

# LITERATURA CORRENTE

## CURRENT LITERATURE

### CIRURGIA

COURTRIGHT, P; KIM, S.H.; TUNGPAKORN, N.; CHO, B-H.; LM, Y-K.; LEE, H-J., LEWALLEN, S. Lagophthalmos surgery in leprosy: findings from a population-based survey in Korea. *Leprosy Rev.*, v.72, n.3, p.285-291, Sep., 2001.

Lagophthalmos continues to be a serious problem in cured leprosy patients. We conducted a population-based survey of lagophthalmos surgical coverage (LSC), barriers to lagophthalmos surgery and outcome of lagophthalmos surgery in leprosy patients in South Korea. In our survey, there were 60 patients with lagophthalmos who had needed surgery (> 5 mm gap), 34 of whom had received surgery, resulting in a lagophthalmos surgery coverage of 57%. Among the 34 patients who had received lagophthalmos surgery, 18 needed further surgery. Among those who had never had surgery, none of the demographic indicators predicted surgical uptake; the primary reason given for failure to have surgery was lack of knowledge about it. Outcome of surgery (by eye) showed that 29% of eyes still had a gap of 5 mm or more. The frequency of symptoms (tearing, blurring of vision, pain, etc.) was high. Even in settings with a good eye care infrastructure, such as Korea, uptake of surgery can still be low and results may not be satisfactory to patients. There is a need for practical guidelines for leprosy control programmes in the areas of (a) patient recognition, (b) patient education, (c) monitoring the uptake of surgery, and (d) monitoring the outcome of surgery to ensure the best possible outcome.

LIWEN, Dong; FUTIAN, Li; JUAN, Jiang; GUOCHENG, Zhang. Transplantation of fibula with vascular pedicle for fusion of ankle in leprotic drop-foot. *Indian J. Leprosy*, v.72, n.4, p.431-436, Oct-Dec., 2000.

Devascularized bone grafts are pieces of dead bone and they simply serve as scaffolds for new bone to grow and fill the gap, taking a long time when they succeed in doing so. In contrast, vascularized grafts being living tissues have short healing time, great vitality and strong infection-resisting capacity. We report here the successful use of vascularized grafts of the lower end of fibula for fusing the ankle in five leprosy patients.

### CLÍNICA

ARUNTHATHI, S.; EBENEZER, G.; DANIEL, E.; SUGUMARAN, S.T. Nocardia farcinica pleuritis in a lepromatous patient with severe necrotizing reaction: an unusual presentation. *Mt. 1. Leprosy*, v.69, n.2, p.104-107, Jun., 2001.

A young, male, lepromatous leprosy patient with a severe necrotizing erythema nodosum leprosum reaction treated with prolonged oral steroids and thalidomide developed pleuritis that was caused by a rare opportunistic pathogen, *Nocardia farcinica*. This organism was resistant to most antibiotics but was susceptible to amikacin and minocycline. During the course of treatment the patient developed severe gastritis which necessitated the removal of clofazimine and the inclusion of an H2 receptor antagonist. Bilateral steroid-induced cataracts needed surgical correction. This case is being presented for its rare opportunistic bacterial infection and for the multiple complications which made treatment difficult

ISHIKAWA, A.; ISHIKAWA, S.; HIRAKAWA, M. Osteoporosis, bone turnover and hypogonadism in elderly men with treated leprosy. *Leprosy Rev.*, v.72, n.3, p.322, 329, Sep., 2001.

In male hypogonadism associated with bone loss, it is important to determine whether bone loss continues with ageing and an increased risk of fracture. We studied bone metabolism in 86 male leprosy patients, who were classified according to the presence or absence of osteoporosis. Osteoporosis was present when men had lumbar compression fractures or a mean BMD-2SD that of normal Japanese men in each age decade. Four men had fractures. Serum concentrations of 1,25-dihydroxyvitamin D and high-sensitivity parathyroid hormone were almost normal in both groups, whereas free testosterone and oestradiol were significantly lower in the osteoporosis group than in the non-osteoporosis group (free testosterone:  $P < 0.01$ , oestradiol:  $P < 0.05$ ). The urinary concentrations of pyridinoline and deoxypyridinoline, as a marker of bone absorption, were significantly higher in the osteoporosis group than in the non-osteoporosis group (pyridinoline:  $P < 0.01$ , deoxypyridinoline:  $P < 0.01$ ). The serum concentration of osteocalcin, a marker of bone formation, was significantly

higher in the osteoporosis group than in the non-osteoporosis group ( $P < 0.01$ ). Elevated concentration means that bone repair is increased possibly because of compensation mechanisms for increased bone loss. In the osteoporosis group, hypogonadism occurred, and high bone turnover continued even in older men. We recommend clinical studies of treatment such as replacement therapy to prevent bone loss and increasing risk of fractures in older men with leprosy.

EBENEZER, G.; DANIEL, S.; SUNEETHA, S.; REUBEN, E.; PARTHEEBARAJAN, S.; SOLOMON, S. Bacteriological study of pus isolates from neuropathic plantar ulcers associated with acute inflammatory phase. *Indian J. Leprosy*, v.72, n.4, p.443-449, Oct-Dec., 2000.

In this retrospective study, sensitivity of organisms cultured from ulcers of leprosy patients without and with diabetes mellitus, diabetic patients without leprosy and patients with ulcers from other causes was examined. The profile of organisms grown from these groups of patients did not differ significantly. However, there was a high prevalence of organisms like *Proteus*, *E. coli* and *Enterococcus* in the ulcers of leprosy patients indicating faecal contamination of the ulcers. Co-trimaxazole and tetracycline were of little value in the treatment of these ulcers. We therefore recommend that in situations where there is no culture facility, the patients be started on a course of penicillin and gentamycin. If these antibiotics fail, it would be necessary to use more advanced antibiotics like norfloxacin, amikacin and ciprofloxacin.

JAGGARAJAMMA, K.; THOMAS, A.; NAGARAJAN, M. Status of long absentees among multibacillary leprosy patients admitted to a controlled clinical study. *Indian J. Leprosy*, v.72, n.4, p.469-475, Oct-Dec., 2000.

Of 210 multibacillary leprosy patients who were admitted to a trial of two drug regimens, fifty-seven were excluded from efficacy analysis at 120 months for various reasons. Thirty-three of these patients were identified as long absentees. Efforts were made to contact these patients through letters and home visits to assess their clinical and bacteriological status and to find out the reasons for default. Twenty-one patients were thus retrieved. Only one patient was found to be having active disease requiring treatment; the rest were clinically inactive and bacteriologically negative.

KANG, T.J.; YOU, J.C.; CHAE, G.T. Identification of catalase-like activity from *Mycobacterium leprae* and the relationship between catalase and isonicotinic acid hydrazide (INH). *J. Med. Microbiol.*, v.50, n.8, p.675-81, Aug., 2001.

As *Mycobacterium leprae* proliferate inside macrophages, it has been speculated that catalase encoded by *katG* may protect the bacilli from deleterious effects of peroxide generated from the macrophage and may also play a crucial role in the survival of *M. leprae* in vivo. However, unlike that of *M. tuberculosis*, the *katG* of *M. leprae* has been reported to be a pseudogene, implicating that isoniazid, which is activated to a potent tuberculocidal agent by catalase, is unlikely to be of therapeutic benefit to leprosy patients. These results raise a question as to how *M. leprae* avoids H2O2-mediated killing inside macrophages. To understand the survival of *M. leprae* in macrophages, the present study attempted to detect catalase-like activity in *M. leprae*. Catalase-like activity was found in *M. leprae* cell lysate by the diaminobenzidine (DAB) staining method with non-denaturing polyacrylamide gel electrophoresis. An ammonium sulphate precipitation study revealed that the catalase-like activity was precipitable with 80% ammonium sulphate. The effect of isoniazid (INH) on *M. leprae* growth was also tested by RT-PCR and radiorespirometric assay to examine catalase-like activity in *M. leprae*, because INH was activated by catalase. It was found that the viability of *M. leprae* was decreased at a concentration of 20 microg/ml by radiorespirometric assay and it was inhibited at higher concentrations as determined by RT-PCR. These data suggest that a catalase-like activity other than that encoded by *katG* is present in *M. leprae*.

KRUPNICK, A.I.; SHIM, H.; PHELPS, R.G.; CUNNINGHAM-RUNDLES, C.; SAPADIN, N.A. Cutaneous granulomas masquerading as tuberculoid leprosy in a patient with congenital combined immunodeficiency. *Mt. Sinai J. Med.*, v.68, n.4-5, p.326-30, Sep-Oct., 2001

Combined immunodeficiency disorders are characterized by abnormalities in cellular and humoral immunity. This classification includes common variable immunodeficiency (CVI), a primary immunodeficiency disorder characterized by hypogammaglobulinemia, recurrent bacterial infections, and significant T-cell abnormalities. Associated autoimmune diseases include rheumatoid arthritis, pernicious anemia, idiopathic thrombocytopenic purpura, and systemic lupus erythematosus. Granulomatous lesions in lymphoid tissues, solid organs, and skin have been reported. We describe a patient with CVI who developed cutaneous granulomas with perineural invasion; to our knowledge, this is a previously undescribed feature.

LIWEN, D.; FUTIAN, L.; F, JUAN, J.; GUOCHENG, Z. Techniques for covering soft tissue defects resulting from plantar ulcers in leprosy: Part V. Use of the flap in the inguinal region and latissimus dorsi musculocutaneous flap. *Indian J. Leprosy*, v.72, n.2, p.227-244, Apr-Jun., 2000.

The area of distribution of the superficial circumflex iliac, superficial epigastric and superficial external pudental arteries is large and flaps based on them can meet the requirement of different recipient sites. We have transplanted free flaps based on the superficial epigastric artery for repairing plantar soft tissue defects in six leprosy patients. During the follow-up examination 58 to 118 months later there has been no recurrence of ulceration in any of these cases. The latissimus dorsi muscle, is mainly nourished by the thoracodorsal artery and the latissimus dorsi musculocutaneous flap is a large sized, composite structure with abundant blood provision and strong anti-infectious property. The latissimus dorsi flap can be used as an artery-pedicled island flap or as a free flap besides its use as a muscle graft, because of its constant vascular position, wide outer-diameter of the vessels and long pedicle. It can therefore be utilized for repairing soft tissue defect or replacement of paralyzed muscle. We have used the latissimus dorsi musculocutaneous free flap for repairing large skin and soft tissue defects resulting from plantar ulceration in three leprosy patients. During the follow-up period, one patient who had complete drop-foot and had refused corrective surgery had recurrence of the ulcer in the 12th post-operative month. No ulcers had recurred in the other two cases during the follow-up at 48 and 114 months.

MAGDORF K; HMS WH; Harms D; Huger PH; Griese M; Rank M. Leprosy - Ein Überblick aus pädiatrischer Sicht. *Klin. Padiatr.*, v.213, n.5, p.266-70, Sep-Oct., 2001.

Worldwide tourism is an increasing industry. One result of this phenomenon is the occurrence of imported infectious diseases, as recently observed even in Germany. Leprosy ranks high among dreaded infectious diseases from tropical and subtropical countries. It remains a major health threat despite marked improvements in diagnosis and therapy. This was achieved by a better understanding of bacteriological and immunological mechanisms over the past decades, resulting in a decline of Leprosy's incidence.

NERY, J.A.; PERISSE, A.R.; SALES, A.M.; VIEIRA, L.M.; SOUZA, R.V.; SAMPAIO, E.P.; SARNO, E.N. The use of pentoxifylline in the treatment of type 2 reactional episodes in leprosy. *Indian J. Leprosy*, v.72, n.4, p.457-467, Oct-Dec., 2000.

It has been suggested that erythema nodosum leprosum (ENL) is associated with enhanced production of TNF-alpha

resulting in increased inflammation of the skin and nerve function impairment. Thalidomide and steroids are the major drugs used in the treatment of ENL, but due to the serious problems associated with their use, alternative therapeutic interventions are being considered. In the present retrospective study, the authors report their clinical observations on the effect of pentoxifylline (PTX) in the treatment of ENL. Parameters, such as the clinical involution of reactional lesions, the regression of the inflammatory symptoms associated with the lesions, and the impact on the systemic symptoms common to ENL were assessed at regular intervals during PTX therapy. It was found that PTX therapy led to total elimination of systemic symptoms within the first week of treatment. This improvement was maintained until the end of the study (60 days of treatment). Moreover, the evolution of nodular lesions showed a 100% improvement within the first 14 days of treatment. However, by the 60th day, worsening of the lesions was noted in 20% of the cases. The impression is that PTX is well tolerated, and it may be used for improving patient's clinical condition during ENL reaction. Nevertheless, a randomized, double blind, controlled trial to compare the effects of the widely-accepted thalidomide and the yet untested pentoxifylline for treatment of type 2 reaction is still necessary.

PATIL, K.M.; JACOB, S. Mechanics of tarsal disintegration and plantar ulcers in leprosy by stress analysis in three dimensional foot models. *Indian J. Leprosy*, v.72, n.1, p. 69-86, Jan-Mar., 2000.

This paper describes three dimensional two arch models of feet of a normal subject and two leprosy subjects, one in the early stage and the other in the advanced stage of tarsal disintegration, used for analysis of skeletal and plantar soft tissue stresses by finite element technique using NISA software package. The model considered the foot geometry (obtained from X-rays), foot bone, cartilages, ligaments, important muscle forces and sole soft tissue. The stress analysis is carried out for the foot models simulating quasi-static walking phases of heel-strike, mid-stance and push-off. The analysis of the normal foot model shows that highest stresses occur at push-off over the dorsal central part of lateral and medial metatarsals and dorsal junction of calcaneus and cuboid and neck of talus. The skeletal stresses, in early stage leprosy with muscle paralysis and in the advanced stage of tarsal disintegration (TD), are higher than those for the normal foot model, by 24% to 65% and 30% to 400%, respectively. The vertical stresses in the soft tissue at the foot-ground interface match well with experimentally measured foot pressures and for the normal and leprosy subjects they are the highest in the push-off phase. In the leprosy subject with advanced TD, the highest

soft tissue stresses and shear stresses (about three times the normal value) occur in push-off phase in the scar tissue region. The difference in shear stresses between the sole and the adjacent soft tissue layer in the scar tissue for the same subject is about three times the normal value. It is concluded that the high bone stresses in leprosy may be responsible for tarsal distintegration when the bone mechanical strength decreases due to osteoporosis and the combined effect of high value of footsole vertical stresses, shear stresses and the relative shear stresses between two adjacent soft tissue layers may be responsible for plantar ulcers in the neuropathic leprosy feet.

MAHAJAN, P.M.; JADHA,V.; JOGAIKAR, D.G.; MEHTA, J.M. Intranasal administration of fusidic acid cream in leprosy. *Indian J. Leprosy*, v.72, n.4, p.451-455, Oct-Dec., 2000.

The effect of local treatment of nostrils with fusidic acid cream was investigated in 30 previously untreated lepromatous leprosy patients. The cream was applied in the nostrils after flushing the nostrils with normal saline, twice a day for a period of four weeks. It was found that 20 mg/gm of sodium fusidate was effective in reducing the morphological index of the nose-blow smear to zero in two weeks in majority of the patients. No untoward side effect was seen in any of the patients. Such nasal treatment along with multidrug therapy may help in reducing the patient's level of infectiousness to their contacts, since the nose is recognized to be an important portal of exit of *M. leprae*.

## COMPLICAÇÕES

HUGHES, R.G.; DRAKE-LEE, A. Nasal manifestations of granulomatous disease. *Hosp. Med.*, v.62, n.7, p.417-21, Jul., 2001.

Granulomatous disease frequently affects the head and neck region, particularly the nose and sinuses. This article describes the most common infectious and non-infectious conditions and their clinical features.

LEWALLEN, S.; COURTRIGHT. P. Blindness in Africa: present situation and future needs. *Brit J. Ophthalmol*, v.85, n.8. p.897-903, Aug., 2001.

AIM: To review the prevalence and causes of blindness in sub-Saharan Africa, the existing services and limitations, and the Vision 2020 goals for the future. METHODS: Methodologically sound population based surveys published in the past 20 years are reviewed and results for prevalence and causes of blindness are tabulated. The current resources and needs according to recent publications and international working groups are described. CONCLUSIONS: Blindness

prevalence rates vary widely but the evidence suggests that approximately 1% of Africans are blind. The major cause is cataract; trachoma and glaucoma are also important causes of blindness. The bulk of blindness in the region is preventable or curable. Efforts should focus on eye problems which are universally present and for which there are cost effective remedies, such as cataract and refractive problems and on those problems which occur focally and can be prevented by primary healthcare measures, such as trachoma, onchocerciasis, and vitamin A deficiency. Major development of staffing levels, infrastructure, and community programmes will be necessary to achieve Vision 2020 goals.

NAKAYAMA, E.E.; URA, S.; FLEURY, R.N.; SOARES, V. Renal lesions in leprosy: a retrospective study of 199 autopsies. *Am. J. Kidney Dis.*, v.38, n.1, p.26-30, Jul., 2001.

In the present work, 199 patients with leprosy who underwent autopsy between 1970 and 1986 were retrospectively studied to determine the prevalence, types, clinical characteristics, and etiologic factors of renal lesions (RLs) in leprosy. Patients were divided into two groups: 144 patients with RLs (RL+) and 55 patients without RLs (RL-). RLs observed in 72% of the autopsied patients were amyloidosis (AMY) in 61 patients (31%), glomerulonephritis (GN) in 29 patients (14%), nephrosclerosis (NPS) in 22 patients (11%), tubulointerstitial nephritis (TIN) in 18 patients (9%), granuloma in 2 patients (1%), and other lesions in 12 patients (6%). AMY occurred most frequently in patients with lepromatous leprosy (36%; nonlepromatous leprosy, 5%;  $P < 0.01$ ), recurrent erythema nodosum leprosum (33%;  $P < 0.02$ ), and trophic ulcers (27%;  $0.05 < P < 0.10$ ). Ninety-seven percent of AMY was found in patients with lepromatous leprosy, 88% showed recurrent trophic ulcers, and 76% presented with erythema nodosum leprosum. NPS was found in older patients with arterial hypertension, neoplastic diseases, infectious diseases, and vasculitis associated with GN. Most patients with AMY presented with proteinuria (95%) and renal failure (88%). The most frequent causes of death were renal failure in patients with AMY (57%), infectious diseases in patients with GN (41%) and TIN (45%), and cardiovascular diseases in patients with NPS (41%). No difference in survival rates was observed among RL- patients and those with AMY, GN, NPS, or TIN.

RU77ENENTI, M.R.; BRUNI, R.; FLORIO, G.; DE LUIGI, M.C.; LERCARI, G.; BARABINO, G.F.; NUNZI, E.; VALBONESI, M. Lepromatous vasculitis successfully treated by plasma exchange (PE). *J. Clin. Apheresis*, v.16, n.1, p.37-8, 2001.

Vascular involvement is presently considered a

"common pathway" in a number of diseases that is mediated by circulating immune complexes (CIC). CIC are found in the circulation when the disease is active and in single patients their level may parallel disease activity. Lepromatous leprosy is characterized by the presence of CIC and deposits of immunoglobulins and complement in vascular lesions of the different organs and an Arthus-like mechanism is considered as the basis for the clinical picture. The same mechanism is considered to play an essential pathophysiologic role in Lucio's phenomenon, which is characterized by lymphohistiocytic vascular infiltrates with or without thrombosis and secondary cutaneous infarction. Lepromatous vascular involvement is mediated by CIC whose antigen composition is known, the same as it is with HCV mediated cryoglobulinemia, HBV positive panarteritis nodosa, rheumatoid vasculitis, or Wagner's granulomatosis, which are usually treated by PE [1-3]. PE has been employed for lepromatous vasculitis since 1979 [4] and other cases have been successfully treated afterwards [5,6]. We report on another patient successfully treated by plasma exchange.

## CONTROLE

BENBOW, C.; TAMIRU, T. The experience of self-care groups with people affected by leprosy: ALERT, Ethiopia. *Leprosy Rev.*, v.72, n.3, p.311-321, Sep., 2001.

This paper describes the development of self-care groups in Ethiopia by ALERT, and the successes and failures experienced in the process. The groups were started in 1995 in response to two main problems, the increasing number of people dependent on ALERT to heal their wounds despite years of health education, and the limited financial resources of ALERT for wound healing supplies. By December 1999, there were a total of 72 established groups. Group membership was voluntary. There have been a number of positive outcomes. Group members have taken up responsibility for managing and monitoring their own wounds and supplying their own wound healing materials. More attention is paid to their personal hygiene and personal appearance. They also report increased confidence to participate in society, restored dignity and self-respect, and a sense of belonging within the community. In addition, some members have started to pay more attention to their local environmental hygiene by building pit latrines and waste disposal sites. The ALERT staff involved in this initiative had to change their role from that of a leprosy service provider to a self-care group facilitator, but not all were successful in making this transition. The remaining challenge for the programme is sustainability and further development through the National Tuberculosis and Leprosy Control Programme, The Ethiopian National Association for Ex-Leprosy Patients and possibly other organizations too.

CHEN, X-S.; LI, W-Z.; JIANG, C.; ZHU, C-B.; YE, G.Y. Studies on mode of detection of leprosy in China during the years 1981-1998. *Leprosy Rev.*, v.72, n.3, p.302-310, Sep., 2001.

Along with the nationwide economic reform initiated in the early 1980s and the rapid decrease of leprosy endemic after the implementation of multi-drug therapy (MDT), the leprosy programme changed from 'vertical' to 'horizontal'. An evolution in the mode of detection of leprosy cases has consequently taken place. Based on the nationwide registration of newly detected cases, the profile of patients at detection has been studied. The proportions of cases corrected significantly with calendar years in detection by dermatological clinics, contact checks, 'clue survey' and mass survey, showing a significant increase in percentage of cases detected through dermatological clinics and contact checks, and decreases through 'clue survey' and mass survey. Detection of cases through dermatological clinics and voluntary reporting have become the main modes of case-finding during 1997-1998, accounting for 37.3% and 28.6%, respectively, where contact check accounts for only 9.1%. In areas with good dermatological services, a significantly higher proportion (75.9%) of cases was detected through dermatological clinics, where voluntary reporting and 'clue survey' were the main modes of detection in endemic areas. As regards confirmation of diagnosis, the great majority of cases were confirmed by leprosy units, even though they were detected in various other situations. Only 6.5% of leprosy cases were detected and subsequently confirmed by doctors in dermatologic clinics. The present modes of detection and their relation to demographical, iological, clinical factors and health services are discussed. This study emphasizes the cardinal importance of the dermatological clinics in the detection of leprosy cases in China at the present time and hence the need to strengthen the training of doctors in these clinics, while continuously encourage their involvement in leprosy control.

CROSS, H.; NEWCOMBE, L. An intensive self care training programme reduces admissions for the treatment of plantar ulcers. *Leprosy Rev.*, v.72, n.3, p.276-284, Sep., 2001.

This paper describes, in detail, an intensive 14 day Self Care Training Programme that is conducted at Lalgadh Leprosy Services Centre in Nepal. An evaluation of the programme was undertaken in which hospital admission for infected plantar ulceration was the outcome measure. It was found that those who had undertaken the programme were less likely to have been admitted for hospital treatment in a 3-month follow-up period ( $\chi^2 = 5.1, P = 0.02$ ). An odds ratio of 1:1.8 (95% CI = 0.15-0.01) was also calculated. This paper presents an overview of the issues related to

impairment, a description of the Self Care Training Programme, an analysis of the evaluation results and a discussion of the findings.

FREERKSEN, E.; ROSENFELD, M.; DEPASQUALE, G.; BONNICI, E.; GATT, P. The Malta Project—a country freed itself of leprosy. A 27-year progress study (1972-1999) of the first successful eradication of leprosy. *Chemotherapy*, v.47, n.5, p.309-31, Sep-Oct., 2001.

The successful conclusion of the first leprosy eradication program carried out with combination therapy is reported. This program started in Malta in June 1972. It was based on extensive experimental and clinical studies and was formally concluded on 31 December 1999. No new infections occurred after the start of this 27-year progress report. The youngest patient was 16, and the eldest 83 years old. Of the total of 261 cases in the project, 201 had already received pretreatment [mainly with diaminodiphenylsulfone (DDS)] at the start. Sixty-one cases had no pretreatment. These were predominantly elderly patients who were late in deciding to have treatment. The very long follow-up period totaling 27 years was consistently maintained in order to be able to refute all potential objections empirically, e.g. with regard to relapses at a late stage. Besides the overall symptoms which are typical for the broad picture of leprosy, the involvement of the eyes was very striking (at least 50%). The therapeutic effect was of very rapid onset in these cases without surgery. Rifampicin (RMP) + isoniazid + prothionamide + DDS (trade name Isoprodian-RMP) was used as medication in a fixed combination. This fixed combination had already proved to be highly effective in the treatments during the course of the project, surprising therapy results (including lifesaving effects) were also noticed in other diseases.

MARLOWE, S.N.; LOCKWOOD, D.N. Update on leprosy. *Hosp. Med.*, v.62, n.8, p.471-6, Aug., 2001.

Leprosy, a result of infection by *Mycobacterium leprae*, is a leading cause of peripheral neuropathy. The World Health Organization aimed to eliminate leprosy as a public health problem by 2000, but this has not been attained. Patients with leprosy continue to present in the UK. The diagnosis of leprosy is frequently not considered, with resultant pathological and psychological problems for patients.

PORTER, J.D.; KESSEL, A.S. Needing to know? Ethical dilemmas in leprosy treatment and control. *Leprosy Rev.*, v.72, n.3, p.246-249, Sep., 2001.

A young man presents to your local clinic in a leprosy endemic country with a small patch of discoloured skin on

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

## EPIDEMIOLOGIA

BOLDSEN, J.L. Epidemiological approach to the paleopathological diagnosis of leprosy. *Am. J. Phys. Anthropol.*, v.115, n.4, p.380-7, Aug., 2001.

In paleopathology it is usually assumed that modern diagnostic criteria can be applied to infectious diseases in the past. However, as both the human species and populations of pathogenic microorganisms undergo evolutionary changes, this assumption is not always well-founded. To get valid estimates of the frequency (the point prevalence at death) of leprosy in skeletal samples, sensitivity, specificity, and sample frequency must be estimated simultaneously. It is shown that more than three symptoms must be evaluated in at least three samples in order to reach estimates with well-described properties. The method is applied to three skeletal samples from Medieval Denmark; the samples were scored for the presence of seven osteological conditions indicating leprosy. For the osteological conditions, sensitivity varied from 0.36-0.80, and specificity from 0.58-0.98. The frequency of leprosy in the three samples was: Odense (a lepers' institution), 0.98, 95% CI 0.64-1.00; Malmö (urban cemetery), 0.02, 95% CI 0.00-0.07; and Tirup (rural cemetery), 0.36, 95% CI 0.23-0.46. It is concluded that it is indeed possible to estimate disease frequencies without reference to modern standards, and that leprosy occurred with widely differing frequencies in different segments of the Medieval population in southern Scandinavia. Copyright 2001 Wiley-Liss, Inc.

KANG, T.J.; CHAE, G.T. Detection of Toll-like receptor 2 (TLR2) mutation in the lepromatous leprosy patients. *FEMS Immunol. Med. Microbiol.*, v.31, n.1, p.53-8, Jul., 2001.

Toll-like receptor 2 (TLR2) is critical in the immune response to mycobacterial infections and the mutations in the TLR2 have been shown to confer the susceptibility to severe infection with mycobacteria. To define this, we screened the intracellular domain of TLR2 in 131 subjects. Groups of 45 lepromatous and 41 tuberculoid leprosy (TT)

patients and 45 controls were investigated. Ten subjects among the lepromatous leprosy (LL) patients had a band variant detected by single-stranded conformational polymorphism. DNA sequencing detected a C to T substitution at nucleotide 2029 from the start codon of the TLR2. The mutation would substitute Arg to Trp at amino acid residue 677, one of the conserved regions of TLR2. In our results, the mutation was involved in only LL, not TT and control. Thus, we suggest that the mutation in the intracellular domain of TLR2 has a role in susceptibility to U.

RU77ENENTI, M.R.; BRUNI, R.; FLORIO, G.; DE LUIGI, M.C.; LERCARI, G.; BARABINO, G.F.; NUNZI, E.; VALBONESI, M. Lepromatous vasculitis successfully treated by plasma exchange (PE). *J. Clin. Apheresis*, v.16, n.1, p.37-8, 2001.

Vascular involvement is presently considered a "common pathway" in a number of diseases that is mediated by circulating immune complexes (CIC). CIC are found in the circulation when the disease is active and in single patients their level may parallel disease activity. Lepromatous leprosy is characterized by the presence of CIC and deposits of immunoglobulins and complement in vascular lesions of the different organs and an Arthus-like mechanism is considered as the basis for the clinical picture. The same mechanism is considered to play an essential pathophysiologic role in Lucio's phenomenon, which is characterized by lymphohistiocytic vascular infiltrates with or without thrombosis and secondary cutaneous infarction. Lepromatous vascular involvement is mediated by CIC whose antigen composition is known, the same as it is with HCV mediated cryoglobulinemia, HBV positive panarteritis nodosa, rheumatoid vasculitis, or Wagner's granulomatosis, which are usually treated by PE [1-3]. PE has been employed for lepromatous vasculitis since 1979 [4] and other cases have been successfully treated afterwards [5,6]. We report on another patient successfully treated by plasma exchange.

WU, X.S.; NING, Y.; SHI, L.; JIN, Z.; YANG, J.W. An epidemiological analysis of leprosy from 1951-1996 in Sichuan. *Indian J. Leprosy*, v.72, n.2, p.215-226, Apr-Jun., 2000.

Through the leprosy surveillance system established in 1990s the authors analysed the epidemiology of leprosy in Sichuan province from 1951 to 1996. By the end of 1996, the total number of registered cases was 32,772, the peak incidence rate (2.44/100,000) was in 1958. The annual average progressively decreasing speed (AAPDS) of the number of new cases, incidence rate, incidence rate among children, number of newly detected patients, detection rate, number of registered cases and registered prevalence rates were 4.7% (xg = 0.9534), 5.9% (xg = 0.9407), 7.4% (xg =

0.9263), 6.7% (xg = 0.9326), 8.1% (xg = 0.9195), 10.9% (xg = 0.8913) and 11.7% (xg = 0.8828) respectively. Among newly detected cases, the proportion of children gradually declined with an AAPDS of 2.9% (xg = 0.9712), but that of household contacts gradually increased, showing a gradual decline of source of infection. The multibacillary (MB) rate among new cases, newly registered cases and active cases also increased gradually. The MB rate among child cases was much lower than that among adults. The disability rates among newly registered cases tended to decline. The peak incidence was in the 20 to 35 years age group, the average age at onset being 31.92 years. Average age at onset gradually increased to 34.19 during 1991-1995. The average interval between onset of symptoms and diagnosis was 4.89 years and that had reduced gradually to 3.24 years during 1991-1995. The authors conclude that: (1) the epidemiological trend of leprosy in Sichuan province shows decline; (2) the case-finding activities have improved and intensified; but (3) the disability rate among newly detected cases is still high (> 20%) and the average delay in diagnosis is still too long, showing that early case finding is still not satisfactory.

## IMUNOLOGIA

HATAGIMA, A.; OPROMOLLA, D.V.A.; URA, S.; FEITOSA, M.E.; BEIGUELMAN, B.; KRIEGER, H. No evidence of linkage between Mitsuda reaction and the NRAMP1 locus. *Mt. Leprosy*, v.69, n.2, p.99-103, Jun., 2001.

Thirty sib-pairs were ascertained through unrelated lepromatous probands. They consisted of 22 healthy individuals and 8 leprosy patients. The Mitsuda reactions of all sibs were evaluated both macroscopically and histologically, and high molecular weight genomic DNA was extracted from the white blood cells of all sib-pairs. Three DNA polymorphisms identified by polymerase chain reaction (274C/T, D543N, 1729 + 55de14) were used as chromosome markers at the NRAMP1 locus. Sib-pair comparisons did not disclose any sign of close linkage between the Mitsuda reaction and the genetic markers.

ROCHE, P.W.; NEUPANE, K.D.; FAILBUS, S.S.; KAMATH, A.; BRITTON, W.J. Vaccination with DNA of the *Mycobacterium tuberculosis* 85B antigen protects mouse foot pad against infection with *M. leprae*. *Int. J. Leprosy*, v.69, n.2, p.93-98, Jun., 2001.

A DNA vaccine composed of the gene for the common mycobacterial secreted protein antigen 85B was demonstrated to protect the mouse foot pad against infection with *Mycobacterium leprae*. The protective effect

was demonstrated by a 61%-88% reduction in the bacterial number, a protective effect less than that of BCG. The same DNA vaccine has been shown to protect mice against *M. tuberculosis* infection, and the importance of testing other candidate tuberculosis vaccines for their potential to protect against leprosy is discussed.

## PATOLOGIA

JOB, C.K. Pathology and pathogenesis of leprosy neuritis; a preventable and treatable complication. *Int. J. Leprosy*, v.69, p.S19-S29, Jun., 2001. (Suppl. 2).

In conclusion, it may be said that many advances have been made in the diagnosis, treatment and prevention of nerve damage. It is now a well accepted fact that the affinity of *M. leprae* for Schwann cells and the property of *M. leprae* to grow in cooler sites of the body have made certain segments of nerve trunks vulnerable. Trauma that supervenes the inflammation and swelling severely aggravates the nerve damage. The reactive phase in all forms of leprosy, the etiology of which is not clearly understood, produces intraneural caseous necrosis in tuberculoid disease and microabscesses in lepromatous disease, causing much irreversible damage to nerves. The steroid treatment that is administered during the reactive phase has helped greatly to stop further damage, although the damage already done to nerves is not always reversible. Preventive measures like detecting the disease before nerve trunks are infected and offering prompt and adequate antileprosy therapy as early as possible have helped to reduce the prevalence of deformities. It is hoped that administering steroids along with antileprosy therapy to prevent active inflammation and or fibrosis of the nerve will reduce the prevalence of nerve damage significantly. Measures which provide rest for the infected nerve to prevent trauma should be explored.

## PREVENÇÃO

CHEN, S.; ZHANG, L.; WANG, Z.; ZHOU, J.; LIU, Y.; MAO, C. Experiences from a collaborative project on the prevention of disability in leprosy patients in Shandong Province, the People's Republic of China. *Leprosy Rev.*, v.72, n.3, p.330-336, Sep., 2001

Shandong Province (present population 89 million) in the People's Republic of China established a leprosy control programme in 1955. Between that year and the end of 1999, allowing for death and migration, the cumulative number of cases registered was 53,618, including 120 cases on multiple drug therapy (MDT) and 18,248 who had completed satisfactory courses of dapsone monotherapy and/or MDT. Of this latter group, 9500 cases (52%) suffered from visible disabilities (grade 2 of the WHO classification). Prevalence and incidence rates of leprosy have decreased

dramatically since 1955 and, on average, only 50-70 new cases are now being detected annually in the entire province. Leprosy is thus no longer a public health problem, but the existence of such a large number of patients with grade 2 disabilities is clearly a matter of serious concern. This paper describes a pilot project to investigate the potential of health personnel in the leprosy programme and the dermatology and sexually transmitted diseases services to (a) prevent deterioration of existing disabilities in ex-patients through self-care and (b) prevent new neuritis in patients on MDT through early detection and the use of steroids.

VAN DEN BROEK J, VAN JAARSVELD T, DE RIJK A, SAMSON K, PATROBAS P. Capture-recapture method to assess the prevalence of disabled leprosy patients. *Leprosy Rev.*, v.72, n.3, p.292-301, Sep., 2001.

The capture-recapture technique was applied in estimating the prevalence of disabled leprosy patients in four States in Northern Nigeria. A two-sample capture-recapture method, using data from hospital admissions during 1997 and 1998 in three leprosy referral hospitals, and from a sample survey on leprosy patients with disabilities in the clinics in 1999. In the sample, 1395 (ex) leprosy patients were found, 393 with a disability. Of these 393 patients, 47 had been admitted during 1997 and 1998 to one of three leprosy referral hospitals. In these hospitals, 151 individuals from the 24 study Local Government Areas (LGA) in four states of Northern Nigeria were admitted in 1997 and 1998. Using the Peterson estimator, we calculated the number of unknown disabled leprosy patients in the studied LGAs to be 1262 (95% confidence interval 991-1533). This was nearly four times greater than the field reported figure. The capture-recapture method can be applied in a leprosy care programme. Limitations of the method are the completeness of reporting after invitation in the field, as well as the probable biased sample of leprosy patients admitted to hospital. Our finding implies that relying on patients to report for prevention of disabilities and rehabilitation to the clinics, causes the real size of the problem to be underestimated by a factor of 3-4. We recommend the use of a special 'care' register for disabled leprosy patients to better address their needs for prevention of disabilities and rehabilitation.

## TERAPÉUTICA

AL-QUBATI, Y.; AL-KUBATI, A.S. Multidrug therapy - the pathway for global leprosy elimination. *Indian J. Leprosy*, v.72, n.4, p.477-490, Oct-Dec., 2000.

Introduction of dapsone therapy paved the way for

better and more humanitarian way of dealing with the leprosy victims who, prior to 1943, were simply rejected and segregated from society. Emergence of dapson-resistant *M. leprae* and mycobacterial persistence provoked our quest for another solution. More drugs were discovered for treatment of leprosy. But the real breakthrough was the recommendation of regimens of multidrug therapy (MDT) for the treatment of leprosy by the WHO Study Group on Chemotherapy of Leprosy in October 1981. Subsequent world wide development of leprosy control activities was phenomenal. The impact of MDT has led to the cure of over eight million leprosy sufferers and the saving of one million patients from becoming crippled. Leprosy prevalence has decreased by 80% in ten years. By the end of May 1999 the leprosy burden remained concentrated in only 12 countries of the world. These achievements are mainly attributed to the development and worldwide adoption of the MDT programme.

DHOPLÉ, A.M. Search for newer antileprosy drugs. *Indian J. Leprosy*, v.72, n.1, p.5-20, Jan-Mar., 2000.

In 1991 World Health Organization proclaimed the goal of global elimination of leprosy as a public health problem by year 2000 by implementing multidrug therapy (MDT). Since then the prevalence rate has declined by 85%. However, during the same period the incidence rate of leprosy has remained constant or even has been increasing. This suggests that it will take a long time for the eradication of leprosy and that without in-vitro cultivation of *M. leprae*, eradication of leprosy is not likely to be achieved. While in-vitro cultivation is a long-term goal, as an immediate measure, there is an urgent need for the development of newer drugs and newer multidrug therapy regimens. Using the in-vitro system for screening potential antileprosy drugs and also using the mouse foot-pad system we have evaluated several compounds in four classes of drugs: dihydrofolate reductase inhibitors, fluoroquinolones, rifampicin analogues and phenazines and identified at least two compounds that appear to be more potent than dapson, rifampicin and clofazimine. Newer combinations of rifampicin analogues and fluoroquinolones have also been identified that seem to be better than the combination of rifampicin and ofloxacin.

GROSSET, J.H. Newer drugs in leprosy. *Int. J. Leprosy*, v.69, p.S14-S18, Jun., 2001. (Suppl. 2).

During the last 15 years, new drugs active against *Mycobacterium leprae* have been identified. All of them belong to the fluoroquinolone, cycline and macrolide drug families. In the mouse model and in humans, minocycline, ofloxacin, and clarithromycin have demonstrated,

individually or in combination, antileprosy activities much superior to those of the standard drugs dapson and clofazimine. In humans, a single dose of the combination ofloxacin 400 mg + minocycline 100 mg was able to kill 68% to 98% of viable *M. leprae* and a single dose of ROM, a three-drug combination of rifampin 600 mg + ofloxacin 400 mg +

minocycline 100 mg, was killing more than 99% of viable *M. leprae*. As a result of a double-blind, control, clinical trial, the Seventh Report of the WHO Expert Committee on Leprosy recommended in 1997 the use of single-dose ROM in the treatment of patients with single-lesion paucibacillary leprosy. Recently moxifloxacin, a new fluoroquinolone, and rifapentine, a long-lasting rifamycin derivative, have demonstrated in the mouse model highly promising antileprosy activities, justifying their assessment in humans.

GUPTA, U.D.; KATOCH, K.; SINGH, H.B.; NATRAJAN, M.; SHARMA, V.D.; KATOCH, V.M. Assessment of viability by normal mouse foot-pad and bacillary ATP bioluminescence assay in multibacillary cases treated with an MDT regimen using conventional as well as newer drugs like minocycline and ofloxacin. *Indian J. Leprosy*, v.72, n.4, p.437-442, Oct- Dec., 2000.

The therapeutic effect of a drug regimen of conventional drugs as well as newer drugs like ofloxacin and minocycline in smear-positive multibacillary (MB) leprosy cases was assessed by mouse foot-pad and ATP bioluminescence methods. Biopsies were taken before starting treatment and after one year of treatment. They were processed for viability assessment by normal mouse foot-pad inoculation and bacillary ATP assay techniques. The test regimen was quite effective in its antibacterial effect as it was found to result in loss of bacillary viability in all the cases, as assessed by both methods.

CHEN, X.S.; LI, W.Z.; JIANG, C.; YE, G.Y. Leprosy in China: epidemiological trends between 1949 and 1998. *Bull. World Health Organ.*, v.79, n.4, p.306-12, 2001.

OBJECTIVE: To report the epidemiological trends of leprosy in China from 1949 to 1998. METHOD: Data for the study were obtained from the computerized database of the National System of Leprosy Surveillance. FINDINGS: A total of 474,774 leprosy patients were detected during this 50-year period. Case detection rates per 100,000 population were highest in the 1950s and 1960s, with peaks appearing in 1957-58, 1963-66, 1969-70, and 1983-84, corresponding to mass surveys or screening surveys carried out in most areas or selected areas of the country. While the duration of the disease at the time of detection fell over the period, the disability rates, which were > 50% in the early

1950s, have decreased gradually to 20.8% by 1997-98 but are still too high. More than 50% of cases were found through active methods in the periods 1955-58, 1965-66, and 1969-76, but in recent years cases are mostly detected through dermatological clinics or by voluntary reporting. The peak prevalences of the 1960s (i.e. > 2 per 10,000 population) decreased annually from the 1970s onwards. By the end of 1998 the prevalence was 0.05 per 10,000 population. CONCLUSIONS: This study shows that leprosy was well controlled in China and that the WHO goal of

elimination of leprosy as a public health problem has been achieved at the national and subnational levels. However, leprosy is still unevenly distributed in the country. According to the criterion for leprosy elimination in China—defined as a prevalence of < 1 per 100,000 in county or city—there are still more than 10% of counties or cities where this target has not yet been reached. Special attention must therefore be given to achieve elimination and final eradication of leprosy in China.