detected.

The study provides histological documentation of complete damage to dermal innervation in 62.85% (22/35) of patients with BT leprosy, of which 14.28% (5/35) occurred during MDT. Of the patients with detectable dermal innervation at the onset of MDT, 27.7% (5/18) suffered continuing damage during MDT.

SHARMA, P. et al. *Mycobacterium* w vaccine, a useful adjuvant to multidrug therapy in multibacillary leprosy: a report on hospital based immunotherapeutic clinical trails with a follow-up of 1-7 years after treatment. *Leprosy* Rev., v.71, n.2, p.179-192, June, 2000.

A vaccine based on autoclaved *Mycobacterium* w was administered, in addition to standard multidrug therapy (MDT), to 156 bacteriologically positive, lepromin negative multibacillary leprosy patients compared to a well matched control group of 145 patients with a similar type of disease who received a placebo injection in addition to MDT. The MDT was given for a minimum period of 2 years and continued until skin smear negativity, while the vaccine was given at 3-month intervals up to a maximum of eight doses. The fall in clinical scores and bacteriological indices was significantly more rapid in vaccinated patients, from 6 months onward until years 2 or 3 of therapy. However, no difference was observed in the fall in bacteriological index in the two groups from year 4 onwards. The number of LL and BL patients released from therapy (RFT) following attainment of skin smear negativity, after 24-29 months of treatment was 84/133 (63.1%) in vaccinated and 30/120 (25.0%) in the placebo group; the difference was highly statistically significant ($P < 0.0001$). In all, 90.2% patients (146/162) converted from lepromin negativity to positivity in the vaccine group, as against 37.9% (56/148) in the placebo group. The average duration of lepromin positivity maintained following eight doses of vaccine administered over 2 years was 3.016 years in the vaccine and 0.920 years in the placebo group. Histological upgrading after 2 years of treatment in the LL type was observed in 34/84 (40.5%) cases in the vaccine and 5/85 (5.9%) cases in the placebo group, the difference being statiscally significant ($P<0.001$). The incidence of type 1 reactions was significantly higher (30.5%) in the vaccine group than (19.7%) in the placebo group ($P = 0.0413$); the difference was mainly observed in LL type ($p = 0.009$) The incidence of type 2 reactions was similar (31.8 and 34.6%) in, vaccine and placebo groups. The vaccine did not precipitate neuritis or impairments over and above that encountered with MDT alone. After 5 years of follow-up following RFT no incidence of bacteriological or clinical relapses was observed in both groups.

SINGH, H.B.; KATOCH, K., SHARMA, R.K., GUPTA, U.D.; SHARMA, V.D.; SINGH, D.; CHAUHAN, D.S.; SRIVASTAVA, K.; KATOCH, V.M. Effect of treatment on PCR positivity in multibacillary leprosy patients treated with conventional and newer drugs ofloxacin and minocycline. Acta *Leprol., v.* 11, nA, p.179-182, 1999.

In order to develop objective criteria to monitor trends of therapeutic responses positivity of PCR signals and ATP assay methods has been compared in multibacillary (MB) leprosy patients. Biopsies from lesions of 95 BL/LL patients before and after one year of treatment with a new drug regimen comprising of conventional and newer drugs ofloxacin and minocycline have been studied. These biopsies were processed for bacillary ATP assay and PCR positivity for a 36 kDa gene target by earlier published methods. In the untreated patients bacillary ATP levels were detectable in all specimens and ranged from 0.02 to more than 36 pg/millions organisms. After one year of treatment ATP levels were not detectable in any of the 57 biopsies specimens available for analysis. However , PCR signals were detectable in 3 out of 57 biopsies. In two specimens signals were very weak detectable only by hybridization. It may be concluded that DNA based PCR assay may be useful in monitoring the trends of therapeutic responses in MB patients under treatment.

SOARES, L. S. et al. The impact of multidrug therapy on the epidemiological pattern of leprosy in Juiz de Fora, Brazil. Cad *Saúde Publ.*, v.16, n.2, p.343 -350, Apr-Jun., 2000.

We investigated the impact of multidrug therapy (MDT) on the epidemiological pattern of leprosy in Juiz de Fora, Brazil, from 1978 to 1995. Evaluation of 1,283

medical charts was performed according to the treatment regimen used in two different periods. Following the introduction of MDT in 1987, prevalence of leprosy decreased from 22 patients/10,000 inhabitants to 5.2 patients/10,000 inhabitants in 1995. Incidence rate of leprosy was lower in period 11 (1987-1995) than in period I (1978-1986). Decreasing prevalence and incidence appear to be related to drug efficacy rather than decreased case identification, since both self-referred and professionally referred treatment increased markedly from period I to period II. For both periods, multibacillary leprosy was the most frequent clinical form of the disease (+/-68%), and the main infection risk factor identified was household contact. Leprosy is predominantly manifested in adults, but an increase in the number of very old and very young patients was observed in period II. The MDT Program has been effective both in combating leprosy and in promoting awareness of the disease.