

HANSENIASE: RESUMOS

HANSENIASIS ABSTRACTS

BACTERIOLOGIA E IMUNOLOGIA

BACTERIOLOGY AND IMMUNOLOGY

ABU AHMED, H.; BELEHU, A.; STONER, G.; TOUW, J.; AT LAW, T. Selection of sites for slit-skin smear. *Lepr. Rev.*, 50(4):283-287, 1979.

The results of slit-skin smears from 18 untreated lepromatous leprosy patients showed high bacteriological index (BI) and morphological index (MI) in the ears, fingers, face, buttocks and toes. Need for standardization of site of smearing is stressed. The ears, fingers, face and buttocks are suggested as standard sites for slit-skin smearing for diagnosis, follow-up and assessment of chemotherapy.

Authors' abstract

COLE, F.S.; BRUSCH, J.L.; TALARICO, L. A circulating anticoagulant in lepromatous leprosy. *Int. J. Lepr.*, 47(2):121-125, 1979.

We observed a patient with lepromatous leprosy and a circulating anticoagulant. Intrinsic pathway inhibition was demonstrated by prolongation of the activated partial thromboplastin time. Extrinsic pathway inhibition was demonstrated by prolongation of the prothrombin time when performed with diluted thromboplastin. A plasma co-factor was required for inhibition. Immunoabsorption with specific antisera and Sephadex G-200 fractionation suggested that the anticoagulant was an IgM immunoglobulin. The similarities between this patient's anticoagulant and those associated with other disease states are discussed.

Authors' summary

HUIKESHOVEN, H.; WIT, M. de.; SOETERS, A.; EGGELTE, T.A.; LANDHEER, J.E.; LEIKER, D.L. ELISA inhibition technique for the demonstration of sulphones in body fluids. I. Sulphones specific antibody-enzyme conjugate. *Lepr. Rev.*, 50(4):275-281, 1979.

A sulphones specific antibody-enzyme conjugate was developed as a basic tool for an enzyme linked immunosorbent assay (ELISA) for dapsone. The conjugate was found to be specific for sulphones without significant cross-reactions with sulphonamides. The sensitivity for dapsone is in the ng/ml range. This may lead to a simple and sensitive ELISA inhibition technique for the qualitative demonstration of sulphones in body fluids.

Authors' abstract

KELKAR, S.S.; MONDKAR, A.D.; WARAWDEKAR, W. Serum immunoglobulins in leprosy. *Lepr. India*, 51(2):189-193, 1979.

Serum immunoglobulins were quantitated by radial immunodiffusion in 25 cases each of tuberculoid and lepromatous leprosy. Immunoglobulins estimated from 50 normal healthy adults were the control. Serum IgG was markedly raised in both tuberculoid (mean 2420 mg/dl) and lepromatous leprosy (mean 2493 mg/dl) when compared with the controls (mean 1288 mg/dl) and the difference was significant ($p < 0.01$). However the difference in serum IgM and IgA levels in cases as compared to controls were not statistically significant. Serum IgM was slightly raised, the mean values obtained being 222 mg/dl in tuberculoid leprosy, 221 mg/dl in

lepromatous leprosy and 202 mg/di in control. Serum IgA was reduced in lepromatous leprosy (mean 129 mg/di) as compared to the controls (mean 168 mg/di) and the cases of tuberculoid leprosy (mean 165 mg/di). The range of values obtained in both groups of patients showed greater scatter than the controls and a few cases of both forms of leprosy showed very low values of both serum IgA and IgM.

Authors' abstract

LAI A FAT, R.F.M.; CHAN PIN JIN, J.; DIESSELHOFF-DEN DULK, M.; VAN FURTH, R. *In vitro* synthesis of humoral factors (immunoglobulins and complement) in lesional skin of leprosy patients. *Infect. Inman.*, 25(3):891-895, 1979.

An *in vitro* culture technique was used to demonstrate the synthesis of immunoglobulins and complement in lesional skin of patients representing the entire clinico-histopathological spectrum of leprosy. The results indicate that immunoglobulin G is produced in different amounts in the various forms of leprosy. Classification of the patients according to the three main groups shows that a small amount of immunoglobulin G synthesis occurred in tuberculoid leprosy, a distinct amount occurred in borderline leprosy, and a large amount occurred in lepromatous leprosy. Contrary to expectation, synthesis of C3 was found only in some of the cultures of these three forms of leprosy. The function of the locally synthesized immunoglobulin G and the findings concerning C3 synthesis are discussed.

Authors' abstract

MASALA, C.; AMENDOLEA, M.A.; NUTI, M.; RICCARDUCCI, R.; TARABINI, C.G.L.; TARABINI, C.G. Autoantibodies in leprosy. *Int. J. Lepr.*, 47(2):171-175, 1979.

The frequency of autoantibodies directed against a variety of tissue constituents (thyroglobulin, thyroid-microsomes, gastric parietal cells, nuclei, smooth muscle, mitochondria) has been assessed in 186 Somalian leprosy patients (living in the leprosy village in Jilib), of whom 111 had lepromatous (LL) leprosy and 75 had the tuberculoid (TT) leprosy, according to the classification of Ridley-Jopling. A significant increase of thyroglobulin (Tg) antibodies, of antinuclear antibodies (ANA) and of smooth muscle antibodies (SMA) was found in leprosy patients as compared to matched healthy controls. The frequency of thyroid microsomal antibodies, of gastric parietal cell antibodies and of mitochondrial antibodies in leprosy patients did not significantly

differ from that found in the control group. Autoantibodies occurred to almost the same extent in both tuberculoid (TT) patients and lepromatous (LL) patients; an increased frequency of thyroglobulin antibodies was found among the tuberculoid patients as compared to lepromatous patients while the opposite was found for SMA.

These results seem to indicate that the hypothesis of a suppressor T cell deficiency leading to an increased autoantibody production in leprosy is too simplistic and that other mechanisms may account for the increased autoantibody production in both the tuberculoid and lepromatous forms.

Authors' summary

MEHRA, V., MASON, L.H.; FIELDS, J.P.; BLOOM, B.R. Lepromin-induced suppressor cells in patients with leprosy. *J. Immunology*, 123(4):1813-1817, 1979.

The possibility of an active mechanism of immunologic suppression in leprosy was explored by assessing the *in vitro* lymphocyte responses of 61 leprosy patients and 30 normal individuals to the mitogen Con A in the presence or absence of Dharmendra lepromin. Lepromin-induced suppression of Con A stimulation was found in 32 of 35 lepromatous patients and 15 of 15 borderline patients, but only 2 of 15 tuberculoid patients and 2 of 30 normal controls. Cell fractionation studies indicated at least two cell populations involved in the *in vitro* lepromin-induced suppressor activity, adherent veils and Ty-cells.

Authors' abstract

MENZEL, S.; BJUNE, G.; KRONVALL, G. Lymphocyte transformation test in healthy contacts of patients with leprosy. I. Influence of exposure to leprosy within a household. *Int. J. Lepr.*, 47(2):138-152, 1979.

Fifty-three household contacts of lepromatous patients, 37 household contacts of tuberculoid patients, and 91 control persons were examined with the lymphocyte transformation test (LTT) for their responses to whole and sonicated antigen preparations from *M. Leprae*, to BCG, *M. avium*, *M. gordonae*, and phytohemagglutinin (PHA). The study was carried out in the Gurage area of Ethiopia in 15 households with a leprosy patient and 15 matched control households. Household contacts of lepromatous patients showed significantly greater LTT responses to antigens from *M. leprae* than the controls, whereas household contacts of tuberculoid patients did not respond differently from controls. Household contacts of lepromatous

patients had significantly greater responses to *M. leprae* antigens when the index patients were "active," i.e., highly bacilliferous, than when they were "inactive," i.e., having a low bacillary load. The degree of sensitization, as indicated by the LTT response, in different exposure groups paralleled the degree of probable infectivity of the index patient. A preparation of antigen from whole *M. leprae* proved to be more sensitive and more specific in the LTT than did a sonicated preparation. A significant degree of cross-reactivity was found among the various mycobacteria in their LTT responses.

Authors' summary

MENZEL, S.; BJUNE, G.; KRONVALL, G. Lymphocyte transformation test in healthy contacts of patients with leprosy. II. Influence of consanguinity with the patient, sex, and age. *Int. J. Lepr.*, 47(2) : 153-160, 1979.

The study was carried out in the Gurage area of Ethiopia, where 53 household contacts of lepromatous patients, 37 household contacts of tuberculoid patients, and 91 control persons were examined with the lymphocyte transformation test (LTT) for their responses to whole and sonicated antigen preparation from *M. leprae* to BCG, *M. avium*, *M. gordonae* and phytohemagglutinin. The potential influence of host factors, namely the state of consanguinity with the leprosy patient, sex and age on the LTT responses was evaluated. In the 35 household contacts of "active," i.e., highly bacilliferous, lepromatous patients, consanguinity with a lepromatous patient was not associated with a significant depression of the LTT responses to *M. leprae* antigens. Male household contacts of active lepromatous patients showed significantly greater LTT responses to *M. leprae* antigens than female household contacts. Possible confounding factors for this finding are discussed. Sensitization of *M. leprae* antigens was present already in a high proportion of the 6 to 14 year old household contacts of active lepromatous patients, which was the youngest age group examined in our study. No significant results were found in any of the other patient contact groups with regard to the host factors examined.

Authors' summary

SAHA, K.; DUTTA, R.N.; DUTTA, A.K.; MOHAN, T.R. Reversal reaction in patients with lepromatous leprosy after transplantation of human fetal thymic grafts. *Vox Sang.*, 35(1-2) :81-90, 1978.

An attempt has been made to reconstitute impaired cell-mediated immunity in I patient

with indeterminate, 4 patients with borderline and 2 patients with polar lepromatous leprosy by grafting three thymus glands obtained from human fetuses of 14-19 weeks gestation. Most of these patients had severe ulcerative erythema nodosum leprosum (ENL) and were intolerant to dapsone. After thymus transplantation these patients were followed for 11/2 years. During this period, all conventional chemotherapy had been withdrawn. In most cases, there was dramatic improvement of the clinical condition, resolution of skin lesions, subsidence of ENL, clearance of bacteria from skin and reconstitution of several immunologic deficits; but late lepromin reactivity returned in none, which indicated permanent loss of resistance to *Mycobacterium leprae*.

From authors' abstract

SCHEINBERG, M.A.; MASUDA, A.; BENSON, M.D.; MENDES, N.F. Serum amyloid protein SAA, C-reactive protein and lysozyme in leprosy. *Int. J. Lepr.*, 47(2) :133-137, 1979.

Serum amyloid protein (SAA) appears to be the precursor of amyloid protein AA, the non-immunoglobulin fibril protein of secondary amyloidosis. Since amyloidosis is known to occur in high frequency associated with lepromatous leprosy (LL), we have examined the SAA levels in untreated LL patients and compared them to the levels observed in patients with tuberculoid leprosy (TT) and a large number observed in healthy controls. We found that SAA is markedly elevated in LL when compared to TT and controls. No clear correlation could be established with C-reactive protein, a well-documented acute phase reactant, or serum lysozyme levels that reflect the presence of monocyte activity. This study showed that SAA levels in leprosy do not appear to be a reflection of inflammatory activity or monocyte turnover. Whether amyloidosis will be more prevalent in patients who have higher SAA levels remains to be determined.

Authors' summary

SENGUPTA, U.; GHEI, S.K.; VENKATESAN, K.; BHARADWAJ, V.P. *In vivo* effect of DDS on phytohemagglutinin (PHA) — induced lymphocyte transformation cultures in normal healthy volunteers. *Int. J. Lepr.*, 47(2) :167-170, 1979.

Depression in PHA-induced lymphocyte transformation in peripheral blood has been observed in 15 healthy volunteers after administration of DDS (100 mg/day) for seven days. *In vitro* culture of lymphocytes obtained

from these volunteers in DDS-free normal AB serum has not altered the blast cell numbers. Lymphocytes of these volunteers have been found to contain a significant amount of DDS, ranging from 0.42 to 3.2 *yg* per 10.6 lymphocytes.

Authors' summary

SHARMA, S.; GANGULY, N.R.; KUMAR, B.; KAUR, S.; CHAKRAVARTY, R.N. T and B lymphocytes and blastogenesis in leprosy. *Lepr. India*, 51 (2):194-202, 1979.

T and B cell percentages and their blastogenic response to PPD and lepromin have been studied in 107 patients of various types of leprosy. T cell counts and their blastogenic response were found to be considerably lower in all types of leprosy as compared to the normal. The counts and stimulation were the lowest for lepromatous leprosy. B cell counts were unaltered in all types of leprosy.

Authors' abstract

YODER, L.; NAAFS, B.; HARBOE, M.; BJUNE, G. Antibody activity against *Mycobacterium leprae* antigen 7 in leprosy: studies on variation in antibody content throughout the spectrum and on the effect of DDS treatment and relapse in BT leprosy. *Lepr. Rev.*, 50(2):113-121, 1979.

Antibodies against *Mycobacterium leprae* antigen 7 were determined by a specific radio-immunoassay. The median value of 4 groups of patients decreased gradually from the lepromatous to the tuberculoid end of the spectrum, but there was a striking variation between the antibody content of individual sera in each group. Prolonged DDS treatment led to only a moderate decline of this antibody activity in lepromatous leprosy. In borderline tuberculoid leprosy, DDS treatment led to a marked decrease in antibody activity and a relapse is associated with renewed synthesis and increased antibody content.

Authors' abstract

HANSENÍASE EXPERIMENTAL E LEPRA ANIMAL EXPERIMENTAL HANSENIASIS AND ANIMAL LEPROSY

ANTHONY, J.; VAIDYA, M.C.; DASGUPTA, A. Immunological methods employed in an attempt to induce erythema nodosum leprosum (ENL) in mice. *Lepr. India*, 50(3):356-362, 1978.

In the mouse foot pad model five different parameters were employed to simulate the condition of ENL as observed in the human. The experimental groups with five to six months leprosy infection were injected intravenously with various antimycobacterial antibodies, *M. leprae* sonicate and 'B' cells obtained from synergic donors. The control group of animals, infected similarly, were treated either with *M. leprae* sonicate or gamma globulins precipitated from normal human serum. All recipients were killed at one day interval excepting those with 'B' cell transfer, which were sacrificed at seven days. The sites of predilection for immune complex deposition viz. foot pad and kidney as well as the spleen were examined by light and fluorescence microscopy. These findings are described and discussed.

Authors' abstract

BHIDE, M.B.; PRADHAN, K.S.; BAPAT, C.V. A vaccine from ICRC bacilli against *M. leprae* infection in mouse foot-pad. *Lepr. India*, 50(3):334-344, 1978.

A vaccine was prepared from ICRC bacilli strain C-44 by γ -irradiation and injected subcutaneously in two batches of CBA mice. An equal numbers of vaccinated and untreated mice were challenged with fresh *M. leprae* infection in foot-pads (7.5×10^6). The first group was challenged at 2 weeks and others at 1, 2 and 3 months after vaccination. The foot-pad harvests were made at monthly intervals from 6th month, to estimate the group of *M. leprae* in a pair of vaccinated and untreated mice. In normal untreated mice, the *M. leprae* exhibited normal growth pattern with final yield 2×10^6 (max.). In vaccinated mice challenged after 2W and IM, the yields of AFB were higher (2.5X) than in normal mice at 6 to 8 months. The number then dropped sharply, and remained low, with a small rise later. In the groups-2M and 3M, the growth of *M. leprae* remained suppressed without initial enhancement. The results expressed as the ratio of yields, Vac/Cont. show that there is early enhancement phase (2.5) followed by sharp drop (0.6) and

suppression (0.2) of growth of *M. leprae* in vaccinated mice in comparison with that in the untreated mice. The results demonstrate that irradiated ICRC bacilli used as vaccine, can induce protective mechanisms against *M. leprae* infection in mouse foot-pad. It appears that CMI develops at about 6 weeks after vaccination. The pattern of growth—enhancement, drop and arise, in the vaccinated mice suggests specificity of action, i.e. antigen-induced CMI. The data also establish the feasibility of the mouse model for the study of anti-leprosy vaccines.

Authors' abstract

CAMARGO, E.E.; KERTCHER, J.A.; LARSON, S.M.; TEPPER, B.S.; WAGNER JR., H.N. Radiometric measurement of differential metabolism of fatty acids by *Mycobacterium lepraemurium*. *Int. J. Lepr.*, 47(2):126-132, 1979.

An assay system has been developed based on automated radiometric quantification of ^{14}C produced through oxidation of (^{14}C) fatty acids by mycobacteria. With this system, the Hawaiian strain of *M. lepraemurium* was studied using the K-36 buffer as a suspending solution for the organisms along with $5.0\ \mu\text{Ci}$ of one of the following fatty acids: acetate, butyric, hexanoic, octanoic, decanoic, lauric, myristic, palmitic, stearic, oleic, linoleic, linolenic, and malonic. The ^{14}C production by this organism was greatest with lauric, decanoic, myristic, octanoic, and stearic acids, in decreasing order. Assimilation studies and radiochromatograms confirmed that most of the oxidized substrates were converted into by-products with no change in those from which no oxidation was found.

These data suggest that the radiometric measurement of differential fatty acid metabolism may provide a basis of radiometric identification of *M. lepraemurium* and assessment of the growth requirements of this organism.

Authors' summary

CHANDI, S.M. & JOB, C.K. The early cellular response to *M. leprae*: and ultra-structural study. *Lepr. India*, 50(3):345-351, 1978.

The ultrastructural changes that develop in mouse peritoneal macrophages from 10 minutes up to 14 weeks after exposure to *Mycobacterium leprae* are presented. Phagocytosis occurred by a process of engulfment by cytoplasmic processes and incorporation into a phagosome, into which lysosomal enzymes were subsequently introduced. Electron transparent zones (E.T.Z.) were not observed around phago-

cytosed bacilli in this study, however discrete droplets of lipid-like material appeared in the cytoplasm of macrophages, between 2 and 4 weeks after ingestion of the micro-organisms. Phagosomes with double limiting membranes were observed in macrophages harvested as early as 40 minutes after exposure to *M. leprae*, contrary to the observations of Evans and Levy (1972).

Authors' abstract

CURTIS, J. & TURK, J.L. Mitsuda-type lepromin reactions as a measure of host resistance in *Mycobacterium lepraemurium* infection. *Infect. Immun.*, 24(2):492-500, 1979.

The footpad reaction to autoclaved whole *Mycobacterium lepraemurium* organisms (ML M lepromin) in high-resistance (C57BL) and low-resistance (BALB/c) mice was studied. Infected C57BL mice gave a prolonged footpad response persisting for 4 weeks after skin testing with high and low doses of lepromin. This was accompanied by mononuclear cell infiltration. Uninfected C57BL mice gave no response. The majority of infected BALB/c mice gave no increase in footpad thickness. However, a high proportion of infected and control BALB/c mice tested with the high dose showed mononuclear cell-infiltration which resembled that in C57BL mice. The low dose caused little infiltration in infected or control BALB/c mice. The course of infection in the two strains was different. Dissemination of organisms from the infected footpad was minimal in C57BL mice 5 months after infection. In BALB/c mice, dissemination to the draining lymph node and to some extent to the liver had occurred by 5 months. The draining lymph node of BALB/c mice showed histological evidence of local antibody formation, which was not found in C57BL mice. On the basis of these findings, it was possible to fit murine leprosy in these two strains into a classification similar to that used for human leprosy.

Authors abstract

DRAPER, P.; HART, P.A.; YOUNG, M.R. Effects of anionic inhibitors of phagosome-lysosome fusion in cultured macrophages when the ingested organism is *Mycobacterium lepraemurium*. *Infect. Immun.*, 24(2):558-561, 1979.

The mouse pathogen *Mycobacterium lepraemurium* is readily phagocytosed by cultured mouse peritoneal macrophages. Ingestion is normally followed by fusion between phagosomes and lysosomes. The influence of some anionic compounds known to inhibit fusion in other systems was investigated by trans-

mission electron microscopy after ingestion of *M. lepraemurium*. Fusion was markedly, although temporarily, inhibited by suramin and moderately inhibited by poly-D-glutamic acid. The effects are, however, not sufficient to permit these agents to be used to study the longterm effects of shutting off the secondary lysosomephagosome fusion system in cultured macrophages infected with *M. lepraemurium*.

Authors' abstract

KAJIWARA, N.M. & MATSUO, Y. Effect of culture supernatants of mouse splenic lymphocytes on the growth of *M. lepraemurium* in mouse peritoneal macrophages. *Jap. J. Leprosy*, 47(4) :103-109, 1978.

Splenic lymphocytes were collected from BCG-vaccinated ddY mice and cultured with or without the antigen. Thus obtained supernatants were tested by tissue culture techniques. Normal mouse peritoneal macrophages were infected with *M. lepraemurium in vitro* and the effects of Myco1F (mycobacterial growth inhibiting factor) in these supernatants on the growth of the bacilli were examined. The multiplications of the bacilli were suppressed in the media added with culture supernatants of splenic lymphocytes from immunized animals, especially the one cultured with antigen for 48 hr.

Authors' abstract

KAWAGUCHI, Y.; MATSUOKA, M.; KAWATSU, K.; SUSHIDA, K.; TANEMURA, M. Pathogenicity of cultivated murine leprosy bacilli of Hawaiian-Ogawa strain in mice. 3. Transmission of bacilli recovered from subcutaneous leproma induced with smooth-colony variants. *Japan. J. Exp. Med.*, 49 (1):27-32, 1979.

CHI and DDD strain mice were subcutaneously inoculated with 0.25 ml of a 1:1000 saline suspension prepared from a malignant leproma in a nude mouse. The malignant leproma was induced with smooth colony variants (HO-S) of cultivated murine leprosy bacilli, strain Hawaiian-Ogawa. In C3H mice, no palpable lesions developed during the initial 35 weeks post-infection, however, at week 40, palpable lesions which were identified as malignant lepromata, were found. In DDD mice, small benign lepromata were present at week 10 and examination at week 40 showed that they had not increased in size. BALB/c mice were subcutaneously inoculated with 0.25 ml of a suspension prepared from the homogenate of subcutaneous tissue from the HO-S bacilli inoculation site of C3H mice. This suspension contained, the same number of bacilli as a 1:2000 leproma suspension. Three

of 4 BALB/c mice developed typically intermediate mouse leprosy and similar results were obtained in BALB/c mice infected with HO-S bacilli grown *in vitro*.

These observations confirmed our previous results and led us to conclude that the pathogenicity of HO-S bacilli grown *in vivo* is identical to that of *in vitro* cultivated HO-S bacilli and that HO-S bacilli do not revert to the more highly virulent parent bacilli of the rough colony (HO-R).

Authors' summary

KAWAGUCHI, Y.; MATSUOKA, M.; KAWATSU, K.; SUSHIDA, K.; TANEMURA, M. Pathogenicity of cultivated murine leprosy bacilli of Hawaiian-Ogawa strain in mice. 4. Visceral lesions in mice produced by intraperitoneal infection. *Japan. J. Exp. Med.*, 49(4) :265-271, 1979.

The pathogenicity of two substrains (HO-R and HO-S) of cultivated murine leprosy bacilli was examined by intraperitoneal inoculation to various strains of mice (C3H, KK, BALB/c, DDD and C57BL/6). HO-R (Rough Form) was first isolated on 1% Ogawa's egg yolk medium from the leprosy lesions produced by original Hawaiian strain (H bacilli). HO-S (Smooth Form) was dissociated *in vitro* during the 9th to 15th subculture of HO-R on the same kind of medium. In all the mice tested, intraperitoneal inoculation with HO-R bacilli produced progressively severe visceral lesions in the manner similar to H bacilli harvested from subcutaneous leproma. The only exception was, however, in DDD strain of mice H bacilli produced only slight visceral lesions even in the later stage of infection. HO-S was much lower in the pathogenicity than the above two strains of murine leprosy bacilli. Visceral lesions produced by intraperitoneal inoculation with HO-S used to be very slight in all the strains of mice except BALB/c. BALB/c strain mice were highly susceptible to intraperitoneal as well as subcutaneous infection with HO-S. From the above observations, it is concluded that the characteristic features of pathogenicity of cultivated murine leprosy bacilli, such as mouse strain differences, are all the same regardless of infection route.

Authors' summary

LAGRANGE, P.H. Active or passive acquired resistance after *Mycobacterium lepraemurium* infection in C57BL/6 and C3H/HeN mice. *Ann. Immunol.*, 190C (4): 561-579, 1979.

Varying doses of living *Mycobacterium lepraemurium* (MLM) injected intravenously

were able to modify to some extent the local granulomatous reaction which was induced after local challenge with the same microorganism in C57BL/6 and C3H mice. Intravenous injection with 10' or more living bacteria was able to facilitate the local infection in both strains. Subcutaneous immunization with 10' living MLM was able to limit the early phase of multiplication of a secondary challenge in C57BL/6 mice. Local and systemic transfers with lymphoid cells from immune donors were associated with an early local reaction, equivalent to a delayed-type hypersensitivity reaction and with a delay of growth of the challenge inoculum in the draining node. Later on, nevertheless, the same number of acid fast bacteria were found in controls and in adoptively immunized recipients. When these recipients were pretreated with cyclophosphamide prior to the adoptive transfer, a significant reduction in multiplication was observed. Spleen or lymph node cells from MLM infected C3H mice, harvested 5 weeks after intravenous or subcutaneous infection respectively, were able to transfer an early local cellular hypersensitivity reaction but unable to modify the growth of the challenge inoculum in the draining node. Also cyclophosphamide pretreatment did not influence the onset if the granulomatous reaction nor the multiplication rate of C3H mice preimmunized with 10' MLM injected intravenously. Macrophage activation, measured by testing the increase of resistance to *Listeria mono cytogenes*, and immunopotentialization of delayed-type hypersensitivity to sheep erythrocytes after MLM infection, given either subcutaneously or intravenously, were observed in C57BL/6 but not in C3H mice. Thus, it is concluded that after subcutaneous injection with an optimal dose of MLM responsive C57BL/6 mice are able to mount a specific acquired resistance associated with hallmarks of cell-mediated immunity such as macrophage activation and cellular hypersensitivity. On the other hand, C3H mice receiving the same immunizing dose are able to mount a cellular hypersensitivity but unable to acquire a specific and a non-specific resistance. Thus the form of cellular hypersensitivity in these two strains of mice after MLM infection are different in nature.

Author's summary

LAGRANGE, P.H. & HURTREL, B. The influence of BCG vaccination on murine leprosy in C57BL/6 and C3H mice. *Ann. Immunol.*, 130C (5):687-709, 1979.

Cross-reactivity between *Mycobacterium lepraemurium* (MLM) and BCG vaccine was found and evaluated in vivo, in C57BL/6

mice, in terms of delayed-type hypersensitivity, local granulomatous response at the injected site and limitation of growth of the challenge inoculum in the draining node. Cross-reactive specific protection and local reactivities were transferred in syngeneic norm& recipients by means of non-adherent lymphoid cells from immune donors. When BCG vaccine was injected either intravenously or subcutaneously in C57BL/6 and in C3H mice, it was able to induce resistance to local infection with living MLM in both strains, but no alteration of the local granulomatous reaction (equivalent to local specific immune response) was observed in C3H mice, as compared to the control. When mice were immunized with one or two injections of heat-killed MLM after the immunomodulating effect of BCG vaccination, better immunization was not achieved. In order to test the presence of strain-related immunosuppressive mechanisms, mice were cyclophosphamide-treated during the immunization process. As expected, higher specific DTH reactions were obtained in both strains, but with only a slight increase of the protective mechanism. Protection was always higher in C57BL/6 than in C3H mice.

The specific and non-specific immune responses to BCG vaccine were then evaluated in both strains with different parameters: in vivo lympho-proliferative response in the draining node, delayed local granulomatous reaction at the injected site after a subcutaneous injection, increase in spleen index, kinetics of the immunopotentialization to a thymus-dependent antigen (sheep red blood cells) after a single intravenous injection of BCG. A striking interstrain difference was observed; C57BL/6 mice were able to mount a more rapid and marked immune response as compared to C3H mice (which only developed a delayed and slight response). Moreover, these differences were associated with the fact that BCG did not seem to multiply properly in C3H mice during the first two weeks after inoculation. Thus, it was concluded that higher natural resistance to pathogens and cross-reactive preimmunization with related microorganisms can interfere with the artificial immunization when living microorganisms are used. Implication for vaccination to mycobacterial infection (tuberculosis and leprosy) are discussed.

Authors' summary

MEHRA, V. & BLOOM, B.R. Induction of cell-mediated immunity to *Mycobacterium leprae* in guinea pigs. *Infect. Immun.*, 23 (3):787-794, 1979.

Guinea pigs immunized with intact or disrupted armadillo-grown human *Mycobacte-*

rium leprae administered in aqueous or oil vehicles were tested with various dilutions of *M. leprae* suspended in saline, water-soluble *M. leprae* extract, purified protein derivative, and a water-soluble extract of normal armadillo tissue. The results demonstrated the following. (i) Under no conditions was any skin test reactivity found to normal armadillo tissue extract. (ii) Positive sensitization to both *M. leprae* and its water-soluble extract was achieved by sensitizing guinea pigs with *M. leprae* suspended in Hanks solution or saline. Autoclaved *M. leprae* in Hanks solution or saline inoculated intradermally was an effective immunogen. Oil suspensions or emulsions were effective at sensitization, but appeared to be no better and, in general, slightly weaker, than simple inoculation in aqueous suspension. (iii) Living BCG failed to reveal a significant adjuvant effect on sensitization to *M. leprae*. However, cord factor appeared to potentiate slightly the sensitization to *M. leprae* in aqueous suspension. (iv) The minimum dose required for sensitization with *M. leprae* in aqueous suspension was 55 µg of purified bacilli. (v) Animals inoculated with *M. leprae* in saline or with *M. leprae* together with BCG showed positive skin test reactivity to the first skin test application made fully 1 year after the initial sensitization. The efficacy of autoclaved, irradiated *M. leprae* in aqueous, oil-free medium suggests a relatively safe approach to human vaccination studies.

Authors' abstract

MORI, T. & KOHSAKA, K. Isolation culture of 7 strains of *Mycobacterium lepraemurium* and isonicotinic acid hydrazide or rifampicin resistant Hawaiian strain. *Jap. J. Leprosy*, 47(3) :87-91, 1978.

Seven strains of *Mycobacterium lepraemurium* (Douglas, Fukuoka-1, Keishicho, Kurume-42, Odessa and Osaka-No. 1 strains) were isolated on the 1% Ogawa yolk medium. These colonies were white yellow, very slow growing and rough at the isolation, but were changed gradually to smooth colony by the successive cultivation. Kurume-42 and Odessa strains were strongly rough type, especially Kurume-42 strain did not change to smooth type until the 17th generation and became extinct on account of failure of cultivation at the 18th generation. Kurume-42 strain differed from the other 7 strains of murine leprosy bacillus on the characteristic of rough type. All strains secreted coproporphyrin on the medium and coloured to red

the medium surface. Many negative tubes were seen every time in the primary isolation culture and some seeded colonies did not grow in the successive cultivation. All strains are difficult to culture.

INH or rifampicin resistant strain was isolated on the 1% Ogawa yolk medium from murine leproma formed with INH or rifampicin resistant Hawaiian strain. Degree of the INH resistant is 16 µg/ml and that of rifampicin resistant is 7 µg/ml. Seven strains and INH or rifampicin resistant strain of Hawaiian were cultivated successively for several generations, thereafter these strains were inoculated to mouse. These strains made murine leproma in the injection site. Many globi were observed on the smear preparation of these murine lepromata.

Authors' abstract

WATSON, S.R.; MORRISON, N.E.; COLLINS, F.M. Delayed hypersensitivity responses in mice and guinea pigs to *Mycobacterium leprae*, *Mycobacterium vaccae*, and *Mycobacterium nonchromogenicum* cytoplasmic proteins. *Infect. Immun.*, 25(1):229-236, 1979.

Antigenic relationships between *Mycobacterium vaccae*, *M. nonchromogenicum*, and *M. leprae* were examined in mice and guinea pigs injected with *M. vaccae* or *M. nonchromogenicum* suspensions. The growth of both organisms in outbred ICR and four inbred mouse strains was followed up to 30 days. *M. nonchromogenicum* persisted in the livers and spleens of the inbred mice substantially better than did the *M. vaccae* population in the same mouse strains. A translucent colony variant of *M. vaccae* isolated from the opossum survived in vivo better than the opaque colony isolated from opossums and cattle. Persistence of *M. vaccae* and *M. nonchromogenicum* was not markedly increased in T-cell-depleted (nude) mice. Normal mice infected with increasing numbers of *M. vaccae* did not develop delayed-type hypersensitivity to the homologous *M. vaccae* cytoplasmic protein antigen. When heat-killed *M. vaccae* were incorporated into Freund adjuvant, both mice and guinea pigs developed delayed hypersensitivity to cytoplasmic antigens prepared from *M. vaccae*, *M. nonchromogenicum*, and *M. leprae*, but not to purified protein derivative. Both *M. nonchromogenicum* and *M. vaccae* vaccines cross-sensitized guinea pigs to the *M. leprae* cytoplasmic antigens.

Authors' abstract

PATOLOGIA, FISIOPATOLOGIA E BIOQUIMICA

PATHOLOGY, PHYSIOPATHOLOGY AND BIOCHEMISTRY

JOPLING, W.H. The saga of the skin smear. Editorial. *Lepr. Rev.*, 50 (4):271-273, 1979.

At this stage in our knowledge we can do no more than surmise as to the reasons why in lepromatous leprosy the skin of fingers is so rich in bacilli, and there are three likely explanations, working in concert: *firstly*, fingers are among the coolest skin sites, and it is well known that leprosy bacilli prefer cooler sites; *secondly*, the dermis of fingers has a good supply of sensory nerves, much favoured by bacilli; *thirdly*, these dermal nerves on the dorsal aspects of fingers are close to the surface because of the thinness of the dermis, and therefore an incision with a scalpel blade can readily collect bacilli from them; this applies particularly to the middle and distal phalanges. The role of repeated minor trauma is more speculative.

From the editorial

KORANNE, R.V.; RATAN SINGH; IYENGAR, B. Lymph-node involvement in tuberculoid leprosy. *Indian J. Dermatol. Venereol. Lepr.*, 45(3):177-180, 1979.

Twenty-two untreated cases of proved tuberculoid leprosy and five healthy persons in the control group were studied histopathologically for involvement of the lymph nodes. 54.54% (12 cases) in the study group showed positive evidence of lymph node involvement. Ten patients (45.45%) showed the presence of granuloma in the lymph nodes. Eight cases (36.36%) had acid fast bacilli in the lymph nodes; six (75%) of them had granulomas as well and in two cases (25%) bacilli were present without granulomatous foci. There was no evidence of tuberculosis. In the control group, none showed any pathology in the lymph nodes. In two cases, the leprosy granuloma and bacilli were seen in lymph nodes which were outside lymphatic drainage area of the cutaneous lesions. 36.84% of these cases also showed evidence of leprosy pathology in the liver.

Authors' summary

KORANNE, R.V.; RATAN SINGH; IYENGAR, B. *Mycobacterium leprae* in the striated muscle of tuberculoid leprosy patients. *Lepr. India*, 50(3):375-380, 1978.

Striated muscle specimens from 24 untreated proved cases of tuberculoid leprosy

and five healthy normal individuals were studied histopathologically for the evidence of leprosy pathology. Atrophy or damage to the muscle fibre was not observed in any patient. Nineteen (79.16%) cases showed evidence of leprosy in striated muscles. Seventeen (70.83%) cases showed scanty histiocytic infiltrate between the muscle fibres. Thirteen (54.16%) cases had acid fast bacilli mostly inside the muscle. There was no correlation between the location of the bacilli and that of the histiocytes; in two cases, acid fast bacilli were seen without the histiocyte. The bacilli were solidly staining and were lying singly in the undamaged muscle. There was no evidence of tuberculosis and, in the control group, none showed any AFB or infiltrate.

Authors' abstract

REA, T.H. & RIDLEY, D.S. Lucio's phenomenon: a comparative histological study. *Int. J. Lepr.*, 47(2):161-166, 1979.

To study further the pathogenesis of Lucio's phenomenon, we have made a comparative histological study of 11 patients with Lucio's phenomenon and 12 with ENL. Confirming the findings of others, Lucio's reaction could be distinguished from ENL by epidermal necrosis and by necrotizing vasculitis manifesting necrosis in the walls of superficial vessels and severe, focal endothelial proliferation of mid-dermal vessels. Furthermore, in Lucio's phenomenon large numbers of AFB were found in evidently normal and in swollen or proliferating endothelial cells.

We hypothesize that patients with Lucio's phenomenon have an exceptionally deficient defense mechanism, allowing unrestricted proliferation of AFB in endothelial cells, facilitating contact between bacterial antigen and circulating antibody and leading to infarction; also, this nadir of resistance allows unimpeded dissemination of AFB, accounting for the clinical features of diffuse non-nodular leprosy. Thus, an explanation is offered for the restriction of Lucio's phenomenon to patients with diffuse non-nodular lepromatous leprosy.

Authors' summary

REZA, K.; TALIB, S.; IMAM, S.K. O-diphenoloxidase concentrations in leprosy. *Br. Med. J.*, 2(6195):900-901, 1979.

O-diphenoloxidase activity was studied in 15 patients with lepromatous leprosy, 15 with tuberculoid leprosy, and 15 controls. O-diphe-

noloxidase isolated from skin and serum samples of patients with lepromatous leprosy had the specificity of a bacterially derived enzyme and not that of a mammalian-derived enzyme. Only the patients who had had lepromatous leprosy for over two years showed enzyme activity in serum, though all showed it in skin tissue. O-diphenoloxidase activity in serum may be a useful diagnostic marker of lepromatous leprosy.

Authors' summary and conclusions

SHARDA, D.P.; PARVEZ, M.; JAIN, A.K.; BHARGAVA, N.C.; MISRA, S.N. A study of serum fibrinolytic activity in leprosy. *Lepr. India*, 51(2):203-208, 1979.

Fibrinolytic activity was studied in 50 patients of leprosy and 30 healthy individuals who served as control. Fibrinolytic activity was determined by measuring euglobulin lysis. No significant alteration in fibrinolytic activity was observed in patients with non-lepromatous leprosy, the levels being approximately similar to control group. However, fibrinolytic activity was found to be significantly decreased in patients of lepromatous leprosy and lepra reaction group. The observed decrease in fibrinolytic activity can be explained on the basis of presence of tissue destruction and vasculitis seen in leprosy more so in patients with lepromatous leprosy and lepra reaction.

Authors' abstract

SMITH, W.C.S. Screening for diabetes mellitus in leprosy patients with complicated ulcers. *Lepr. India*, 51(2):236-238, 1979.

All patients admitted to an ulcer ward in a leprosy hospital over the period of one year were screened for glycosuria. Out of 154 patients screened 4 showed glycosuria. These

4 patients had more severely complicated ulcers evidenced by their longer duration of admission. Early diagnosis and treatment of diabetes in leprosy patients with complicated ulcers is important.

Author's abstract

SREEVATSA; SENGUPTA, U.; RAMU, G.; DESIKAN, K.V. Evaluation of bacteraemia in leprosy patients. *Lepr. India*, 50(3):381-387, 1978.

Thirty five patients of leprosy have been screened for bacteraemia by haemolysis (HL), leucocyte adherence (LA) and buffy coat (BC) methods and the results have been compared. The HL method has yielded not only higher number of acid-fast bacilli (AFB) but also has detected more frequently AFB in blood of leprosy patients as compared to other methods. Further, it has been established that the skin over the cubital fossa does not play any significant role in contaminating blood samples while sampling blood by venepuncture.

Authors' abstract

STONER, G.L. Importance of the neural predilection of *Mycobacterium leprae* in leprosy. *Lancet*, 2(8150):994-996, 1979.

It is suggested that continuous leakage of bacilli into the circulation from a primary focus of intraneural infection may simultaneously initiate bacillary dissemination and the suppression of cell-mediated immunity. Both these features are essential for the development of lepromatous leprosy. Nerve involvement in leprosy, previously thought of as a diagnostic feature of the disease and as a complication of therapy, may represent an essential phase in the cycle of infection and reinfection by *Mycobacterium leprae*.

Author's summary

GENETICS

GENÉTICA

CHAKRABARTY, M.S.; MUKHERJEE, K.K.; CHAKRABARTY, S.K.; GHOSH, S.; CHOUDHURY, S. Hepatitis B surface antigen (HBsAg) in leprosy patients of Calcutta: its prevalence and subtypes. *Lepr. India*, 51(2):182-188, 1979.

High incidence of Hepatitis B surface antigen (HBsAg) in lepromatous leprosy patients have been reported by many workers.

This paper reports on a study undertaken over a period of more than two years to determine the prevalence of HBsAg and its major antigenic subtypes amongst the various clinical types of leprosy and apparently healthy individuals of Calcutta population. The overall incidence of HBsAg in lepromatous leprosy is found to be 3.8% (9 out of 234) in our study. The incidence of HBsAg in tuberculoid leprosy and non leprosy control

cases were almost identical, 2.5% (11 out of 431) and 2.7% (14 out of 519) respectively. The incidence of HBsAg in lepromatous leprosy in the present study was apparently higher than tuberculoid or non leprosy cases, although statistically not significant. Hence the association between HBsAg and lepromatous leprosy could not be established in our study. None of the major antigenic subtypes of HBsAg could be related to any particular type of leprosy. The subtypes 'ad', 'ay' and 'ar' were present at varying proportions in all the groups tested. The antigenic subtype "ay" was found to be prevalent in Calcutta population in higher proportions.

Authors' abstract

CHIRON, J.P.; MAUPAS, Ph.; DENIS, F. Infection par le virus de l'hépatite B chez les hanséniens. IV. — Recherche de nouveaux marqueurs (Hbe Ag, anti-HBe, anti-HBc) dans le sérum. *Bull. Soc. Méd. Afr. Noire. Lang. Fr.*, 24(1):79-84, 1979.

HB V new markers in 553 patients with leprosy have been researched. HBe Ag and anti-HBe have been found respectively in 15% and about 50% of HBs Ag + hanséniens. The leprosy not carrying the coat markers (33%) were anti-HBe and/or anti-HBc positive. This new class of infected patients by HB V, rare in Europe and America, exists in Africa in the non-leprosy population but with a frequency less than that observed in the hanséniens.

Authors' summary

CHIRON, J.P.; LANGUILLON, J.; ROUX, G.; DENIS, F. Infection par le virus de l'hépatite B chez les hanséniens. III. Relation entre les marqueurs d'enveloppe du virus de l'hépatite B et la transaminasémie. *Bull. Soc. Méd. Afr. Noire Lang. Franc.*, 23(4):406-409, 1978.

The quantity of glutamoxaloacetic and glutamopyruvic transaminases have been determined in the serums of 445 lepers and the results analysed according to the markers of the envelopes of the hepatitis B virus (HBs and anti-HBs). It appears that the leprosy HBs Ag (+) have higher rates of SGOT and SGPT than leprosy HBs Ag (—) and also than the tuberculoids HBs Ag (+).

Authors' summary

CHIRON, J.P.; DENIS, F.; MAUPAS, Ph.; ROUX, G.; LANGUILLON, J. Infection par le virus de l'hépatite B chez les hanséniens. II. Titre sérique des antigènes de surface du virus de l'hépatite B et des

anticorps homologues. *Bull. Soc. Méd. Afr. Noire Lang. Fr.*, 23 (4):402-405, 1978.

The quantity of surface antigens (HBs Ag) has been determined in the serum of 143 leprosy patients and the homologous antibodies (anti-HBs) for 243 lepers having synthesized such discernable antibodies. The technique used in these two cases is radioimmunological quantity determination. There does not appear to be any statistically significant difference (whether HBs Ag or HBs) between the titres according to the form of leprosy or the sex of the patient.

Authors' summary

DATAR, S.V.; PANSARE, M.S.; KATTI, V.A. Leprosy and ABO blood groups. *Lepr. India*, 50 (3):388-391, 1978.

250 patients of Lepromatous and Non-lepromatous Leprosy were studied. The statistical analysis showed that there is no relationship between the blood groups and Lepromatous or Non-lepromatous Leprosy. The results are discussed in comparison with the work of other authors.

Authors' abstract

HITZEROTH, H.W.; WALTER, H.; HILLING, M.; MUNDERLOH, W. Genetic markers and leprosy in South African negroes. Part II. Erythrocyte enzyme polymorphisms. *S. Afr. Med. J.*, 56(13):507-510, 1979.

The phenotype frequencies of the erythrocyte enzyme polymorphisms acid phosphatase (aP), phosphoglucomutase loci 1 and 2 (PGM) and PGM₂, adenylate kinase (AK), adenosine desaminase (ADA), esterase D (EsD) and 6-phosphogluconate dehydrogenase (6-PGD) were determined on a sample of 234-248 South African Negroes with leprosy. These results were compared with data of 841-997 healthy Negro controls of similar geographical and ethnic origin, in order to determine whether or not any association exists between specific phenotypes and the manifestation of leprosy. A part of the data included in the present study were compared with the data of a similar comparative analysis on Mozambican Negroes. With regard to the polymorphisms aP, PGM₂, and PGMc, the results derived from South Africa and Mozambique exhibit reverse patterns of deviations from the null hypothesis. From this it does not appear justified to postulate an association between these genetic markers and the occurrence of leprosy. For the enzyme polymorphisms ADA, AK and EsD (data are confined to South African Negroes only) the distribution of phenotypes between patients

and controls was very similar. The differences were not statistically significant. However, observations on the 6-PGD polymorphism (data are confined to South African Negroes only) showed an excess of phenotype PGD A among leprosy patients as compared with controls. The difference was statistically

highly significant. Further studies based on additional samples are required to substantiate whether or not the statistical outcome reflects a true association between this phenotype and leprosy.

Authors' summary

CLÍNICA E DIAGNÓSTICO

CLINICAL ASPECTS AND DIAGNOSIS

CARRICA, A.; FAUXPOINT, B.; LABAT, P.; RIVAUD, C.; VEDY, J. Manifestations ophtalmologiques de la lepre. *Med. Trop.*, 39(3):301-306, 1979.

Modern authors estimate from 47 p. 100 to 78 p. 100 the frequency of ocular lesions in leprosy. This frequency varies according to the duration and type of the disease. These lesions may result from a paralysis of the V or VII cranial nerves, or from a bacteremia, but, more probably, from a spreading of the bacilli from the nasal cavity through the lacrymal ducts. The various lesions of each ocular structure are described with reference to the T. or L. type of leprosy.

Authors' summary

DUTTA, R.B. A study of patients with Erythema Nodosum Leprosum syndrome *Lepr. India*, 51(2):209-212, 1979.

25 cases of Erythema Nodosum Leprosum (ENL) Syndrome have been clinically evaluated. Majority patients (84%) were males in the middle age group. Fever (56%), arthralgia (100%) and neuritic pains (100%) were common presenting constitutional symptoms. ENL was not related to DDS therapy or to any precipitating factors. Severity of reaction graded by clinical scoring was well correlated with fibrinolytic activity. Fibrinolytic activity was found decreased in all the cases. The decreases in fibrinolytic activity was more so pronounced in patients having higher clinical scorings.

Author's abstract

JOPLING, W.H.; REES, R.J.W.; RIDLEY, D.S.; RIDLEY, M.J.; SAMUEL, N.M. The fingers as sites of leprosy bacilli in pre-relapse patients. *Lepr. Rev.*, 50(4):289-292, 1979.

Two dapsone treated patients with apparently quiescent lepromatous leprosy were found to have solid-staining acid-fast bacilli (AFB) in the fingers. The viability of the

bacilli from both patients was proved and dapsone resistance was established in one patient by mouse foot-pad inoculation. Subsequently both patients relapsed bacteriologically, one clinically in addition. Thus solid-staining AFB in the fingers, though there may be none seen in skin lesions, may be the prelude to relapse.

It is suggested that the dorsum of fingers is a favourable site for persisting bacilli because it is cool and nerve bundles are more superficial there than in most other areas.

Authors' abstract

LOWY, G. & MEILMAN, I. Hanseniasis em urn hospital infantil. *J. Ped.*, 47(3):88-98, 1979.

From 1966 to 1977 forty four patients with leprosy have been followed at Hospital Jesus. A progressive higher incidence of the infection has been noted since 1974. Most of the patients were between 5 and 14 years old. In 54.54% the beginning of the clinical signs occurred between 5 and 9 years. According to the clinical forms the Tuberculoid form was the most frequent (52.2%), followed by the Indeterminate form (25.0%), Lepromatous (15.0%) and the nodular variety in 6.8%. The main skin lesions were plaques with well defined edges (36.7%); hypopigmented macules (24.5%), erythematous and swollen plaques (10.2%), nodules (6.1%), anaesthetic and atrophic plaques (8.2%), ichthyosis scaling (6.1%), lepromas (4.0%) and hypopigmented macules with swollen edges (4.0%). The most impressive neurologic manifestations were: cubital nerve thickening (33.3%), hypotenar atrophy (35.0%). History of familial contact could be confirmed in 18.1% of patients. Treatment consisted in diamino diphenyl sulphone (DDS) once in a while associated with rifampicine. Clinically 18.2% are cured, 40.9% up to now are in treatment and 18.2% were transferred to peripheral Health Departments and 22.7% did not come back to follow-up. The authors emphasise the medical and

social aspects of the problem. They alert pediatricians to recognise the early signs of the disease in order to avoid its progression and dissemination.

Authors' summary

REA, T.H. Lucio's phenomenon: an overview. Editorial. *Lepr. Rev.*, 50: (2) :107-112, 1979.

Lucio's phenomenon is a distinctive reactional state as judged by clinical, histopathological and therapeutic criteria. The reaction occurs in patients with a variant of lepromatous leprosy, PPDL. Circulating immune complexes are associated with Lucio's phenomenon and may be important in its pathogenesis. The restriction of Lucio's phenomenon to patients with PPDL can be partially understood by hypothesizing that these patients have a singularly deficient defence mechanism (Rea and Ridley, to be published). Thus this nadir of resistance permits the replication of *M. leprae* in endothelial cells, enhancing the exposure of bacterial antigen to circulating antibody, eventually resulting in vasculitis and infarction. This low resistance also allows the unopposed dissemination of organisms through

out the skin and in other tissues as well, giving rise to the clinical picture of PPDL. For leprologists outside of Mexico and Central America, Lucio's phenomenon should not be regarded as a faraway curiosity but rather approached as an experiment of nature, one that when understood will help illuminate the entire problem of leprosy. For example, what are the environmental or genetic determinants that restrict Lucio's phenomenon to Mexico and Central America? What deficiency in resistance allows the development of Lucio's phenomenon and PPDL but is present in other lepromatous patients? Why do no nodules form or what is the mechanism of nodule formation?

From the editorial

SINHA, H.K. & PRAKASH, A.P.S. Syndrome of crocodile tears caused by lepra bacilli. *Lepr. India*, 50 (3) :392-395, 1978.

A case of the Syndrome of Crocodile tears as a result of tuberculoid type of leprosy is reported to lend support that the Syndrome may be caused by this disease after a long period of its onset.

Authors' abstract

TERAPÉUTICA

THERAPY

EKAMBARAN, V. Duration of treatment for "disease arrest" of non-lepromatous cases and relapse rate these patients. *Lepr. Rev.*, 50 (4) :297-302, 1979.

This is a study of 1879 patients declared disease arrested in the Elep Leprosy Project, Dharmapuri. The study analyses the duration of treatment needed for rendering a patient disease inactive and disease arrested and the number of relapses occurring among these cases. The relapses have been analysed with references to the maintenance and total treatment the patients had before relapse, and the periodicity of relapse, after being declared disease arrested with a view to determining the minimum treatment needed of disease arrest, the surveillance needed after discharge from treatment, etc.

Author's abstract

GIDOH, M.; SAKAMOTO, Y.; TSUTSUMI, S.; NAKAGAWA, H. Fundamental studies on the metabolism of rifampicin (RFP). *Jap. J. Leprosy*, 47(4) :110-121, 1978.

Metabolism of RFP and of the representative metabolites was individually compared by tracer method. The results were discussed especially concerning the metabolites remaining for long-term *in vivo*. A new derivative of RFP named as ADP was synthesized. Through the similar reaction between RFP or DARFP and aromatic or alicyclic carboxylic acid chloride the presumable position in RFP skeleton of conjugation such as glucuronide conjugation was discussed. *In vivo* inhibitory effect of protein on the oxidation of RFP series to their respective quinone-forms was examined using cysteine as a model of *in vivo* SH residue. The predominant adsorption of RFP series on IgM of calf serum was concluded. The low efficacy of RFPQ and ADP on the growth of leprosy bacilli was concluded by mouse footpad method. The uselessness of DARFP was also presumed. The antibacteroidal effects of RFP was compared with those of some antileprosy drugs and the influence of RFP on *in vivo* enterobacteria was mentioned. The relation between these findings and RFP therapy was discussed.

Authors' abstract

GIRDHAR, B.K.; SREEVATSA; DESIKAN, K.V. Primary sulphone resistance: a preliminary report. *Lepr. India*, 50(3): 352-355, 1978.

A case of lepromatous leprosy proven to be a primary sulphone resistant one, has been reported. Bacilli from the case were found to be resistant as checked by their continued growth in the foot pads of mice receiving diet containing 0.001% D.D.S. A study to identify such cases is being systematically pursued.

Authors' abstract

GIRDHAR, B.K.; RAMU, G.; SREEVATSA; DESIKAN, K.V. Introductory rifampicin therapy in lepromatous leprosy: a six month follow-up study. *Lepr. India*, 50(3):363-370, 1978.

A double-blind comparative trial of 300 mg of Rifampicin given daily as against 50 mg D.D.S. administered like wise for an initial period of 3 months has been undertaken on 24 untreated cases of lepromatous leprosy. All the patients have been followed up for 6 months. The results revealed that patients in the former group became non-infective, as concluded from M.I. and mouse foot-pad results, within 3-4 weeks and their nasal ulcers healed faster. Clinical improvement was slightly better in the former group while no bacteriological differences were noticed in the two groups. E.N.L. was milder and slightly less common in the Rifampicin group.

Authors' abstract

GUPTE, M.D. Dapsone treatment and deformities: a retrospective study. *Lepr. India*, 51(2):218-235, 1979.

Gandhi Memorial Leprosy Foundation conducted a study from 1963-72. Records of 2608 patients pertaining to type of leprosy, year of detection and registration, involvement of nerves, treatment, reactions, deformities, were available for a retrospective study. Patients having problems like neuritis and deformities and of the types lepromatous and borderline were the ones who tended to be regular clinic attenders. Lepromatous and Borderline and Polyneuritic types and N3 group were prone to develop deformities. There seemed to be association between reaction and causation of deformities. Because of the neurotoxic effect and ability to concentrate in the affected nerves, dapsone might enhance the risk of deformities. Low deformity rates in N1 and N2 types of nerve involvement reaffirmed the necessity of early diagnosis of leprosy.

Author's abstract

HAGAN, B.J. & SMITH, S.E. Variability of urinary dapsone/creatinine concentration ratios in leprosy patients fully compliant with dapsone therapy. *Lepr. Rev.*, 50(2): 129-134, 1979.

A highly sensitive and reproducible assay procedure for the determination of dapsone (DDS) and hydrolyzable metabolites in urine is described. DDS/creatinine (D/C) concentration ratios, which are used to monitor compliance with DDS therapy, have been determined on samples of all urine voided throughout a 24-h period by 7 leprosy in-patients fully compliant with their therapy. The D/C concentration ratios varied both within and between patients over the 24 h and the time-course of variation showed no closely predictable pattern. Urinary excretion of DDS over the 24 h was found to be 74.8%±5.7% (S.E.M.) uncorrected or 90.2%±6.8% corrected for recovery. Our results indicate an unreliability in the use of single urine samples to determine D/C ratios and hence compliance by individual patients with their DDS therapy.

Authors' abstract

JOPLING, W.H. & PETTIT, J.H.S. Interaction between rifampicin, steroids and oral contraceptives. *Letter. Lepr. Rev.*, 50(4): 331-332, 1979.

We wish to warn leprosy workers to expect a poor response to steroid therapy for severe type 2 lepra reaction (ENL reaction) if rifampicin is being given at the same time. Rifampicin also impairs the effectiveness of oral contraceptives, and this could lead to an undesired pregnancy in a lepromatous woman of child-bearing age; worse still, if the woman is given thalidomide to control a prolonged and severe lepra reaction on the strength that the contraceptive pill will prevent pregnancy, the consequences could be disastrous.

From the letter

NIGAM, P.; DAYAL, S.G.; GOYAL, B.M. Erythema multiforme bullosum due to rifampicin. *Lepr. India*, 51 (2):249-251, 1979.

A case of Erythema Multiforme Bullosum in patient of lepromatous leprosy with pulmonary tuberculosis due to Rifampicin is described. It is stressed that ethambutol may act as a trigger factor to the toxic effects of Rifampicin.

Authors' abstract

PATTYN, S.R.; BOURLAND, J.; WARNSDORFF, J.; CAP, A.; SAERENS, E.J. Short course two months treatment of paucibacillary leprosy with rifampicin preliminary results. *Ann. Soc. Beige. Méd. Trop.* 59(1):79-85, 1979.

The possibility of treating paucibacillary leprosy by a short course rifampicin regimen was investigated in a pilot trial in Bujumbura and a controlled trial in Addis Ababa. Rifampicin was administered once weekly in a dose of 900 mg during 8 weeks. Clinical improvement continued after the administration of RMP was stopped and no systemic adverse effects associated with the intermittent RMP administration were observed. The follow-up period was one year. The clinical observations and examination of biopsies give the impression that this short course RMP treatment is not as good as standard dapsone therapy. Three patients in the RMP group developed neuritis, this was not significantly different when compared with the dapsone group and the neuritis developed after the RMP treatment had been stopped. Continuing observation of the patients is necessary.

Authors' summary

PETERS, J.H.; MURRAY, J.F.; GORDON, G.R.; LEVY, L.; RUSSEL, D.A.; SCOTT, G.C.; VINCIN, D.R.; SHEPARD, C.C. Acedapsone treatment of leprosy patients: response versus drug disposition. *Am. J. Trop. Med. Hyg.*, 26(1):127-136, 1977.

In 22 lepromatous Filipino patients receiving their first injection of 225 mg acedapsone (DADDS), dapsone (DDS), and monoacetyl DDS (MADDS) were present in plasma in approximately equal quantities. Peak levels of parent drug, DDS, and MADDS occurred between 22 and 35 days. The half-times of disappearance ($T_{1/2}$) from plasma were 43 days for DDS and MADDS and 46 days for DADDS. Acetylator phenotyping with sulfamethazine (SMZ) and DDS showed that 17 patients were rapid and 5 patients were slow acetylators. Correlations between acetylation of SMZ and DDS after DDS and of acetylation of DDS after DDS and DADDS were highly significant. However, acetylation of DDS after DADDS did not differentiate the patients into acetylator phenotypes. The $T_{1/2}$ of DDS after DDS in the patients was directly related to the minimum levels of DDS at 77 days after DADDS treatment. These minimum levels were 8-fold higher than the minimum inhibitory concentration (MIC) of DDS for *Mycobacterium leprae* in mice and rats, but not all patients responded satisfactorily. No relationship

could be demonstrated between the bacteriologic response and any of the pharmacologic parameters examined in these Filipino patients. In a companion study, minimum levels of DADDS, MADDS, and DDS were determined in 447 leprosy patients of all disease types from the Karimui District of Papua New Guinea who had been receiving 225 mg DADDS every 70 of 80 days for the past 5 years. All patients exhibited DDS levels above the MIC of DDS for *M. leprae*, no significant differences in plasma sulfone levels were found among disease types, no relationship between rate of healing in paucibacillary patients and sulfone levels were found, and type of response in multibacillary patients and sulfone levels were unrelated. No substantial accumulation of the sulfones in the Karimui patients receiving continuous therapy with DADDS for 5 years was indicated from a comparison with the levels in the Filipino patients following a single injection of DADDS.

Authors' abstract

SAHOO, S.K.; TRIPATHY, N.; DEBI, B.P. Acute fatal DDS poisoning: report of 4 cases. *Lepr. India*, 51(2):244-248, 1979.

We here report 4 cases of fatal suicidal DDS poisoning in adults resulting death in 3 cases. The reported acute symptoms include nausea, vomiting, hyperexcitability followed by depression, Carpopedal spasm or convulsions. The most marked signs are dyspnoea and cyanosis. The symptoms are due to methaemoglobinaemia, and or sulphaemoglobinaemia.

From authors' abstract

TOUW-LANGEDIJK, E.M.J. & NAAFS, B. Relapses in leprosy after release from control. *Lepr. Rev.*, 50(2):123-127, 1979.

In 1974, 678 patients, originally classified as suffering from various types of leprosy from LL to TT, were released from control. During the next 3 years, 105 of them reported back on their own accord, with evidence of relapse which was confirmed by clinical, bacteriological and electrophysiological observations. During this period the overall relapse was 15%, but patients in the LL/BL group, the indeterminate group, and the BT group treated for less than 5 years, had a relapse rate of over 30%. Reasons for these disconcertingly high figures are discussed and a plea is made for the collection of more data on relapse rates in similar groups of patients from different countries, in order to revise the criteria for releasing patients from treatment.

Authors' abstract

CIRURGIA, FISIOTERAPIA E REABILITAÇÃO FÍSICA.

SURGERY, PHYSIOTHERAPY AND PHYSICAL REHABILITATION

GIRAUDEAU, P. & DEPINAY, J. Place et importance de la chirurgie "spécialisée" dans un programme national de lutte contre la lépre. *Med. Trop.*, 39(5) :577-579, 1979.

In order to get a representative sample of the population, a survey was conducted in an rural district of the Republic of Mali. The data collected give evidence that the number of specific surgical indications can be correctly evaluated not from the number of leprosy patients numbered, but by applying a ratio of 5,5 per cent to the whole population. This easy evaluation is important for the management of any public health programme.

Authors' summary

LAKHAN PAL, V.P.; YADAV, S.S.; NAIR, M.N. Reconstructive surgery of claw hand in leprosy. *Lepr. India*, 51(2):213-217, 1979.

32 hands in 31 known cases of leprosy were operated using the Paul-Brand technique for the intrinsic minus deformity. 29 hands revealed good results whereas remaining 3 also had definite improvement in their function and cosmesis. Bunnel's opponens plasty was performed in 7 cases to restore back the power of opponens in the thumb. Meticulous pre and postoperative management proved to be very necessary.

Authors' abstract

EPIDEMIOLOGIA E PREVENÇÃO

EPIDEMIOLOGY AND CONTROL

ABREU, A.; WERTHEIN, L.J.; RUIZ DE ZARATE, S. Evaluación del nuevo programa de control de lepra en Cuba. *Rev. Cub. Hig. Epid.*, 17(1):83-92, 1979.

The new leprosy control program which has been put in force in May, 1977 involves the controlled administration of rifampicin to all lepers (prevalence figure, 4936) as well as to every single patient who has accounted for the incidence of this disease. The daily dose was 600 mg of rifampicin during 6 months in the case of bacterioscopic-positive patients and during 3 months in bacterioscopic-negative patients. The treatment was prescribed for every clinical type. The different preparatory activities previously related to the implementation of the program are pointed out. The drug was daily administered both in general health services (policlinics) by the nursing personnel or in the patients' homes whenever they were physically handicapped. A monthly clinical and bacterial control in the case of bacterioscopic-positive types and a three-month control in the case of bacterioscopic-negative types were obtained. 98,6% of patients received the drug during the stroke phase according to the program. At the end of the stroke phase a clinical improvement was found in

73,8%; a bacterial negativization was found in 43,1%; and the morphological index equalized 0 in 83,1% of patients with positive results. Taking into account the negative morphological index as an expression of the bacillus nonviability, a cut of the transmission chain has been achieved during the stroke phase in 83,1% of patients who had yielded positive results at the beginning of the program.

Authors' summary

CHATTERJEE, B.R. Leprosy endemicity in the light of population genetics. Editorial. *Lepr. India*, 50(3) :327-333, 1978.

The appreciation and acknowledgement of all that has been said here can be summed up in a few lines quoted from Dharmendra (loc cit) — "It may be said that *leprosy in India is in the long-drawn-out plateau phase of the epidemic, and ultimately it is bound to follow the downward curve*. Our concerted efforts, the availability of *potent drugs* against the disease and a *rise in economic status of the masses will no doubt accelerate the downward trend*". (Emphasis mine).

From the editorial

McDOUGALL, A.C. & ROSE, P. El control integrado de la lepra en Guyana. *Sol. Of. Sanit. Panam.*, 86 (2):105-112, 1979.

El problema de la lepra en Guyana es pequeño en comparación con el de otros países de América del Sur. Por otro lado, existe una persistente incidencia de nuevos casos, a pesar de la existencia de servicios satisfactorios de diagnóstico y tratamiento, que es similar a la situación que se advierte en otras unidades políticas vecinas del Caribe y algunas otras partes del mundo. Después de más de un siglo de tratamiento basado casi exclusivamente en la hospitalización en leproserías, en 1971 se dio comienzo a un programa de 'búsqueda y tratamiento' aprovechando los servicios de atención de consulta externa que se encontraban en funcionamiento. Este programa ha tenido éxito y ha sido bien acogido por los pacientes, los médicos y el público en general.

Actualmente se está prestando especial atención a la incidencia anual de nuevos casos a fin de evaluar la eficacia permanente del programa. Es posible que mediante la intensificación de las actividades de educación para la salud — incluida la clausura definitiva de la leprosería Mahaica, que todavía sigue funcionando — el tratamiento regular durante periodos prolongados (especialmente de los pacientes con bacilos positivos) y el examen intensivo de escolares y contactos en el hogar, se logre disminuir la incidencia y se dé nuevo ímpetu a la actividad de erradicación. Por otra parte, si no se advierte

una disminución de la incidencia puede ser útil considerar la realización de un análisis más detallado de la situación. A decir verdad, bien puede justificarse llevar a cabo un estudio epidemiológico detallado de todos los casos nuevos diagnosticados desde 1971. Dicho estudio podría facilitar la erradicación de la lepra, no solo en Guyana, sino también en otros países que presentan una reducida incidencia anual, y en los cuales la enfermedad probablemente se pueda controlar, aun cuando no esté bajo control en ese momento.

Resumen de los autores

REVANKAR, C.R.; DEWARKER, P.R.; MULCHAND, S.; GANAPATI, R. Leprosy in preschool age. *Lepr. Rev.*, 50(4): 293-296, 1979.

Examination of 4235 preschool age (1-5 years) children from various slums in Bombay revealed 20 active leprosy cases (prevalence rate of 4.7 per 1000). An analysis of pooled figures from clinics showed that preschool children formed 1.3% of the total number of patients attending these clinics. 5% were smear positive; 45% had one or more family members with leprosy (25% of the latter being bacteriologically positive). The high proportion of associated infectious cases (as compared to corresponding data for school age) indicates a strong possibility of intrafamilial infection in children of preschool age.

Authors' abstract

PSICOLOGIA, EDUCAÇÃO E REABILITAÇÃO SOCIAL

PSYCHOLOGY, EDUCATION AND SOCIAL REHABILITATION

MEISELS, L. HD, the vicious circle of the stigma. *Star*, 89 (1):5-7, 1979.

It appears that among the patients, their families and the medical staff there is a general consensus as to the severity of the stigma that may be designated as "the stigma of the stigma": they see the stigma as far more severe than it actually is; they attribute importance to religious factors which, in reality, have no influence, and resort to tactics of hiding the disease/the stigmatized place of work, which causes them to adopt the hard way of coping with their difficulties. A few negative social reactions are sufficient to encourage "the stigma of the stigma", to "prove" its severity, and to add substance to the wall of secrecy with which they

surround their disease. The phenomenon exists in all its intensity amongst in patients who are unable to confront their conceptions with prevailing social views. This contributes to understanding their high degree of self-stigmatization in comparison with that of out-patients. It seems that the approach of hiding the information about the existence of the patients and the disease from public knowledge and encouraging the patients to keep the fact of their disease a perfect secret, is of little avail to break "the vicious circle of the stigma": society stigmatizes the disease because of lack of knowledge, hence the patients keep their disease a secret, hence they are unable to fight the stigma in the open, hence society continues lacking knowledge and stigmatizing, and so on. In this

way the stigma is perpetuated, at the same time perpetuating the patients' suffering. Thus it appears imperative to involve the mass media for the purpose of increasing and developing the knowledge and awareness of the modern medical approach towards the disease and of the patients' ability to live within the framework of society. This is not enough, however. It is necessary to devote special efforts to giving psychological assistance to the patients and their families, to be concentrated on liberating them from "the stigma of the stigma" by putting the severity of the stigma in its right place.

From the article

OSAKA, R. A survey of the social situations of leprosy patients in JALMA Leprosy Centre, Agra, India. I. Survey on the medical aspects of inpatients. *Jap. J. Leprosy*, 47(3):92, 1978.

This is a report of a sociological study on 240 inpatients hospitalized in JALMA Leprosy Centre, India. This survey was carried out during the time ranging from October 20, 1971 to January 10, 1976. Results of the survey on the medical aspects of these patients are summarized as follows: Onsets of the disease were most frequently noticed by the patients at the ages between 11 and 15 (39.1%). 75% of the patients came to the hospital because of patches on their body surface. However, many of them did not know the nature of the disease until the medical staffs explained it to them. There were considerable number of patients defaulted from the regular treatment (46.2%). Their reasons for the drop-out were the absence of pain and the frustration for the retarded improve-

ment of the clinical symptoms of leprosy. Many of them changed to other treatment centres in expectation for the better treatment. 45% of inpatients had leprosy patients in their families or relatives. Cases with leprosy parents were the most frequent (43.1%). Most of the patients changed more or less their food habits after the onset of the disease. 59.7% of them stopped taking animal foods such as meat, fish and egg after they had leprosy.

Author's abstract

PHILLIPS, M.A. Health education in leprosy: the problem of overcoming fear and misconceptions. *Int. J. Health Educ.*, 21(2):130-136, 1978.

Leprosy is still one of the most dreaded diseases. Fear and misunderstanding persist in all parts of the world. Possibly people cling to the picture presented in the Bible, where the sufferer was cast out of the city as unclean and compelled to carry a bell which he would use to warn people to keep their distance. The fact that the disease described in the Bible is quite unlike the disease which we call leprosy today, does not seem to remove the stigma. Not only is leprosy a dreaded disease, it is also an important public health problem in many countries, as indicated by a report presented to the World Health Assembly held in May 1977. The total number of cases in the world is conservatively estimated to be between 10 and 12 million. A rough breakdown by regions gives the following figures: Asia, 6.5 million; Africa, 3.5 million; the Americas, 350,000. Yet, in 1970, there were only 2,877,481 registered patients in the world.

From the article

GENERALIDADES E HISTÓRIA

GENERAL AND HISTORY

BRASIL. Ministério da Saúde. Divisão Nacional de Dermatologia Sanitária. *Guia para o controle da Hanseníase*. Brasília, 1978. 44p.

Introdução. Orientação para o diagnóstico da hanseníase. Classificação. Tratamento. Controle.

BRASIL. Ministério da Saúde. Divisão Nacional de Dermatologia Sanitária. *Hanseníase: prevenção e tratamento das incapacidades físicas, mediante técnicas simples*. Rio de Janeiro, 1977. 116p.

Introdução. Membros superiores. Membros inferiores. Olhos. Educação em saúde. Levantamento de incapacidades físicas.

BRASIL. Ministério da Saúde. Divisão Nacional de Dermatologia Sanitária. *Manual de normas e procedimentos de enfermagem de tipo ambulatorial no controle da hanseníase*. Brasília, 1978. 41p.

Introdução. Objetivos do manual. Diretrizes da política de controle da hanseníase relacionadas com a enfermagem. Assistência de enfermagem de tipo ambulatorial no con-

trole da hanseníase. Atribuições do pessoal de enfermagem no controle da hanseníase, Aspectos normativos de enfermagem de tipo ambulatorial no controle da hanseníase. Anexos.

BROWNE, S.G. La lèpre — une vue d'enA
semble. Ann. Soc. Beige. Méd. Trop.,
59 (1) :5-9, 1979.

Epidémiologie. Immunologie. Microbio-
logie. Les nerfs périphériques. Thérapeutique.

DHARMENDRA. *Leprosy*. Bombay, Kothari
Med. Publ. House, 1978. v.1.

Aetiology, History and Present Distri-
bution. Clinical manifestations. Diagnosis.
Differential diagnosis. Classification of lep-
rosy. Treatment of leprosy. Prognosis in
leprosy. Microbiology. Pathology. Experi-
mental transmission of *Mycobacterium leprae*
to animals. Immunopathology. Epidemiology
of leprosy. Leprosy control. Appendices.

DHARMENDRA. Transfusion of blood from
leprosy patients. Editorial. *Lepr. India*,
51 (2) :176-181, 1979

Even apparently cured cases of the LL
and BL types should not be used as donors
as would be evident from the fact that a large
proportion of patients suffering from these
types relapse after apparent arrest or cure
of the disease with treatment. Transfusion
of blood from cases of the non-lepromatous
leprosy can also not be considered safe as
they may have in circulation some bacilli
which cannot be detected by the normally
used methods of examination or even by the
mouse foot pad technique. Thus, it is much
better to avoid transfusion of blood from
leprosy patients, although the risk from some
cases may be much more than from others.
Of course in case of emergency a strongly
positive typical tuberculoid (TT) case may
be used for donation of blood for transfusion,

From the editorial