CURRENT LITERATURE

This department carries selected abstracts of articles published in current medical journals dealing with leprosy and other mycobacterial diseases.

General and Historical

Wozel, G. The story of sulfones in tropical medicine and dermatology. Int. J. Dermatol. **28** (1989) 17–21.

The course of development is obviously comparable to that of sulfonamides. All the names that have become well known in the context of this chemotherapeutically important class of substances are recorded in the annal of the medic and the pharmaceutical industry. The facts are different when referring to the chemically similar sulfones. Names that have to be associated with the history of sulfones remained unjustifiedly in the shadow of sulfonamide research and are hardly known today. This is the background for recalling the discoverers of sulfones and for honoring the pioneers on the occasion of the 50th anniversary of the introduction of DDS in medicine.—(*From the* Article)

Chemotherapy

Balakrishnan, S., Karthikeyan, S. and Ramu, G. Investigations into the haemolytic effects of dapsone therapy in leprosy patients. Indian J. Lepr. **61** (1989) 10–16.

Investigations into the hemolytic effects of dapsone therapy were carried out in 44 leprosy patients admitted to the Sacred Heart Leprosy Centre, Kumbakonam. They received weight-based dapsone dosages varying from 1.3–3.3 mg/kg body weight. Blood levels and urinary dapsone/creatinine ratios were assessed at 1 day, 7 days and 30 days of dapsone treatment. At the same points of time, hematological observations were also carried out. Serum bilirubin as well as blood methemoglobin were also examined. The findings showed a reduction in hemaglobin levels at 30 days' observation in a good proportion of cases on 100 mg. In one case (child) weighing 15 kg and receiving 50 mg dapsone increased methemoglobin was observed. It is suggested that dapsone dosage be regulated to body weight and preferably not to exceed 1.5 mg/kg body weight.—Authors' Abstract

Chen, J., *et al.* [Tridrug regimen in multibacillary leprosy for two years.] China Lepr. J. **4** (1988) 216–218. (in Chinese)

Fifty-three cases of multibacillary leprosy have been treated with rifampin, clofazimine and dapsone for 2 years in leprosaria, and all of them are on the mend either clinically or bacteriologically. The regimen did not show marked toxicity or side effects, was able to control lepra reaction and was also effective for relapsed cases. But after 2 years of the treatment 12 of the patients still have slight erythema nodosum leprosum, suggesting that their disease is active and needs continuous treatment. Therefore, the authors propose that for relapsed, severe and resistant cases the therapy should be continued to negativity of the skin smear.—Authors' English Abstract

dos Santos, I. B., Amorim, M. G. M., Sant'Anna, I. P. and Maris, M. M. [Hanseniasis and pregnancy; an evaluation of sulfone therapy.] An. Bras. Dermatol. **63** (1988) 447–449. (in Portuguese)

The authors present the results of the follow up of 53 pregnancies in 31 patients with leprosy in its several clinical forms, evaluating the possible consequences of the disease and the usage of dapsone over the pregnancy as well as to the newborn. A comparative study is made with 35 healthy pregnant women.—Authors' English Summary

Ekambaram, V. and Rao, M. K. Changing picture of leprosy in North Arcot District, Tamil Nadu, after M.D.T. Indian J. Lepr. **61** (1989) 31–43.

This paper discussed the effect in a 5-year period (1983–88) of multidrug therapy (MDT) on the leprosy situation in North Arcot District where MDT was started in 1983. The cases at the start of MDT were 68,351 and 29,511 cases were detected in the year period and the total case load was 97,862. Out of this total case load 84,810 cases were deleted by release from control (RFC), deaths, or patient left control area (PL). The causes for deletions are discussed in detail. The remaining case load at the end of the 5-year period is 13,052 or 13.35% of the cases at the start. MDT has definitely played a part in the drastic reduction of the case load since the major number of cases have been deleted as RFC due to cure of the disease. The future planning of leprosy work when the case load becomes very low is also discussed.—Authors' Abstract

Garg, S. K., Kumar, B., Bakaya, V., Lal, R., Shukla, V. K. and Kaur, S. Plasma dapsone and its metabolite monoacetyldapsone levels in leprotic patients. Int. J. Clin. Pharmacol. Ther. Toxicol. **26** (1988) 552–554.

Dapsone (DDS) is a drug of choice in the treatment of leprosy. The DDS and monoacetyldapsone (MADDS) levels and different pharmacokinetic parameters after a single dose of dapsone and at steady state in leprotic patients have been studied. At steady state, all the patients showed plasma DDS and MADDS levels above 0.5 μg/ml throughout the 24-hr duration. There was no significant difference in the elimination half-lives of DDS and MADDS after a single dose as compared to at steady state, but AUC_0^∞ for both DDS and MADDS were significantly increased at steady state. From these results, it could be concluded that a 100 mg daily dose is sufficient to maintain plasma therapeutic concentration in leprotic patients in Indian populations.—Authors' Abstract

Hazra, S., Chaudhury, S., Chaudhury, S. K., Das, P. K. and Dey, S. K. Paucibacillary leprosy and WHO regimen. Indian J. Dermatol. **32** (1987) 99–101.

Ninety cases of tuberculoid leprosy were selected for multidrug study with the WHO regimen. They were treated with dapsone 100 mg daily and rifampin 600 mg monthly for 6 months. Clinical activity of the disease was observed thereafter. Five patients showed reactivation of lesions 3–8 months after stopping the treatment. The rest of the patients did not show any clinical activity.—Authors' Abstract

Papaiordanou, P. M. de O., Branchini, M. L. M., Gonçales, F. L., Jr., Aoki, F. H., Boccato, R. S. B. S., Ramos, M. de C. and Pedro, R. de J. [Adverse effect of intermittent use of rifampin for leprosy treatment.] Rev. Inst. Med. Trop. São Paulo **30** (1988) 383–386. (in Portuguese)

The authors present a case of acute renal failure, acute hemolysis and thrombocytopenia due to intermittent use of rifampin for leprosy. These adverse reactions have rarely been described in the medical literature. During follow up there was recovery of renal function and complete remission of the hematological alterations. To our knowledge, this has been the first report of such adverse effects of rifampin during leprosy therapy in Brazil. Pathogenetic aspects are discussed and current literature is reviewed.—Authors' English Summary

Clinical Sciences

Abdulkadir, S. Bacteriology of infected hands and feet in leprosy patients. Indian J. Lepr. **61** (1989) 65–67.

Seventy cases of infected hands and feet admitted to ALERT Hospital during 1986/1987 (3/10/86–5/5/87) were studied for the

infecting organisms and the sensitivity of these organisms to available antibiotics. Single organisms were isolated in 56 cases (95%), two organisms were isolated in 3 cases (5%), no organisms were isolated in 11 cases (15.7%). *Proteus* was the commonest organism. The most effective drug was ampicillin. Three organisms isolated in 7 cases proved resistant to all drugs tested. The study shows that commonly available drugs are effective in the great majority of secondary infections in leprosy patients.—Author's Abstract

Arora, S. K., Mukhija, R. D., Mohan, L., Girdhar, M., Matreja, V. S., Saxena, R. and Sharma, S. P. Calcification of ulnar nerve in leprosy—a case report. Indian J. Lepr. **61** (1989) 111–112.

A case of tuberculoid leprosy who had taken irregular treatment for 5 years and had thickened ulnar nerve, which on radiological examination showed calcification, is reported.—Authors' Abstract

Ghei, S. K., Katoch, K., Girdhar, B. K., Ramu, G. and Sengupta, U. Dermatoglyphics in leprosy: (III) Creases of palm. Indian J. Lepr. **61** (1989) 96–102.

Palmar configurations of triradii and creases of 100 leprosy patients [50 lepromatous (BL/LL) and 50 tuberculoid (BT/LL)] were compared with those of 100 normal persons selected from families of these patients. The patterns of position of triradii were similar in controls and leprosy patients as such, but the patterns in the two types of leprosy patients were different. As for palmar creases patterns, there was significant difference between those of controls and patients, the double radial base crease occurring more often in patients. However, the differences between the two types of patients were not statistically significant.—Authors' Abstract

Majoroh, T. O. and Imongan, W. I. Carcinoma in plantar ulcers of leprosy patients. Trop. Geogr. Med. **40** (1988) 365–368.

Three cases presenting clinically with carcinomas developing from long standing plantar ulcers are presented. Intra-operational histopathological examination confirmed two cases of squamous cell carcinoma and one case of malignant melanoma. Two of the patients had developed distant metastases in the brain, chest and regional lymph nodes at presentation. All had below-knee amputation. The regional lymph nodes were not interfered with in any of them. One finally died, one was discharged home fully fit, while the third's clinical condition has been deteriorating.—Authors' Abstract

Meeran, K. Prevalence of HIV infection among patients with leprosy and tuberculosis in rural Zambia. Br. Med. J. **298** (1989) 364–365.

Mycobacterial infections have been associated with HIV infection. Much evidence exists of tuberculosis as a presenting feature of HIV infection or AIDS-related complex. High-grade pathogens such as *Mycobacterium tuberculosis* develop early, whereas low-grade pathogens such as *M. avium-intracellulare* emerge only when immune deficiency is more advanced. There are few reports of a direct association between HIV infection and leprosy, although clinical leprosy has long been associated with a defect in cell-mediated immunity. I studied patients in Zambia to see whether an association between leprosy and HIV infection existed similar to that shown for tuberculosis.

Of 18 new patients with leprosy, six (33%) were positive for HIV antibody. Of 54 patients with suspected tuberculosis, 27 (50%) were positive for HIV antibody. Eighteen of the 54 had active pulmonary tuberculosis, with results of smears of sputum positive for acid-fast bacilli, and eight of these (44%) were also positive for HIV antibody. By comparison, only 7 out of 63 blood donors (11%) and 2 out of 42 surgical patients (5%) were positive for HIV antibody.

The prevalence of HIV infection was significantly higher among patients with leprosy than among blood donors ($p < 0.05$) or surgical patients ($p < 0.01$). Some patients came from Lusaka, which may have a higher prevalence of HIV infection than rural Zambia. When the analysis was restricted to rural residents, patients with leprosy still had a higher prevalence of HIV infection than surgical patients or blood donors ($p < 0.001$).—(*From the* Article)

Mohan, L., Sharma, N. K., Sangal, R. and Arora, S. K. A report on six cases of histoid variety of lepromatous leprosy in children. Indian J. Lepr. **61** (1989) 103–106.

Six cases of the histoid variety of lepromatous leprosy among children below 12 years of age were detected over a 3-year period. Bacteriological index was high (3 to 5+). None of the patients had received any antileprosy treatment. A public health problem because of the infectious nature of the disease, early detection and management of this entity among children is important.—Authors' Abstract

Moudgil, K. D., Irshad, M., Gandhi, B. M. and Mishra, R. Serological pattern of hepatitis B virus markers (HBsAg, anti-HBs, IgM anti-HBc and HBV specific DNA polymerase) in leprosy patients. Indian J. Lepr. **61** (1989) 54–60.

Sera of 134 lepromatous (LL/BL) and 57 tuberculoid (TT/BT) leprosy patients were analyzed for four HBV markers. HBsAg was detected in 6.71% of lepromatous and 3.5% of tuberculoid sera. The percent positivity of lepromatous and tuberculoid sera for anti-HBs antibodies was 30.59% and 35.08%, respectively. The positivity of normal sera for HBsAg and anti-HBs was 3.60% and 21.69%, respectively. The difference in the positivity of three groups of sera (lepromatous, tuberculoid and normal) for HBsAg or anti-HBs was not statistically significant. Anti-HBc (IgM) antibodies were detected in 6% of lepromatous sera. HBV-specific DNA-polymerase activity was found in 22.22% of HBsAg-positive (but anti-HBc-negative) sera, and 66.66% of anti-HBc-positive (but HBsAg-negative) sera. The pattern of acute HBV infection in leprosy patients followed the typical pattern prevalent in the normal population.—Authors' Abstract

Nayak, K. C., Gupta, R. K., Aggarwal, T. D., Chadda, V. S. and Kumar, K. K. A study of incidence of Australia antigen and derangements in liver function tests in leprosy. Indian J. Lepr. **61** (1989) 23–30.

The present study was conducted in 50 patients of various subtypes of leprosy (lepromatous, tuberculoid, borderline borderline) and 25 healthy controls, for detection of Australia antigen and various liver function tests (serum protein, cholesterol, alkaline phosphatase, SGOT, SGPT, bilirubin and liver biopsy) to see the incidence of Australia antigen and derangement in liver function. It was concluded that incidence of Australia antigen in the study and control groups was zero. Total serum protein and serum globulin were increased in lepromatous leprosy. A/G ratio was reversed in 34.3% and 50% in lepromatous and tuberculoid leprosy, respectively. Granulomatous hepatitis was seen in 66.66% and 50% of the cases of lepromatous and tuberculoid leprosy, respectively. No relationships were established between hepatic lesion, Australia antigen and liver function tests.—Authors' Abstract

Okhandiar, R. P., Sinha, E., Sinha, R. K. and Mishra, A. D. Morphometric study of stratum corneum in leprosy. Indian J. Lepr. **61** (1989) 49–53.

Abnormalities in the stratum corneum (SC) in leprosy lesions have been demonstrated as evidenced by the poor hydration power of SC and increased SC turn-over. In continuation of the same study, morphometric studies of the SC in leprosy were undertaken as per measurement of the thickening of the SC, mean epidermal thickness and basal layer : granular layer cell ratio (B:G ratio) of the H&E, stained tissues. Further, on freshly frozen tissues the SC-cell layers were also counted. The findings suggest increased proliferative activity of the epidermis which may lead to formation of defective SC in leprosy.—Authors' Abstract

Patki, A. H., Jadhav, V. H. and Mehta, J. M. A study of dermatological conditions in leprosy in-patients. Indian J. Lepr. **61** (1989) 92–95.

Three-hundred sixty-six inpatients in a leprosy hospital were examined for other dermatological conditions. Eighty-eight of them displayed ichthyosiform changes. A peculiar condition of a verrucous hyperkeratotic growth on the anterior aspect of ankle, not described previously, was observed in four patients. It was noted that 11 out of

12 patients with scabies did not have the classical lesions in web spaces of the hands.—Authors' Abstract

Pavithran, K. Vitiligo following type II lepra reaction. Indian J. Lepr. **61** (1989) 44–48.

A middle-aged male with lepromatous leprosy developed bouts of skin lesions of depigmented macules and patches of vitiligo, just following attacks of type 2 lepra reaction each time. In view of the present concept of autoimmunity playing a role in the pathogenesis of vitiligo as well as lepra reaction, their association in our patient appears to be more than fortuitous. The depigmented macules persisted even after regression of skin lesions of leprosy following chemotherapy. The vitiligo macules responded partially to topical and systemic psoralen therapy.—Author's Abstract

Siddappa, K., Inamadar, A. C., Basavaraj, G. C. and Chandrasekhar, H. R. Calcification of ulnar nerve in a patient with tuberculoid leprosy—a case report. Indian J. Lepr. **61** (1989) 107–110.

A case of tuberculoid leprosy who showed evidence of calcification of the right ulnar nerve at the elbow on radiological examination is reported.—Authors' Abstract

Siddappa, K., Inamadar, A. C. and Reddy, L. S. Destruction of ala nasi and loss of columella in borderline tuberculoid leprosy—a case report. Indian J. Lepr. **61** (1989) 113–114.

A case of BT leprosy who showed destruction of ala nasi and loss of columella is reported.—Authors' Abstract

Immuno-Pathology

Benjamins, J. A., Callahan, R. E., Runft, D., Gerras, G. and Lefford, M. J. Antineural antibodies in leprosy sera: further characterization of the antigens. J. Neuroimmunol. **21** (1989) 125–135.

Sera or plasmas from 129 leprosy patients were tested by immunoblotting for antibodies that bound to proteins in a Triton-insoluble fraction enriched in neural intermediate filaments (IF fraction) from human or bovine spinal cord. Sixty samples (47%) showed positive staining of proteins at 35 kDa, 42 kDa or both. The presence of these antibodies appeared to be evenly distributed across the spectrum of disease. The frequency of these antibodies in samples from 12 healthy Ethiopians was similar to that in the leprosy group. Similar antibodies were found in only 3 of 28 samples from U.S. patients with neurologic diseases and in 7 of 35 normal U.S. sera. Sera from U.S. tuberculosis patients stained multiple bands in the 50–30 kDa region of the blots; 11 of 16 stained bands corresponding to the 35 kDa or 42 kDa bands along with a number of other bands in this region.

The 35-kDa and 42-kDa antigens do not appear to be breakdown products of neural filaments or glial fibrillary acidic protein, since antibodies to these proteins do not react with the 35-kDa or 42-kDa antigen. Further, the staining pattern with the leprosy sera is unchanged following Ca^{2+}-mediated proteolysis of the IF-enriched fraction. The two antigens differ from one another in isoelectric point: the p*I* of the 35-kDa antigen is 5.9, and the p*I* of the 42-kDa antigen is 4.8. Staining of the immunoblots with antibodies against a number of known neural antigens failed to identify the 35-kDa and 42-kDa antigens. The 42-kDa antigen appears to be a component of axolemma, since 42-kDa-positive leprosy sera stained a protein with identical migration in preparations of bovine peripheral nervous system and human central nervous system axolemma. In some sera, antibodies reacting with the 35-kDa antigen were adsorbed by D-O bovine serum albumin, a synthetic analogue of the terminal disaccharide portion of the phenolic glycolipid-1 of *Mycobacterium leprae*. Antibodies to the 42-kDa antigen were not removed by this treatment.—Authors' Summary

Brennan, P. J. Structure of mycobacteria: recent developments in defining cell wall carbohydrates and proteins. Rev. Infect. Dis. **11** Suppl. 2 (1989) S420–S430.

Work from this laboratory on the immunogens of *Mycobacterium* species has focused on those based on carbohydrates (with a view to the development of specific tools for the serodiagnosis of mycobacterioses) and on the cell-wall proteins, as a source of protective immunity and as a means of observing specific delayed-type hypersensitivity. Most mycobacteria are endowed with specific, highly antigenic glycolipids that are powerful for the serodiagnosis of individual mycobacterial infections: e.g., the phenolic glycolipids of *Mycobacterium leprae* and *M. bovis,* the glycopeptidolipids of the *M. avium* complex, and the acylated trehalose-containing lipooligosaccharides of species such as *M. kansasii, M. szulgai,* and *M. malmoense.* A search for analogous structures in *M. tuberculosis* has revealed an antigenic diglycosyl diacylglycerol and the immunogenic phosphomannoinositides. Others have reported on the presence of a novel phenolic glycolipid in the Canetti strain of *M. tuberculosis.* The dominant carbohydrate-containing antigen of *M. tuberculosis* (responsible for the high-titer anti-arabinofuranosyl activity in tuberculous sera) is lipoarabinomannan, which has been purified in the native state from *M. tuberculosis* and shown to contain both phosphatidylinositol and phosphoinositol side-branches. The cell wall of *M. tuberculosis*—more precisely, the peptidoglycan skeleton—is a source of a few distinct, highly immunogenic protein antigens. The recognition, isolation, and characterization of these antigens will also be described.—Author's Abstract

Chatterjee, D., Cho, S.-N., Stewart, C., Douglas, J. T., Fujiwara, T. and Brennan, P. J. Synthesis and immunoreactivity of neoglycoproteins containing the trisaccharide unit of phenolic glycolipid I of *Mycobacterium leprae.* Carbohydr. Res. **183** (1988) 241–260.

The trisaccharide segment, *O*-(3,6-di-*O*-methyl-β-D-glucopyranosyl)-(1 → 4)-*O*-(2,3-di-*O*-methyl-α-L-rhamnopyranosyl)-(1 → 2)-3-*O*-methyl-L-rhamnopyranose, of the *Mycobacterium leprae*-specific phenolic glycolipid-I has been synthesized as its 8-(methoxycarbonyl)octyl glycoside and coupled to a carrier protein, to produce a leprosy-specific neoglycoprotein, the so-called natural trisaccharide-octyl-bovine serum albumin (NT-O-BSA). Special features of the synthetic strategy were the use of silver trifluoromethanesulfonate (triflate) to promote glycosylation, resulting in the rhamnobiose in high yield and absolute stereospecificity. The terminal 3, 6-di-*O*-methyl-D-glucopyranosyl group was introduced after *O*-deallylation of the rhamnobiose. Removal of protecting groups yielded the trisaccharide hapten suitable for coupling to carrier protein. Poly(acrylamide)-gel electrophoresis of the neoglycoprotein demonstrated its purity, and subsequent immunoblotting with a monoclonal antibody directed to the terminal 3,6-di-*O*-methyl-β-D-glucopyranosyl epitope of the native glycolipid demonstrated its antigenicity. Comparative serological testing in enzyme-linked immunosorbent assays of NT-O-BSA, the corresponding disaccharide-containing products, and another trisaccharide-containing neoglycoprotein, *O*-(3,6-di-*O*-methyl-β-D-glucopyranosyl)-1 → 4)-*O*-(2,3-di-*O*-methyl-α-L-rhamnopyranosyl)-(1 → 2)-(3-*O*-methyl-α-L-rhamnopyranosyl)-(1 → 4′)-oxy-(3-phenylpropanoyl)-BSA (NT-P-BSA) [Fujiwara, *et al.,* Agric. Biol. Chem., 51 (1987) 2539–2547] against sera from leprosy patients and control populations showed concordance; the presence of the innermost sugar did not contribute significantly to sensitivity or specificity. The di- and trisaccharide-containing neo-antigens, on account of ready availability and solubility, provide greater flexibility than the native glycolipid for the serodiagnosis of leprosy—Authors' Abstract

Desai, S. D., Birdi, T. J. and Antia, N. H. Correlation between macrophage activation and bactericidal function of *Mycobacterium leprae* antigen presentation in macrophages of leprosy patients and normal individuals. Infect. Immun. **57** (1989) 1311–1317.

The killing of *Mycobacterium leprae* by resting and gamma interferon (IFN-γ)-activated macrophages in normal subjects and leprosy patients was assessed. Resting macrophages from normal individuals demonstrated the ability to kill *M. leprae*. For macrophages from tuberculoid patients, killing of *M. leprae* was only achieved in the presence of IFN-γ, suggesting that initial T-cell activation occurs prior to the killing of *M. leprae*. In contrast, though activation with IFN-γ rendered the lepromatous macrophage microbicidal, it failed to induce lymphocyte proliferation, suggesting a defect at either the antigen-presenting cell or the lymphocyte level or both. The concept that T-cell anergy is primarily due to lack of lymphokine generation was ruled out by our results, since responsiveness was restored in only a small proportion of lepromatous patients after exogenous lymphokine addition. In conclusion, this study demonstrated that killing and antigen presentation are two independent events. It appears that the ability of the macrophages per se to kill *M. leprae* may be of greater importance than lymphocyte-mediated activation for protection against *M. leprae* infection.—Authors' Abstract

de Vries, R. R. P. Regulation of T cell responsiveness against mycobacterial antigens by HLA class 2 immune response genes. Rev. Infect. Dis. **11** Suppl. 2 (1989) S400–S403.

Helper T lymphocytes can only recognize mycobacterial antigens when they are presented by HLA class 2 molecules. Thus, these molecules may play an important role in the regulation of the immune response against mycobacteria. In this paper it is demonstrated that the T cells from individuals with different HLA class 2 molecules react to different mycobacterial antigens. These data indicate that HLA class 2 molecules are the products of immune response (Ir) genes for mycobacteria. Such genetically controlled differences in antimycobacterial T-cell reactivity may explain the association of certain HLA class 2 alleles with a different course of mycobacterial infections and may have implications for vaccine development.—Author's Abstract

Hunter, S. W., McNeil, M., Modlin, R. L., Mehra, V., Bloom, B. R. and Brennan, P. J. Isolation and characterization of the highly immunogenic cell wall-associated protein of *Mycobacterium leprae*. J. Immunol. **142** (1989) 2864–2872.

In a recent study, we demonstrated that certain reactivities crucial to the immune response in leprosy are due to protein associated with the cell wall peptidoglycan "core" of *Mycobacterium leprae*. We now describe a primary method for the isolation of a highly immunogenic, large molecular-size, cell wall protein (CW-P) complex from *M. leprae*, freed of soluble proteins, bound mycolates, arabinogalactan, and much of the peptidoglycan. The complex is of apparent relative molecular size 2×10^6 to 20×10^6 Da, is distinguished by a high content of Ala, Gly, Leu, Asx, and Glx, and some peptidoglycan, and represents up to 7% of the bacterial mass. It is stable to a variety of dissociation and reductive processes and, in accord with its size, is not resolvable by polyacrylamide gel electrophoresis. The monoclonal antibodies (MAb) to the CW-P complex also react with the heat shock 65-kDa protein of *M. leprae*. Conversely, antibodies that recognize internal epitopes within the polypeptide chain of the heat-shock protein also react with CW-P; however, antibodies that recognize the N and C termini of the 65-kDa protein fail to react with CW-P, and some anti-CW-P MAb do not recognize any of the soluble proteins of *M. leprae*. Alternate methods to derive the large peptidoglycan-associated protein result in lower yield and less of the associated heat-shock protein, implying that the 65-kDa protein may not be crucial to the immunogenicity of the complex. In an accompanying paper, we demonstrate that T-cell clones raised to CW-P also selectively recognize soluble proteins, primarily of 7-kDa and 16-kDa size. Thus, the image of the CW-P complex of *M. leprae* is of a few immunoreactive polypeptides in avid association with a modicum of peptidoglycan to which the 65-kDa polypeptide may be variably attached, perhaps due to involvement in assembly of the complex.—Authors' Abstract

Kalyanasundaram, K., Elangeswaran, N., Bhatia, V. N., Thiagarajan, M. and Sirumban, P. Observations on T-cell subpopulations in type II reactions. Indian J. Lepr. **61** (1989) 79–83.

Fifteen cases each of type 2 reaction, LL and TT leprosy and 50 endemic controls were studied for phenotypic markers T_2, T_4 and T_8 by the two-step immunoperoxidase technique. There was statistically significant increase in T_4 (helper) cells in type 2 reaction. There was also a decrease in T_8 cells but this was not statistically significant.—Authors' Abstract

Kaplan, G., Kiessling, R., Teklemariam, S., Hancock, G., Sheftel, G., Job, C. K., Converse, P., Ottenhoff, T. H. M., Becx-Bleumink, M., Dietz, M. and Cohn, Z. A. The reconstruction of cell-mediated immunity in the cutaneous lesions of lepromatous leprosy by recombinant interleukin 2. J. Exp. Med. **169** (1989) 893–907.

Human rIL-2 (10-30 μg) was injected intradermally into the skin of patients with lepromatous leprosy with high bacillary loads. All patients responded to the lymphokine with local areas of induration that peaked at 24 hr and persisted for 4–7 days irrespective of whether the site was "normal skin" or a nodular lesion. Within 24 hr there was an extensive emigration of T cells and monocytes into the site. The percentage of the dermis infiltrated by mononuclear cells increased by more than sevenfold, peaking at 4 days and persisting for > 15 days. Both CD4+ and CD8+ T cells entered the site. T cells of CD4+ phenotype predominated at 2–7 days but by 11 days, CD8+ cells were predominant. Considerable numbers of T6+ Langerhans' cells appeared in the dermis by 72 hr and persisted for 3 weeks. By 4 days the thickness of the overlying epidermis had increased twofold, and keratinocytes were expressing MHC class II antigen and the IFN-γ induced peptide IP-10.

Starting at 48 hr, there was an extensive destruction of mononuclear phagocytes that contained structurally intact or fragmented *Mycobacterium leprae* observed at the electron microscope level. The organisms, either free or contained within endocytic vacuoles, were discharged into the extracellular space and then reingested by blood-borne monocytes. This was followed by marked reductions in the number of acid-fast organisms in the injected site, evident as early as 4–7 days and more marked at 2–3 weeks after injection; 13 of 15 patients exhibited a disposal of acid-fast bacilli ranging from 5- to 1000-fold with a mean value of ~100-fold.

The administration of IL-2 leads to the generation of an effective cell-mediated immune response, recapitulating an antigen-driven event and leading to striking local reductions in *M. leprae*. In comparison with the purified protein derivative of tuberculin reaction, bacilli are cleared more promptly, although emigratory cells persist for a shorter time.—Authors' Summary

Lamb, J. R., Lathigra, R., Rothbard J. B., Sweetser, D., Young, R. A., Ivanyi, J. and Young, D. B. Identification of mycobacterial antigens recognized by T lymphocytes. Rev. Infect. Dis. **11** Suppl. 2 (1989) S443–S447.

The development of vaccines capable of inducing protective immunity against mycobacterial infection depends in part on the identification of antigenic determinants that activate T cells with antimycobacterial effector function. Various approaches designed to analyze the recognition of mycobacterial antigens by T-cells are reviewed. In addition to the established approach of using serologically defined antigens, alternative methods independent of antibody preselection, such as polyacrylamide gel electrophoresis-fractionated immunoblots of mycobacteria, can be used to probe the specificity of the T-cell repertoire. Furthermore, the application of recombinant DNA expression combined with that of synthetic peptides whose sequences are predicted to constitute T-cell determinants allow the localization of T-cell epitopes within a protein. The use of these techniques in defining potentially "pathogenic and protective" T-cell epitopes in mycobacteria is discussed.—Authors' Abstract

Marino-Albernas, J., Verez-Bencomo, V., Gonzalez-Rodriquez, L., Perez-Martinez, C. S., Gonzalez-Abreu Castell, E. and Gonzalez-Segredo, A. Chemical synthesis of an artificial antigen containing the tri-

saccharide hapten of *Mycobacterium leprae*. Carbohydr. Res. **183** (1988) 175–182.

The trisaccharide allyl *O*-(3,4-di-*O*-methyl-β-D-glucopyranosyl)-(1 → 4)-*O*-(2,3-di-*O*-methyl-α-L-rhamnopyranosyl)-(1 → 2)-3-*O*-methyl-α-L-rhamnopyranoside was synthesized from partially methylated monosaccharide derivatives. Condensation of 1,4-di-*O*-acetyl-2,3-di-*O*-methyl-α-L-rhamnopyranose promoted by boron trifluoride etherate with the appropriate alcohol proceeded stereoselectively and with very high yields. Selective deacetylation and glycosylation with 2,4-di-*O*-acetyl-3,6-di-*O*-methyl-α-D-glucopyranosyl bromide led to a trisaccharide. The acrylamide copolymers of mono-, di-, and trisaccharide were compared in their ability to specifically bind antibodies from leprosy patients.—Authors' Abstract

Mehra, V., Bloom, B. R., Torigian, V. K., Mandich, D., Reichel, M., Young, S. M. M., Salgame, P., Convit, J., Hunter, S. W., McNeil, M., Brennan, P. J., Rea, T. H. and Modlin, R. L. Characterization of *Mycobacterium leprae* cell wall-associated proteins with the use of T lymphocyte clones. J. Immunol. **142** (1989) 2873–2878.

Development of a vaccine against leprosy depends on the identification of antigens (Ag) that stimulate cell-mediated immune responses. We have previously demonstrated that cell-wall proteins of *Mycobacterium leprae* are highly immunogenic. By using human cell wall-specific T-cell clones we have begun to characterize soluble proteins that integrate into the cell-wall skeleton. T cells from leprosy lesions were expanded with IL-2 *in vitro* yet retained specificity to Ag of the insoluble cell wall core (CWC) *in vitro,* indicating that T cells had been activated by CWC Ag *in vitro.* A cell-wall protein-peptidoglycan complex and cell-wall protein preparations lacking carbohydrates and lipids from CWC retained T-cell reactivity. To identify immunogenic protein component(s) of cell-wall protein, T-cell lines were established to cell walls and tested against *M. leprae* proteins separated by SDS-PAGE and transferred to nitrocellulose. Greatest T-cell reactivity was observed to proteins of M_r 7 kDa, 16 kDa, and 28 kDa. T-cell clones reactive with 7-kDa and 16-kDa Ag from gels failed to respond to proteins of other M_r separated under either reducing or nonreducing conditions, indicating that these molecules are not subunits of larger proteins and may represent monomeric units polymerized into cell walls. The approaches described herein for characterization of immunodominant T-cell Ag of *M. leprae* may be useful for study of T-cell Ag in cell walls of bacterial pathogens of man.—Authors' Abstract

Ramu, G. Ten-year study of lepromin response in child contacts of leprosy patients. Indian J. Dermatol. Venereol. Leprol. **54** (1988) 295–299.

In this study, 484 leprosy contact children were tested with Dharmendra lepromin and the early and late responses were recorded. These were followed up for a period of 10 years. They were compared with lepromin reaction in 135 children who were living in the households where there were no leprosy cases. All the contacts and noncontacts belonged to villages in the Chingleput Taluk. Among contacts, the early lepromin was positive in 283 and negative in 201. Forty-six contacts developed leprosy from mostly among lepromin-positive (Fernandez) reactors. Only two lepromin-negative contacts developed leprosy. Out of the 46 children who developed leprosy, there were only two who had a 3+ late lepromin reaction (Mitsuda). Four contacts who developed borderline leprosy were negative for late lepromin reaction (Mitsuda). Among 135 noncontacts, only 15 children had a positive early lepromin response; whereas 90 had a positive late reaction. There was a significant disagreement between the positive early lepromin response and the late reaction. Late lepromin reaction may be an index of protective immunity; whereas the early reaction which indicates delayed hypersensitivity, is not.—Author's Abstract

Sasiain, M. del C., de la Barrera, S., Valdez, R. and Balina, L. M. Reduced suppressor cell response to *Mycobacterium leprae* in lepromatous leprosy. Infect. Immun. **57** (1989) 951–956.

We have previously shown that concanavalin A (ConA) induction of suppressor-cell activity is impaired in patients with lepromatous leprosy (LL). In this study, we demonstrated that the proportion of cells bearing the Leu8 antigen (associated with suppressor-inducer cells) is low in LL patients and tends to normalize during the erythema nodosum leprosum (ENL) episode. Antigen-induced suppressor-cell function was evaluated by a two-stage assay. In the first stage, peripheral blood mononuclear cells (PBMC) were cultured for 5 days either in the presence of gamma-irradiated *Mycobacterium leprae* or in tissue culture medium as a control. In the second stage, mitomycin-C-treated suppressor or control cells were added to phytohemagglutinin (PHA)-or ConA-stimulated autologous PBMC. The results indicate that the ability of *M. leprae* to induce suppressor activity was lower in LL patients than in patients with tuberculoid (TT) and intermediate clinical (BB, BL, BT) forms and *M. bovis* BCG-immunized normal controls. In ENL patients, the percent suppression was between that of TT and normal individuals. *M. leprae*-induced suppression was more effective on ConA- than on PHA-triggered T-cell proliferation in all groups. In contrast, normal PBMC cultured for 5 days in RPMI 1640 medium (N-C) and cells from patients with leprosy (TT-C and LL-C) had effects of their own on PHA- or ConA-induced proliferation. LL-C depressed the response to ConA and enhanced PHA-induced proliferation of autologous cells. Conversely, TT-C reduced PHA-induced proliferation and increased the ConA response. Suppression of proliferation could not be overcome with exogenous interleukin-2 and was not related to the induction of the Tac antigen. The abilities of LL, TT, ENL, and normal cells to proliferate upon PHA or ConA stimulus were similar, indicating that the defect in the generation of *in vitro* suppression by *M. leprae* in LL patients occurred during the induction period (step 1 of assay).—Authors' Abstract

Sehgal, V. N., Sharma, V. and Sharma, V. K. Comprehensive evaluation of complement components in the course of type I (lepra) and type II (ENL) reactions. Int. J. Dermatol. **28** (1989) 32–35.

Complement components C1q and C4 of classic pathway; C3d, a breakdown product of C3, and factor B of alternate pathway; and C3, a component both of classic and alternate pathways, were studied in 35 patients, comprising 18 type 1 (lepra) and 17 type 2 (ENL) reactions. There was a significant decrease in C3 and factor B with a concomitant rise of C3d during ENL. These changes indicate their preeminent role in immunogenesis of type 2 (ENL) reaction. The changes in the classic pathway components, on the other hand, were insignificant, apparently suggesting its limited involvement in ENL. Furthermore, reversion of factor B and C3d after subsidence of reaction is intriguing and may indicate that they are not substantially affected even with contemporary treatment. Complement components, of both classic and alternate pathways, showed no significant alterations either during type 1 (lepra) reaction or after its amelioration.—Authors' Abstract

Shetty, V. P., Antia, N. H. and Jacobs, J. M. The pathology of early leprous neuropathy. J. Neurol. Sci. **88** (1988) 115–131.

A qualitative and quantitative study was made of early changes in nerves from 10 patients with the tuberculoid or lepromatous type of leprosy. Five nerve biopsies, taken from sites remote from skin lesions, were considered to be unaffected when examined by paraffin histology but showed abnormalities in semithin resin sections and by electron microscopy; 5 showed mild to moderate involvement by paraffin histology. Changes in "unaffected" nerves in both types of leprosy included the presence of subperineurial edema; occasional evidence of fiber regeneration, sometimes with atypical features; increased numbers of small myelinated fibers, possibly a consequence of axonal atrophy; a few thinly remyelinated fibers, probably due to secondary demyelination, and some loss of unmyelinated axons. In more affected nerves there was variable loss of axons, both myelinated and unmyelinated. Demyelination was not a conspicuous feature; there was evidence of axonal atrophy in some fibers. Similarities in some of the changes observed in tuber-

culoid and lepromatous types of leprosy suggest a common mechanism of nerve damage, at least in the early stages. The presence of abnormalities in nerves at a distance from skin lesions implies a more diffuse nerve involvement than might have been expected in both types of leprosy.—Authors' Summary

Silva, C. L. and Foss, N. T. Tumor necrosis factor in leprosy patients. J. Infect. Dis. **159** (1989) 787–790.

Tumor necrosis factor (TNF) functions as an immunoregulatory cytokine, with several important biologic effects. Two that dominate—antiproliferative and anti-infective functions—can be easily demonstrated both *in vitro* and *in vivo.* TNF is produced primarily by monocytes. Since *Mycobacterium leprae* infect monocytes, we investigated TNF production by peripheral blood mononuclear cells (PMBC) from patients with the polar forms of the disease. The results demonstrate that PBMC from some LL subjects are unable to produce TNF spontaneously or in response to potent stimulation. However, PBMC from tuberculoid patients either secrete TNF spontaneously or produce it in normal amounts after stimulation. Thus, the spontaneous release of TNF may indicate an activated immune response that is not present in controls or in LL patients. High TNF levels were also demonstrated in the plasma of tuberculoid patients; however, plasma levels of TNF were low in LL patients and in healthy subjects. These observations show that TNF is produced in human beings and extend our previous findings that TNF can be detected in serum from patients with chronic disease. There seems to be a relation between plasma TNF levels and severity of the disease.

The decreased TNF production by PBMC from LL patients may have been a result of either an intrinsic cellular defect or deficient production of other cytokines. Decreased production of TNF in these patients may contribute significantly to the evolution of the infection because TNF, when present at effective concentrations, may act to improve the host defense.—(*From the* Article)

Singh, N. B., Lowe, A. C. R. E., Rees, R. J. W. and Colston, M. J. Vaccination of mice against *Mycobacterium leprae* infection. Infect. Immun. **57** (1989) 653–655.

Intradermal immunization with killed *Mycobacterium leprae* renders mice immune to infection with viable *M. leprae.* This protection is long lasting and systemic in that immunization in the left flank results in protection in both the left and right foot pads. Immunization with *M. vaccae* was ineffective in protecting mice against *M. leprae* infection, while *M. bovis* BCG provided partial protection. *M. habana* TMC 5135 (now known as *M. simiae*) was found to be as effective as *M. leprae* in protecting mice against foot pad infection.—Authors' Abstract

Steinhoff, U., Golecki, J. R., Kazda, J. and Kaufmann, S. H. E. Evidence for phagosome-lysosome fusion in *Mycobacterium leprae*-infected murine Schwann cells. Infect. Immun. **57** (1989) 1008–1010.

Murine Schwann cells were infected with viable armadillo-derived *Mycobacterium leprae in vitro,* and the lysosomal marker enzyme, acid phosphatase, was stained by the Gomori reaction. Electron-microscopic analysis revealed that Schwann cells infected with *M. leprae* possess acid phosphatase and that lysosomes fuse with infected phagosomes.—Authors' Abstract

Thole, J. E. R., van Schooten, W. C. A., Keulen, W. J., Hermans, P. W. M., Janson, A. A. M., de Vries, R. R. P., Kolk, A. H. J. and van Embden, J. D. A. Use of recombinant antigens expressed in *Escherichia coli* K-12 to map B-cell and T-cell epitopes on the immunodominant 65-kilodalton protein of *Mycobacterium bovis* BCG. Infect. Immun. **56** (1988) 1633–1640.

In gene libraries of *Mycobacterium bovis* BCG, *M. tuberculosis,* and *M. leprae* recombinants were frequently encountered that expressed an immunodominant 65-kilodalton (kDa) protein antigen that was shown to react with a high proportion of mycobacterium-reactive human and murine T cells and murine monoclonal antibodies. In this study, recombinant antigens were used

to map T-cell and B-cell epitopes on the *M. bovis* BCG 65-kDa protein that was previously designated MbaA. Four different T-cell-epitope-containing regions (amino acid residues 1 through 16, 17 through 61, 85 through 108, and 235 through 279) were defined that were recognized by seven T-cell clones from patients with tuberculoid leprosy. These regions are distinct from two previously described T-cell epitopes recognized by T cells from a tuberculosis patient. As T-cell clones restricted by different class II determinants were shown to be specific for different regions on the 65-kDa protein, the presented data suggested that the products of different human leukocyte antigen class II loci and alleles present different parts of MbaA to the immune system. B-cell-epitopes recognized by 20 monoclonal antibodies were assigned to eight different regions of MbaA. Using 15 of these antibodies, we previously showed that MbaA was antigenically related to a common antigen present in many bacterial species. The dispersed localization of the involved epitopes defined here shows that various different parts of MbaA are indeed conserved. These results show that well-defined recombinant antigens are useful tools for the localization of both B- and T-cell-epitope-containing regions of a protein. Peptides synthesized from the sequences of such regions may then exactly define the epitopes relevant for the development of specific diagnostic tests or of vaccines against mycobacteria.—Authors' Abstract

Vachula, M., Holzer, T. J. and Andersen, B. R. Suppression of monocyte oxidative response by phenolic glycolipid I of *Mycobacterium leprae.* J. Immunol. **142** (1989) 1696–1701.

Mycobacterium leprae synthesizes a unique phenolic glycolipid (PGL-I) in abundant quantities. We studied the effect of PGL-I on the generation of superoxide anion (O_2^-) by stimulated human monocytes. Peripheral blood monocytes pretreated with PGL-I released less O_2^- when stimulated with *M. leprae* than did control monocytes. Monocytes pretreated with dimycocerosyl phthiocerol, mycoside A of *M. kansasii,* or mycoside B of *M. microti,* on the other hand, released O_2^- in quantities comparable to control monocytes in response to *M. leprae* stimulation.

Monocyte O_2^- release in response to other stimuli of the oxidative metabolic burst, such as PMA, zymosan, *M. bovis* bacille Calmette-Guérin, or *M. kansasii,* was unaffected by lipid pre-treatment. These findings demonstrate that PGL-I has a direct effect on monocyte O_2^- generation in response to *M. leprae* and suggest that PGL-I is a modulator of phagocytic cell function.—Authors' Abstract

Vaishnavi, C., Thakur, M., Kaur, S., Ganguly, N. K., Nanda, A. and Kumar, B. Effect of suppressor cells on antibody producing cells in mice infected with *Mycobacterium leprae.* Indian J. Lepr. **61** (1989) 72–78.

Swiss albino mice were transfused with suppressor cells obtained after *in vivo* stimulation of mice with ConA (NS group). Some of the animals were infected with *Mycobacterium leprae* (NSI-group). Half of these animals were treated with dapsone (NSIT group). Adequate normal (NC) and infected (NI) controls were included. A plaque assay was carried out at different time periods to elucidate the effect of suppressor cells on antibody-producing cells. No significant difference was seen in the number of plaque-forming cells (PFC) in infected and dapsone-treated animals (NSIT) when these were compared with controls. However, a significant increase seen in the number of IgM PFC at 6 months in NI and NSI groups and IgG PFC in NI group could be due to the peak foot pad infection during this period. The significant decrease in the number of IgG PFC in NS and NSIT group compared to NC at 0 month is probably due to the suppressor-cell activity in these groups.—Authors' Abstract

Wu, Q., *et al.* [Assay of antibody level in sera of leprosy patients with a *Mycobacterium smegmatis* ELISA.] China Lepr. J. **4** (1988) 210–214. (in Chinese)

The establishment of a *Mycobacterium smegmatis* (Ms) ELISA and comparison of the Ms-ELISA with PGI-ELISA are reported. The sera for the tests were collected from leprosy patients (142 cases), tuberculosis

patients (20), and normal persons (120 from a nonendemic area of leprosy). The results indicated that Ms-ELISA is of high sensitivity (99%) and specificity (95%), and a significantly positive correlation ($r = 0.6106$, $p < 0.0001$) with agreement rates of more than 90%, and that there was highly significant correlation ($r = 0.955$, $p < 0.01$) between OD and BI values. These data suggest that the Ms-ELISA is valid and reliable for the detection of antibody in leprosy. On the other hand, because Ms-ELISA is more simple and it is easier to get the antigen and reagents used for the test, it may be useful in leprosy control programs, both for screening subclinical infection in leprosy and in following responses to therapy.—Authors' English Abstract

Xiong, S., *et al.* [Determination of ability of producing IL-2 and activity of NK in multibacillary leprosy.] China Lepr. J. **4** (1988) 207–209. (in Chinese)

The ability of produce interleukin-2 and natural killer activity of the circulating mononuclear cells, under stimulation with PHA, has been determined with radioimmunoassay in 20 cases of multibacillary (MB) leprosy and 20 healthy controls. The results show that the ability and activity in the MB patients are obviously lower than those in healthy people ($p < 0.01$), proving still further that MB patients have defects in their cell-mediated immunity.—Authors' English Abstract

Young, D. B. and Mehlert, A. Serology of mycobacteria: characterization of antigens recognized by monoclonal antibodies. Rev. Infect. Dis. **11** Suppl. 2 (1989) S431–S435.

Analysis of the antibody response to mycobacterial extracts has identified a limited set of proteins that are recognized as immunodominant in the BALB/c strain of mice. Detailed characterization has revealed that several of these antigens are homologues of proteins known to be induced in response to environmental stress stimuli in other prokaryotic and eukaryotic cell types. It is proposed that differential gene expression may play a role in determining which antigens are recognized during infection and that highly conserved stress proteins could be involved in generation of autoimmune responses.—Authors' Abstract

Microbiology

Doherty, T. M., Booth, R. J., Love, S. G., Gibson, J. J., Harding, D. R. K. and Watson, J. D. Characterization of an antibody-binding epitope from the 18-kDa protein on *Mycobacterium leprae*. J. Immunol. **142** (1989) 1691–1695.

A murine mAb, designated L5, appears to be specific for an epitope on a protein from *Mycobacterium leprae* of restricted distribution within the mycobacteria. This protein of M_r 18,000 (18 kDa) is of interest because monoclonal antibodies raised against it do not appear to crossreact with other mycobacterial pathogens. The L5 antibody-binding epitope has been mapped by two complementary methods; expression of gene fragments and synthesis of short peptides. This L5-binding region of the 18-kDa protein (amino acids 109 to 115) shows some homology to a region of the GroEL heat shock family of proteins. Characterization of this antibody-binding epitope may lead to a reagent of use in early diagnosis of infection.—Authors' Abstract

Grosskinsky, C. M., Jacobs, W. R., Jr., Clark-Curtiss, J. E. and Bloom, B. R. Genetic relationships among *Mycobacterium leprae, Mycobacterium tuberculosis,* and candidate leprosy vaccine strains determined by DNA hybridization: identification of an *M. leprae*-specific repetitive sequence. Infect. Immun. **57** (1989) 1535–1541.

Comparative DNA hybridization studies of genomic DNA indicated that, while dif-

ferent isolates of armadillo-derived *Mycobacterium leprae* have a high degree of homology, binding of *M. leprae* genomic DNA to DNA of other species of mycobacteria or to corynebacteria was low, establishing that *M. leprae* is only remotely genetically related to any of the species examined. Several candidate leprosy vaccine mycobacterial strains were similarly found to have little genetic similarity to *M. leprae*. In contrast, the DNAs of the slow-growing mycobacteria *M. tuberculosis, M. africanum, M. bovis,* and *M. microti* were found to be very closely related. In the course of these studies, an *M. leprae*-specific repetitive sequence, greater than 15-fold per genome equivalent, was identified that might be useful for diagnostic and epidemiological studies.—Authors' Abstract

Prabhakaran, K., Job, C. K., Harris, E. B. and McCormick, G. T. An electron microscopic study of alterations in the morphology and permeability of purified *Mycobacterium leprae*. J. Basic Microbiol. **29** (1989) 41–48.

This communication reports the association of changes in ultrastructure of *Mycobacterium leprae* with alterations in its permeability. To study morphologic changes of the organisms under different conditions (of temperature and exposure to NaOH and trypsin), ultrathin sections of the bacteria were cut and examined in an electron microscope. In the untreated bacilli and those washed with trypsin, the cytoplasmic membrane and the cell wall (peptidoglycan layer) remained intact; dapsone showed little effect on diphenoloxidase of the bacteria. *M. leprae* is unique among mycobacteria in possessing an unusual form of the enzyme diphenoloxidase. The antileprosy drug dapsone is a potent inhibitor of the enzyme, but it does not readily penetrate the bacteria where the cell envelope remains intact. The cell wall of *M. leprae* exposed to −80°C or washed with NaOH was partially detached from the cell membrane; dapsone readily penetrated these organisms and inhibited the bacterial enzyme. In the above preparations, the cytoplasmic membrane appeared undamaged and the bacteria remained viable, as evidenced by multiplication in mouse foot pads. At 50°C, the peptidoglycan layer became completely separated from the membrane and the cytoplasm was partially denatured. These organisms were permeable to dapsone, but were no longer viable. At 100°C, the structural organization of the bacilli was completely destroyed and, of course, they lost their enzyme activity as well as viability. Evidently, the intact cell-wall layer mediates the exclusion of dapsone from *M. leprae* and there is no correlation between its viability and permeability. The ultrathin sections also reveal the internal organization and cytoplasmic inclusions of *M. leprae* as never before seen.—Authors' Abstract

Wheeler, P. R. Pyrimidine biosynthesis *de novo* in *M. leprae*. FEMS Microb. Lett. **57** (1989) 185–190.

Mycobacterium leprae can synthesize pyrimidines *de novo*. Although pyrimidine synthesis could not be detected in intact bacteria, extracts contained all four enzymes unique to the *de novo* pathway which are detectable in mycobacteria by the methods used. Inhibition of aspartate transcarbamylase by UTP and ATP suggested that lack of pyrimidine synthetic activity in whole *M. leprae* could be a result of strong feedback inhibition.—Author's Summary

Wheeler, P. R. Pyrimidine scavenging by *Mycobacterium leprae*. FEMS Microb. Lett. **57** (1989) 179–184.

Mycobacterium leprae incorporated exogenously supplied pyrimidines as bases or nucleosides, but not as a nucleotide, into its nucleic acids. Notably, thymine was incorporated ~ 5 times more rapidly than thymidine by both suspensions of, or intracellular *M. leprae*. Thymine incorporation was significantly inhibited by clofazamine and dapsone at near-pharmacological levels. Therefore, incorporation of thymine is preferable as an activity for assessing viability of *M. leprae*. Nucleosides were converted to nucleotides through kinases, bases through phosphoribosyltransferases. Alternatively, thymine and uracil could first be converted to nucleosides. Cytosine and uracil bases were interconvertible, and uracil alone could supply all the pyrimidine requirements of *M. leprae*, though conversion

to the thymine base was extremely slow. Overall, pyrimidine scavenging occurs at a slower rate than, and appears not to be so important as purine scavenging in *M. leprae.*—Author's Summary

Zainuddin, Z. F., Kunze, Z. M. and Dale, J. W. Transformation of *Mycobacterium smegmatis* with *Escherichia coli* plasmids carrying a selectable resistance marker. Mol. Microbiol. **3** (1989) 29–34.

One limiting factor in studies of tuberculosis and leprosy is the difficulty of genetic analysis and manipulation of mycobacteria. Two approaches were adopted for the construction of vectors, based on different *Escherichia coli* plasmids and using *Mycobacterium smegmatis* as the host. In both cases we found that the original *E. coli* plasmid is capable of being replicated in *M. smegmatis,* yielding chloramphenicol-resistant colonies. One such plasmid has been recovered from a *M. smegmatis* transformant and used to re-transform both *M. smegmatis* and *E. coli* to chloramphenicol resistance. This plasmid is indistinguishable from the original plasmid by restriction analysis, and can be used as a shuttle vector for the genetic manipulation of mycobacterial species.—Authors' Summary

Experimental Infections

Job, C. K. and Hastings, R. C. Recent advances in experimental leprosy: a brief review. Ann. Natl. Acad. Med. Sci. (India) **25** (1988) 85–90.

Animal models for the study of leprosy in the laboratory are reviewed. In 1960 Shepard reported the limited and localized growth of *Mycobacterium leprae* in the foot pads of normal mice. Thymectomized irradiated mice allow *M. leprae* to multiply to a higher ceiling and athymic nude mice allow even higher levels of bacterial growth. Armadillos are highly susceptible to leprosy bacilli. Armadillos have leprosy in the wild and naturally acquired leprosy has been seen in sooty mangabey monkeys and chimpanzees. Thus, animal models are used for a variety of purposes in the laboratory.—RCH

Nakamura, K. and Yogi, Y. The nude mouse as an experimental lepromatous leprosy model (continued): The NFS/N nude mouse as a new model using the intra-upper lip inoculation method. Jpn. J. Lepr. **57** (1988) 129–136.

We compared the susceptibilities to growth of *Mycobacterium leprae* by using several strains of nude mice which were NFS/N, CBA/N, C3H/HeN + MTV, C57BL/6 and BALB/cA. *M. leprae* were inoculated at the site of their right intra-upper lip (mystacial vibrissae located part) and the right hind foot, respectively. To summarize the results, NFS/N nude mice were confirmed as a powerful tool as an experimental lepromatous leprosy model using the intra-upper lip inoculation. NFS/N nude mice also developed heavier infection than the other nude strains used with the hind foot inoculation. Susceptibilities to *M. leprae* on the CBA/N and C3H/HeN + MTV nude mice at the site of inoculation into the right hind paw were observed with similar findings; likewise the case of NFS/N nude mice at a late stage after inoculation, while lip lepromas of them after intra-upper lip inoculation did not develop such as in the NFS/N nude mice. In C57BL/6 and BALB/cA nude mice, these findings were poor compared with that of NFS/N, CBA/N and C3H/HeN+MTV nude mice. Thus, the development of a severe lepromatoid formation in nude mice was influenced by the genetic backgrounds of the animals in addition to the nude gene.—Authors' Summary

Tsutsumi, S. and Gidoh, M. Inefficacy of thalidomide on rat adjuvant-induced arthritis and lack of arthrogenicity of Hansen bacilli. Jpn. J. Lepr. **57** (1988) 122–128.

The response to adjuvant-induced arthritis (AIA) was compared between male SD rats and a strain of rats (female) named DA which originated from Australia. The response was found to be much higher in

the latter rats than in the former covering several inoculated quantities of heat-killed *Mycobacterium tuberculosis* Aoyama B (TB). Thalidomide (Th) in the dosage of 10 mg/kg once daily covering experimental term exhibited neither hypnotic appearance nor the suppression of AIA; whereas clofazimine suppressed AIA at 20 mg/kg, which was coincidental with a preceding report. The inoculation of Hansen bacilli (HB) into hind foot paws of female DA rats did not induce AIA even at high dosages. The primed inoculation of TB markedly suppressed AIA due to the secondary inoculation. Standing on the basis of these results, the suppression mechanism of Th against ENL was discussed.—Authors' Summary

Yogi, Y. and Nakamura, K. *Mycobacterium leprae*-susceptibility of NOD hybrid nude mice. Jpn. J. Lepr. **57** (1988) 117–121.

The animal model of insulin-dependent diabetes mellitus, NOD mice were established by Makino, *et al.* as inbred mice through isolation from Jcl:ICR mice. NOD hybrid nude mice (N1) developed by the introduction of the Crj:Cd-1 (ICR) nude gene were found to produce marked lepromatous lesions. The results of NOD hybrid nude mice obtained in the present study were indicative of the importance of the genetic background of Swiss mice in relation to the development of lepromatous lesions, likewise the case of NFS/N and N:N1H(s) nude mice. The NOD hybrid nude mice developed by introduction of the nude gene failed to show insulitis or overt diabetes as reported by other investigators. On the other hand, they maintained the genetic gene of a large litter size possessed by Crj:CD-1 (ICR) nude mice. In conclusion, the NOD hybrid nude mice were found to be highly beneficial experimental animals for lepromatous leprosy on the basis of their large litter size and high susceptibility to *M. leprae*.—Authors' Summary

Epidemiology and Prevention

Bagshawe, A., de Burgh, S., Fung, S. C., Chuah, J. and Berry, G. The epidemiology of leprosy in a high prevalence village in Papua New Guinea. Trans. R. Soc. Trop. Med. Hyg. **83** (1989) 121–127.

In a village of about 1000 people in Papua New Guinea the prevalence of clinical leprosy was 8.6% compared to about 3% in surrounding villages. This exceptionally high prevalence could not be explained by recent introduction of the disease or by social factors. Dapsone-resistant disease and faulty compliance with treatment are considered to be contributory to persistent infectivity of old cases which, together with the presence of 20 previously undiagnosed cases, comprised a large infective source. Social ostracism of cases was not observed and the extensive social mixing of all ages would facilitate widespread dissemination of infection. A high prevalence, particularly in children, of elevated levels of IgM antibody to phenolic glycolipid-I *Mycobacterium leprae*-specific antigen suggests frequent subclinical infection. The greater prevalence of clinical leprosy following childhood in the village favors altered susceptibility following exposure in childhood. There was a higher prevalence of leprosy in close relatives of cases when compared with the same relatives of age- and sex-matched leprosy-free controls. The occurrence of familial clustering of leprosy in a hyperendemic area with intense transmission suggests that unidentified inherited factors influence susceptibility to clinical leprosy. It is suggested that the clustering of adverse inherited traits through intermarriage may explain this hyperendemic focus on leprosy.—Authors' Abstract

Cartel, J.-L., Boutin, J.-P., Plichart, R., Roux, J. and Grosset, J. H. [Leprosy in French Polynesian archipelagoes from 1967–1987.] Bull. Soc. Pathol. Exot. Filiales **81** (1988) 819–826. (in French)

Between 1967 and 1987, 255 new cases of leprosy were detected in French Polynesia (FP)—that means on average a 8.6 ‰ detection rate. Average detection

rate calculated in seven 3-year periods did not vary significantly during the 21 year period of time studied. In two remote archipelagoes of FP, average detection rate of leprosy is especially high: Gambier archipelago and Southern Marquesas archipelago with, respectively, a 54.7 and a 48.9 $‰$ detection rate. To control leprosy, the network of treatment and active case-finding should be strengthened in archipelagoes, and chemoprophylaxis programs could be planned in places where the problem is especially important.—Authors' English Summary

Chu, Z., *et al.* [Investigation of occurrence of the disease in 2261 children of parents with leprosy.] China Lepr. J. **4** (1988) 205–207. (in Chinese)

The analysis of leprosy incidence in 2261 descendants of leprosy patients indicates that the sulfone drugs had a good protective effect on the leprosy onset in the descendants of leprosy patients. The use of combined chemotherapy should result in better achievement. The incidence in the descendants, who were born before their multibacillary (MB) parents were treated with sulfone drugs, was 3.94/1000 person years. By contrast the incidence in the descendants, who were born after their parents with MB leprosy were treated with sulfone drugs, was 0.35/1000 person years. This fact suggests that chemotherapy has a role in protecting from the infection and it will be unnecessary to isolate the patients in leprosaria. For the descendants of leprosy patients, especially in those whose parents did not take any antileprosy drug, the incidence of leprosy was significantly higher than that in the normal population. It is obvious that their high incidence was related to close contact with their leprosy parents and, therefore, the authors suggest that the descendants of leprosy patients should be checked each year for at least 5 years and, if possible, for 15–20 years.—Authors' English Abstract

Gonçalves, A., Ribeiro, M. A. C. L., Opromolla, D. A., Padovani, C. R., da Silva e Gonçalves, N. N., Beline, J. and Consorte, J. [Generation of a linear discriminant function of dermatoglyphics for the detection of high risk groups in leprosy.] An. Bras. Dermatol. **63** (1988) 395–400. (in Portuguese)

Although leprosy is clearly an important public health problem, especially in Third World countries and above all in Brazil, early diagnosis techniques are still infrequently used. Among these techniques, dermatoglyphics are of low cost, easy to use and totally innocuous in their effects. As an important genetic marker, they have supplied considerable etiological and diagnostic evidence for a variety of diseases. In the case of leprosy, where the nature of manifestations depends greatly upon the constitution of the host, dermatoglyphics have provided merely descriptive results, given the methodological variations of the studies undertaken to date. In face of these findings, a dermatoglyphic study of leprosy-affected subjects of both sexes, bearers of the indeterminate form of the disease, was undertaken. When paired with normal control subjects of the same sex, age group, race and ancestral background, a linear discriminant function was designed in an attempt to permit detection of high-risk groups and, consequently, early identification of carriers of the disease in its different phases (infection, subclinical and manifest disease).

Clinical and laboratory procedures were undertaken at Lauro de Sousa Lima Hospital in Bauru, state of São Paulo. Dermatoglyphic data were collected and quantified according to standardized techniques and processed at the Biostatistics Department of the Biosciences Institute of the Universidade Estadual Paulista, Botucatu Campus.

The comparison of means for nine quantitative dermatoglyphic variables was investigated using Hotelling's T^2 statistics. The two groups were formed by 49 affected subjects (25 men and 24 women) paired to corresponding healthy control subjects. The means and coefficients of variation of the dermatoglyphic variables showed homogeneity in their distributions. Statistical tests revealed F statistics of 2.385 for male and 2.439 for female subjects, with corresponding probabilities of 0.062 and 0.061, respectively. This leads to a discussion of dermatoglyphic, leprological and experimental aspects involved.—Authors' English Summary

Jeyaseelan, L. and Rao, P. S. S. Determination of sample sizes for epidemiological surveys using cluster sampling technique. Indian J. Lepr. **61** (1989) 84–91.

Cluster sampling often provides a convenient and low-cost device in epidemiological surveys. The sample size needed under cluster sampling is generally larger than that in an individual-based scheme due to the intra-class correlation existing in a cluster. This intra-class correlation coefficient is usually not known and some assumptions or estimates are essential. The strengths and weaknesses of cluster sampling over other sampling plans are presented and briefly discussed in this paper with particular reference to leprosy control programs. One particular model of multistage cluster sampling technique is suggested in the evaluation of a district level program, which includes determining the effectiveness of multidrug therapy, monitoring efficiency of paramedical workers and estimating the incidence of leprosy.—Authors' Abstract

Ly, H. M., Trach, D. D., Long, H. T., Thuy, N. K., Tuan, N. A., Tran, N. T., Stanford, J. L., Hendriks, J. T. and Wright, E. P. Skin test responsiveness to a series of new tuberculins of children living in three Vietnamese cities. Tubercle **70** (1988) 27–36.

A skin-test survey was conducted among 1035 children aged 7–19 years living in three cities in Vietnam. Fifteen new tuberculins, including leprosin A, were applied; an induration of 2 mm diameter or more was considered positive. Compared to some other tropical countries, low levels of sensitization were recorded and remarkable regional differences were found. Positivity to any tuberculins (pooled data) among non-BCG-vaccinated children was significantly lower in Hanoi (13.1%) and HoChiMinh-City (HCMC) (15.5%) than in Nha Trang (25.7%) ($p = 0.001$ and $p = 0.012$, respectively). The proportion of nonvaccinated children responding to tuberculin ranged from 18.4% in Hanoi to 54.5% in Nha Trang. Leprosin A elicited a response in 14.9% of the children in Nha Trang, but in very few of those in Hanoi (4.3%) or HCMC (3.0%). Thus, of the three cities studied, significant sensitization to both *Mycobacterium tuberculosis* and *M. leprae* was demonstrable only in Nha Trang. In Hanoi most of the response was to fast-growing species while in HCMC and Nha Trang it was mainly to slow-growing species. These results may account in part for the observed differences in the prevalence of tuberculosis and leprosy between the north and the south of Vietnam.—Authors' Summary

Martinez, A. R., Resoagli, E. H., De Millan, S. G., Resoagli, J. P., Ramirez, M. M., Cicuta, M. E., De Rott, M. I. O. and Sandoval, A. [Wild leprosy in *Dasypus novemcinctus.*] Arch. Argent. Dermatol. **34** (1984) 21–30. (in Spanish)

The object of this work is to communicate the presence of a natural mycobacteriosis in a nine-banded armadillo captured in the northeastern part of Argentina. The pathology was accompanied with the presence of a mycobacterium which was preferentially localized to the lymphatics, spleen, and liver with involvement of peripheral nerves and skin. The identification of the microbial agent was based on specific staining techniques (Ziehl-Neelsen, Fite-Faraco and King-Young) for the recognition of *Mycobacterium leprae,* loss of acid-fastness by extraction with pyridine, the D-DOPA oxidase test, microbiologic cultures in Lowenstein-Jensen and Stonebrink media, injection into the mouse foot pad following the technique proposed by Shepard, and the preparation of lepromin by the technique of Hanks. The lesions encountered in the armadillo with the natural disease coincided with those produced experimentally in the nine-banded armadillo inoculated with *M. leprae.* Because of the staining characteristics, the results of the other tests carried out and the anatomical and histological lesions caused by this mycobacterium, we face a natural leprosy. This has been described by different authors in armadillos captured in the U.S.A. but until now has not been reported as natural pathology in the South American armadillo.—(*From the* Authors' English Summary)

Tan, D., *et al.* [Endemicity and control of leprosy in Hebai Province.] China Lepr. J. **4** (1988) 214–216. (in Chinese)

There are 150 counties and municipalities in Hebei Province with a population of about 5 million. Two leprosy hospitals were established in Wangdu County and Baoding

City in 1953. Most of the hospitalized patients originated chiefly from Hebei Province, some from Beijing and Tianjin and a few from Inner-Mongolia, Shanxi and other provinces. From 1954 through 1986, 532 leprosy patients were found in Hebei, of whom 467 cases were cured and 22 still are active. Most of the 532 patients originated from marshy areas such as Baiyangdian, and patients from Anxin, Baxian, Wenan counties and Renqiu city accounted for 45%. Anxin County is a moderately endemic area, 87 counties and municipalities are lower ones and no leprosy patients have been found, to date, in the other 62 counties of the province. In the patients, multibacillary cases accounted for 62% and paucibacillary for 38%; male cases were 443 and female cases 89, the ratio being 5.98:1; and persons aged 15–39 made up 61%. The highest prevalence was 0.004/1000 and it decreased to 0.0004/1000 in 1984. The incidence was 0.07/100,000 in 1956–1960 and decreased to 0.002/100,000 in 1981–1985. By the end of 1986, 104 counties and municipalities have reached the goal of basic eradication of leprosy, but Anxin County's prevalence is still 0.017/1000.—Authors' English Abstract

Rehabilitation

Beine, A. O., Sampath, S. R. And Cordeiro, R. A. A modification of the surgical correction of the thumb—a long term follow up. Indian J. Lepr. **61** (1989) 17–22.

A modification of the commonest surgical procedure to restore abduction–rotation using the flexor superficialis transfer with Y-insertion is described. The modification consists of doing a triple insertion at the thumb instead of a Y-insertion. After introducing the triple insertion the procedure shows 80%–90% or more good results; whereas 50% or more failures are reported in the existing literature when a Y-insertion only is used which cannot safely prevent "Z" deformity. Sixty cases were followed up.—Authors' Abstract

Birke, J. A., Cornwall, M. W. and Jackson, M. Relationship between hallux limitus and ulceration of the great toe. J. Orthop. Sports Phys. Ther. **10** (1988) 172–176.

Torque range of motion (TROM) measurements of the metatarsophalangeal joint (MTPJ) of the great toe were made to determine the relationship of joint stiffness and plantar ulceration. Subjects included 20 patients with a history of plantar ulceration of the great toe (GTU), 20 patients with a history of ulceration on the plantar surface of the foot excluding the great toe (NGTU), and 20 normal controls. Peak MTPJ extension was significantly reduced in the GTU group compared to NGTU and control groups ($p < 0.0001$). The slopes of the TROM and stiffness curves were significantly steeper ($p < 0.0001$) in the GTU group compared to the control group ($p < 0.0001$). Results support the hypothesis that stiffness is a factor in plantar ulceration of the great toe.—Authors' Abstract

Nawoczenski, D. A., Birke, J. A. and Coleman, W. C. Effect of rocker sole design on plantar forefoot pressures. J. Am. Pod. Med. Assoc. **78** (1988) 455–460.

The authors quantify rocker sole designs currently used in the management of the insensitive foot and examine their effectiveness in reducing forefoot pressures. Twenty subjects were tested with six different shoe soles modified with various radii or curvature and locations of the take-off or pivot point. Relative pressure was measured at four sites on the forefoot while subjects walked in each shoe design. Analysis of variance of relative pressure was highly significant at all sites tested. Further analysis demonstrated that the traditional rocker design was the most effective in reducing forefoot pressures. The curved sole design with a take-off point at 50% of the sole length was also effective in reducing pressures. This design is more conventional in appearance and may be of greater practical value in the clinical setting.—Authors' Abstract

Nawoczenski, D. A., Birke, J. A., Graham, S. L. and Koziatek, E. The neuropathic foot—a management scheme: a case report. Phys. Ther. **69** (1989) 287–291.

The purpose of this case report is to present a management approach that was effective in the healing and long-term care of a neuropathic plantar ulcer in a patient with diabetes mellitus. The report demonstrates that a successful management program must go beyond the stage of healing and include patient education and techniques for reducing plantar pressures to prevent the recurrence of plantar ulcers.—Authors' Abstract

Pe, H. A 15 year survey of Burmese amputees. Prosthet. Orthot. Int. **12** (1988) 65–72.

A 15-year retrospective study of 2228 civilian amputees was conducted at the Hospital for the Disabled, Thamaing, Rangoon. It was demonstrated that utilization of appropriate technology for development of essential components had enabled the hospital to serve more amputees. The ratio of male to female was 4.23:1. The mean age was 31 years, males slightly older than females. Trauma was the leading cause of upper limb amputations (87%). In the lower limb, although trauma (47%) was the prominent cause, disease (41%) was a close second. Major specific causes of trauma were gun-shot/explosion (25%), railway accident (20%), and road accident (19%). Leading specific causes of disease were leprosy (25%), vascular disease (24%), and gangrene (23%). Unless appropriate and effective preventive measures are instituted man-power drainage and demand for prosthetic services will continue.—Author's Abstract

Thompson, D. E., Buford, W. L., Jr., Myers, L. M., Guirintano, D. J. and Brewer, J. A., III. A hand biomechanics workstation. Comput. Graph. **22** (1988) 335–343.

Interactive graphics for hand surgery was used to apply mathematical modeling and describe the kinematics of the hand and its resultant effect on hand function. Dynamic high resolution displays and three-dimensional images were tailored for use with a specific patient's hand and a new and powerful design and analysis tool produced. Methods were developed to portray kinematic information, such as muscle excursion and effective moment arm, and extended to yield dynamic information such as torque and work. This prototype workstation has been developed in concert with leading orthopedic surgeons and therapists.—Authors' Abstract

Zheng, T., *et al.* [A survey of deformity and disability among 1480 cases of leprosy.] China Lepr. J. **4** (1988) 198–204.

In order to obtain some basic data on disability in leprosy, a survey has been carried out in two leprosy hospitals and in a city and a county in 1987. WHO disability grading (with minor modifications) was used for the survey. The factors associated with disability were investigated.

A total of 1480 cases were examined: females 372, males 1108, aged 8–92 years (mean 49.45 years), including active patients and cured leprosy patients. Among them there were 999 disabled patients, a disability rate of 67.5%. Among the 999 there were 241 (24.12%) active and 753 (75.38%) cured patients. The percentage in the disabled cases whose antileprosy treatment had not yet begun was 55.8% (340/690). The number of patients, who suffer from deformity within 4 years after leprosy was diagnosed, was 36.5% (365/999). The number of patients with WHO disability grade 3 was 418 (41.8%), although in grade 1 there were only 120 (12.0%). Leprosy reaction and nerve pain were the most commonly associated with disability.

The authors note that all the above-mentioned factors indicate the severity of the leprosy disability problem in China today. It should be emphasized that arrested disease is not synonymous with the arrest of disability. Therefore, objectives of leprosy control should have the following precedence: 1) to reduce the incidence, 2) to cure patients and attain complete rehabilitation, and 3) to prevent deformities. Finally, the problems involved in the disability surveys are discussed.—Authors' English Abstract

Zhou, D., *et al.* [A nutriological survey in leprosy and tuberculosis patients.] China Lepr. J. **4** (1988) 218–221. (in Chinese)

Leprosy is a chronic and consumptive social disease. The eradication of leprosy is tightly associated with social and economic development and better nutrition of the population. A nutritional survey has shown that, at present, the living standard for patients with leprosy is very low and it is hard to maintain basic nutrition for them. The authors suggest a raise in welfare funds for the patients and help for them to develop their production for bettering themselves.—Authors' English Abstract

Other Mycobacterial Diseases and Related Entities

Akuffo, H. O., Fehniger, T. E. and Britton, S. Differential recognition of *Leishmania aethiopica* antigens by lymphocytes from patients with local and diffuse cutaneous leishmaniasis. J. Immunol. **141** (1988) 2461–2466.

Data are presented to suggest that differential antigen (Ag) expression by parasites derived from diffuse (DCL) vs local (LCL) cutaneous leishmaniasis patients may be responsible for the Ag-specific anergy seen in DCL patients. The evidence suggests that promastigotes derived from DCL patients express epitopes which preferentially stimulate suppressor activities in DCL patients. These determinants appear to be expressed less, if at all, by promastigotes derived from LCL patients. The Ag-specific suppression or nonresponsiveness which dominates the immune response in DCL patients during an active infection can be abrogated by drug treatment or removal of live DCL parasites, which suggests that Ag-induced regulatory cells, probably of T-cell lineage, are most likely responsible for the nonresponsiveness seen in untreated DCL patients. Thus, the mechanisms of immune regulation operating in this disease differ from that of lepromatous leprosy where the specific unresponsiveness (anergy) is irreversible even after successful treatment.—Authors' Abstract

Anderson, R., Joone, G. and van Rensburg, C. E. J. An *in vitro* evaluation of the cellular uptake and intraphagocytic bioactivity of clarithromycin (A-56268, TE-031), a new macrolide antimicrobial agent. J. Antimicrob. Chemother. **22** (1988) 923–933.

Erythromycin base and its 6-0-methyl derivative clarithromycin were actively accumulated 7.3 ± 1.2-fold and 9.2 ± 2-fold, respectively, by human neutrophils *in vitro*. The intraphagocytic bioactivities of the antimicrobial agents were investigated using the combination of a radioassay, colony counting method and a fluorescence microassay which facilitates the distinction between intracellular bacteriostatic and bactericidal mechanisms. *Staphylococcus aureus, Listeria monocytogenes* and *Legionella micdadei* were used as the test intraphagocytic microbial pathogens. Both agents were found to possess intracellular bioactivity for all three species of bacteria with clarithromycin being consistently more active than erythromycin. Under the assay conditions used, both agents were bacteriostatic (intracellularly) for *S. aureus* and *Leg. micdadei* and bactericidal for *List. monocytogenes*. Clarithromycin is clearly a potent intraphagocytic antibiotic and potentially superior in this respect to erythromycin.—Authors' Abstract

Bothamley, G. H., Swanson Beck, J., Schreuder, G. M. T., D'Amaro, J., de Vries, R. R. P., Kardjito, T. and Ivanyi, J. Association of tuberculosis and *M. tuberculosis*-specific antibody levels with HLA. J. Infect. Dis. **159** (1989) 549–555.

In the search for HLA-linked immune response genes that control susceptibiilty to tuberculosis, we performed HLA typing and measured antibody titers to well-defined *Mycobacterium tuberculosis* antigenic determinants in 101 patients with sputum smear-positive pulmonary tuberculosis and 64 healthy controls from Surabaya, Indonesia. HLA-DR2 and DQwl were associated with sputum smear-positive pulmonary tuberculosis (attributable risk = 36% and 39%, respectively), while DQw3 was associated even more strongly with the con-

trol group (preventive fraction = 57%). Antibody titers to the TB71 and TB72 epitopes of the 38-kDa protein, present only on tubercle bacilli, were strongly associated with DR2 (p_{corr} = 0.001 and 0.024, respectively). The association of both the disease and the antibody response to the 38-kDa antigen of *M. tuberculosis* with Class II HLA genes HLA-DR2 indicates that Ir-gene-mediated regulation of the immune response to this antigen may be of pathogenic significance for the development of sputum smear-positive tuberculosis.—Authors' Abstract

Collins, C. G. and Uttley, A. H. C. *In vitro* activity of seventeen antimicrobial compounds against seven species of mycobacteria. J. Antimicrob. Chemother. **22** (1988) 857–861.

Within attainable serum concentrations, quinolones, especially ciprofloxacin, inhibited strains of *Mycobacterium tuberculosis, M. xenopi, M. kansasii, M. fortuitum* and *M. marinum*; vancomycin inhibited *M. tuberculosis,* the *M. avium-intracellulare-scrofulaceum* complex, *M. kansasii, M. xenopi* and *M. chelonei*; erythromycin was active against *M. kansasii, M. xenopi* and *M. fortuitum*; minocycline against *M. kansasii* and *M. marinum* and netilmicin and cefuroxime against *M. xenopi.* Aztreonam showed some activity against *M. tuberculosis* but little or no effect was shown by five cephalosporins or imipenem.—Authors' Abstract

Dhandayuthapani, S., Nalini, N. and Bhatia, V. N. LDH isoenzyme as a tool for the identification of mycobacteria. Indian J. Lepr. **61** (1989) 61–64.

Using the polyacrylamide gel electrophoretic technique, the lactate dehydrogenase (LDH) isoenzyme patterns have been studied in four slow-growing mycobacteria—*Mycobacterium tuberculosis, M. avium, M. microti,* and *M. bovis*—and four rapid-growing mycobacteria—*M. fortuitum, M. parafortuitum, M. thermoresistible* and *M. diernhoferi.* Each mycobacterial species exhibited a distinct isoenzyme pattern for LDH.—Authors' Abstract

Eng, R. H. K., Bishburg, E., Smith, S. M. and Mangia, A. Diagnosis of *Mycobacterium* bacteremia in patients with acquired immunodeficiency syndrome by direct examination of blood films. J. Clin. Microbiol. **27** (1989) 768–769.

Thirty acquired immunodeficiency syndrome patients with mycobacterial bacteremia documented by Du Pont Isolator (Du Pont Co., Wilmington, Delaware, U.S.A.) blood cultures underwent microscopic examination of buffy coat blood smears. Of 30 patients, 14 were culture positive for *Mycobacterium avium*-M *intracellulare* complex and 1 was positive for *M. tuberculosis.* Of 15 culture-positive patients, 13 had identifiable organisms on Kinyoun- or auramine-stained direct blood smears.—Authors' Abstract

Fine, P. E. M., Ponnighaus, J. M. and Maine, N. The distribution and implications of BCG scars in northern Malawi. Bull. WHO **67** (1989) 35–42.

Reported are data on the BCG scar status of more than 112,000 individuals who were surveyed in Karonga District, northern Malawi, between 1979 and 1984. The age and sex patterns of apparent BCG scars reflect the history of BCG vaccination activities in the district. Repeated independent examinations of large numbers of people revealed that the proportions remaining with the same observed scar status among those initially classified as being scar "positive" or scar "negative" were each approximately 90%. The repeatability of positive scar reading was lower among children and older adults than among young adults aged 15–24 years, and blind follow-up of children known to have been vaccinated as infants in child health clinics indicated that less than 60% had a detectable scar 3 years after receiving the vaccine. "Negative" repeatability increased consistently with age. The implications of these findings for estimating BCG vaccine uptake and for assessing its efficacy in case-control and cohort studies are discussed. The finding that BCG scars may be difficult to read suggests there is a danger of observer bias that could lead to distortion—in particular, to overestimates of vaccine efficacy.—Authors' Abstract

Källenius, G., Hoffner, S. E. and Svenson, S. B. Hypothesis: Does vaccination with bacille Calmette-Guérin protect against AIDS? Rev. Infect. Dis. **11** (1989) 349–351.

In the United States a majority of patients with AIDS are infected with bacteria of the *Mycobacterium avium* complex (MAC), while in Sweden only ~10% of AIDS patients are so infected. It is proposed that general vaccination with bacille Calmette-Guérin (BCG) in Sweden may have induced protection not only against tuberculosis but also against infections with MAC, accounting for the lower incidence of MAC infection in Swedish patients with AIDS. The current AIDS pandemic may indicate a need for reevaluation of national BCG vaccination policies.—Authors' Abstract

Kaufmann, S. H. E. *In vitro* analysis of the cellular mechanisms involved in immunity to tuberculosis. Rev. Infect. Dis. **11** Suppl. 2 (1989) S488-S454.

Tuberculosis is a chronic infectious disease caused by *Mycobacterium tuberculosis.* Protection against and pathogenesis of tuberculosis greatly depend on specific T lymphocytes, and it is generally assumed that CD4+ T cells—through lymphokine-mediated macrophage activation—are the major mediators of the host response to tuberculosis. In the present report, results from experimental tuberculosis studies in mice are summarized which indicate that both CD4+ and CD8+ T lymphocytes are generated during tuberculosis. Furthermore, evidence is presented that both T-cell populations are involved in protection against and pathogenesis of tuberculosis and that the final outcome of the host response depends on an intricate balance between these two types of T cells.—Author's Abstract

Ketova, N. A. [HLA-DR phenotype and B/DR haplotype in patients with sarcoidosis.] Probl. Tuberk. **12** (1988) 49–50. (in Russian)

Examination of 40 patients with sarcoidosis and 70 healthy persons revealed that in the patients with sarcoidosis the frequency of antigens HLA B7 and DR3, haplotypes B7DR2 and B8DR3 and some other haplotypes including antigens HLA B7 and DR3 was increased. These data suggested that the immunological mechanisms relevant to sarcoidosis pathogenesis are under genetic control of the HLA complex.—Author's English Summary

Mehta, P. K. and Khuller, G. K. Serodiagnostic potentialities of enzyme-linked immunosorbent assay (ELISA) using mannophosphoinositides of *Mycobacterium tuberculosis* H37Rv. Med. Microbiol. Immunol. **177** (1988) 285–292.

The serological response to mannophosphoinositides of *Mycobacterium tuberculosis* H37Rv and to tuberculin-purified protein derivative (PPD) was examined by enzyme-linked immunosorbent assay (ELISA) in patients suffering from tuberculosis and related diseases. In sputum-positive cases 94% of samples were found to be positive to mannoside antigens and 77% to PPD; while in sputum-negative cases, 71% of samples gave a positive reaction to mannosides and 54% to PPD. The high specificity of mannoside ELISA was demonstrated to be 97% in healthy individuals and 100% in patients suffering from other respiratory diseases; whereas PPD ELISA was 84% and 82% in healthy and infected patients respectively. Thus, ELISA is more specific and sensitive for mannosides than for PPD for the diagnosis of tuberculosis. However, antibodies to mannosides and PPD were detected in lepromatous as well as tuberculoid leprosy patients.—Authors' Abstract

Murphy, P. M., Mayers, D. L., Brock, N. F. and Wagner, K. F. Cure of bacille Calmette-Guérin vaccination abscesses with erythromycin. Rev. Infect. Dis. **11** (1989) 335–337.

Postvaccination subcutaneous abscess due to bacille Calmette-Guérin (BCG) is an uncommon complication and is especially rare in the United States, where the general population is not vaccinated with BCG. This type of abscess is usually chronic, and optimal therapy has not been defined. Two Americans, a husband and wife, underwent primary BCG vaccination abroad and de-

veloped chronic subcutaneous abscesses at the primary inoculation site. Four months after vaccination, *Mycobacterium bovis* strain BCG was cultured from material aspirated from both lesions. Direct susceptibility studies revealed a minimal inhibitory concentration of < 3.0 μg of erythromycin/mL for both isolates. Erythromycin was given orally to the husband and wife for 3 and 4 weeks, respectively, during which time complete healing occurred in both cases.—Authors' Abstract

Parenti, F. New experimental drugs for the treatment of tuberculosis. Rev. Infect. Dis. **11** Suppl. 2 (1989) S479–S483.

New antitubercular agents are needed for two main purposes: to further simplify therapy (through reductions in the number of medicaments used, the number of doses administered, and the duration of treatment required), thus facilitating supervision and improving compliance, and to combat resistant mycobacteria. Reduction in the number of medicaments has been achieved by combining two or more drugs in a single tablet while retaining a degree of bioavailability similar to that of the single components. The adverse effects observed with once-weekly high doses of rifampin have limited the development of widely spaced intermittent regimens of treatment. For this reason new rifamycins have been developed that are as active as rifampin against mycobacteria but that also offer the advantage of high and prolonged serum levels and thus have the potential for once-weekly administration. The *in vitro* and *in vivo* properties of these drugs have been studied. Three classes of drugs show promise for the treatment of drug-resistant tuberculosis: spiropiperidyl rifamycin, the fluoroquinolones, and combinations of β-lactam agents and β-lactamase inhibitors.—Author's Abstract

Patel, R. J., Piessens, W. F., David, J. R. and Wirth, D. F. A cloned DNA fragment for identification of *Mycobacterium tuberculosis.* Ref. Infect. Dis. **11** Suppl. 2 (1989) S411–S419.

The identification of *Mycobacterium tuberculosis* is a lengthy process. Attempts were made to develop a more rapid, specific, and sensitive assay for identifying tubercle bacilli in biologic specimens by differentially screening plasmid libraries of *Sau*^{3}AI-digested *M. tuberculosis* H37Rv (ATCC 25618) DNA with homologous and heterologous DNA for clones that hybridized strongly with *M. tuberculosis* DNA alone. Three clones, pMTB1, pMTB2, and pMTB3, were selected for further study. Southern analysis indicated that these clones reacted strongly with DNA from strains of *M. tuberculosis* isolated in different parts of the world, weakly with DNA from other mycobacterial species, and not at all with *Escherichia coli* or human DNA. Smaller fragments of mycobacterial DNA contained in plasmid pMTb3 were subcloned into pBR322 (pMTb4) or pUC12 (pMTb5). These recombinant plasmids hybridized with DNA from *M. tuberculosis, M. bovis,* and *M. bovis* BCG (bacille Calmette-Guérin) Montreal and may provide the reagents needed for the development of new methods for rapid diagnosis of *M. tuberculosis* infections.—Authors' Abstract

Ramkisson, A., Coovadia, Y. M. and Coovadia, H. M. A competition ELISA for the detection of mycobacterial antigen in tuberculosis exudates. Tubercle **89** (1988) 209–212.

An enzyme-linked immunosorbent assay (ELISA) was designed to detect the inhibition of BCG-antiBCG reactions by soluble antigens of *Mycobacterium tuberculosis.* Eighty-four samples were tested of which 59 were of cerebrospinal fluid (CSF) (25 control, 10 bacterial, 14 viral and 10 tuberculous meningitis); and 25 were of pleural or ascitic fluid (15 tuberculous exudates and 10 nontuberculous samples). A statistically significant difference ($p < 0.01$) was found between the tuberculous and control groups. The sensitivity and specificity of this test was almost 100%—no false-negative and only one false-positive results occurred among the samples of CSF tested.—Authors' Summary

Rastogi, N., Lévy-Frèbault, V., Blom-Potar, M.-C. and David, H. L. Ability of smooth and rough variants of *Mycobacterium avium* and *M. intracellulare* to multiply and survive intracellularly: role of C-mycosides. Zbl. Bakt. Hyg. A **270** (1989) 345–360.

A spontaneous rough (Rg) mutant of *Mycobacterium avium* ATCC 15769 was mutagenized using N-methyl-N-nitro-nitrosoguanidine (MNNG). Out of 54 clones initially chosen on the basis of their morphological appearance on the 7H11 agar, seven Rg clones were selected on the basis of their response to current biochemical tests, and were later characterized for their cell wall amphiphilic contents (analysis of loosely bound surface lipids for mycosides, peptidolipids, phospholipids, and mycolic acids by thin-layer chromatography, and fatty acids by gas chromatography), and ability to grow intracellularly inside J-774 macrophages. A parallel study was also performed on a previously reported Rg mutant of *M. intracellulare* serovar 20 which lacked the ability to synthesize mycosides C (MYC^-). The results obtained were compared to parental smooth (Sm) colony-types of the respective *M. avium-intracellulare* strains. Our results showed that neither the ninhydrin-reacting lipids (probably peptidolipids) nor the glycopeptidolipids (mycosides C) were primary factors responsible for the intracellular survival and multiplication of these bacteria. Ultrastructural studies showed that although the polysaccharide-rich outer wall layer (POL) in case of MYC^- Rg strain was not uniformly distributed and contained blebs, these bacteria formed the characteristic electron-transparent zone (ETZ) upon phagocytosis by macrophages. Furthermore, the multiplication of MYC^- Rg strain inside macrophages did not result in intracellular selection of MYC^+ bacteria, nor in Rg to Sm transition.—Authors' Abstract

Ratcliffe, G. E. Amoebic disease precipitated by corticosteroids prescribed for tuberculous pleural effusions. Tubercle **69** (1988) 219–221.

The author reports on a Nepalese man and woman who after treatment with prednisolone to hasten resolution of tuberculous pleural effusion developed, respectively, an amoebic liver abscess and amoebic dysentery. Neither patient had a history of amoebic disease and stool examination of both, before steroid treatment, was negative for *Entamoeba histolytica*. The author cautions that clinicians treating tuberculosis patients should be aware that steroids may unmask asymptomatic amoebic disease, particularly in endemic areas.—C. A. Brown (Trop. Dis. Bull.)

Roggero, E., Botasso, O. and Morini, J. C. [Development of experimental infection with *Mycobacterium lepraemurium* in two strains of mice.] Rev. Argent. Microbiol. **20** (1988) 25–35. (in Spanish)

A model of experimental leprosy in two strains of mice, namely CBA/J and CBi, has been developed based on: 1) the histological examination of a granuloma in the hind foot pad 200 days after inoculation of 0.30 μl of *Mycobacterium lepraemurium* (MLM) (6×10^8 MLM/ml); 2) the assessment of T lymphocytes in the granuloma identified by the α-naphthyl acetate method for esterase, and c) dissemination of the infection. The histological findings in the low resistance CBA/J strain included positive acid-fast bacilli, vacuolated cells, without lymphocytic infiltration, scarce number of T lymphocytes and a generalized and important dissemination similar to the one observed in human lepromatous leprosy. The histological findings in the hind foot pad granuloma of 30%–40% of the medium- to high-resistant CBi strain consisted of vacuolated cells and lymphocytic infiltration, a large number of T cells and a scarce dissemination, similar to the human borderline leprosy. Both strains present a different susceptibility to a unique challenge with the mycobacterium which could be useful to disentangle the immunogenetic components involved by means of appropriate selection and crosses. Furthermore, it could be of interest to perform immunoprotection assays in CBi mice, which might have some bearing on the development of a vaccine in human leprosy.—Authors' English Summary

Saito, H., Tomioka, H., Sato, K., Tasaka, H., Tsukamura, M., Kuze, F. and Asano, K. Identification and partial characterization of *Mycobacterium avium* and *Mycobacterium intracellulare* by using DNA probes. J. Clin. Microbiol. **27** (1989) 994–997.

We attempted to identify the *Mycobacterium avium* complex (MAC) isolated in Japan by using DNA probes specific for *M. avium* or *M. intracellulare* (Gen-Probe Rap-

id Diagnostic System for MAC; Gen-Probe, Inc., San Diego, Calif.). The source and drug susceptibility distributions were examined. This assay system proved to be rapid, sensitive, specific, and reliable for identification of MAC and of the species as either *M. avium* or *M. intracellulare*. The DNA probe test showed that of the generally accepted MAC serovars, serovars 1 to 6, 8 to 11, and 21 belonged to *M. avium* and 7 and 12 to 20 belonged to *M. intracellulare*. Moreover, with the DNA probe test we found that the distribution patterns of *M. avium* and *M. intracellulare* isolates in Japan differed depending on the district in which MAC was isolated. The ratio of *M. avium* was much higher in eastern Japan. In Tokai and Shimane districts, the ratio of *M. avium* and *M. intracellulare* isolates significant in human disease was related to that of isolates from soil and house dust (natural sources). In *M. avium*, human disease-associated isolates were more resistant to rifampin, streptomycin, and kanamycin than were isolates from natural sources. However, this source dependence was not evident for *M. intracellulare*. In human disease-associated MAC, *M. avium* isolates were more resistant to most agents, except for quinolones, than were *M. intracellulare* isolates.—Authors' Abstract

Tseng, H. M., Yu, H. S., Lee, A. M., Chien, C. G. and Chang, F. K. Disseminated cutaneous infection caused by *Mycobacterium kansasii*: report of a case. J. Formosan Med. Assoc. **87** (1988) 836–839.

A 35-year-old woman seen in Taiwan had a history of retroperitoneal leiomyosarcoma with liver metastasis. Four months after cancer surgery she presented with multiple erythematous skin nodules, persistent high fever (of 4-months duration) and bilateral pleural effusion. From culture characteristics and histopathological examination of biopsy specimens the causative organism was identified as *Mycobacterium kansasii*. Treatment with antituberculosis drugs (details are given) was successful.—C. A. Brown (Trop. Dis. Bull.)

Vogelsang, G. B., Hess, A. D. and Santos, G. W. Thalidomide for treatment of graft-versus-host disease. Bone Marrow Transplant. **3** (1988) 393–398.

We have used thalidomide in a rat major MHC mismatch model of graft-versus-host disease (GVHD). When given prophylactically, most animals do not develop GVHD and those developing mild GVHD respond to continued therapy. Treatment of established acute GVHD, likewise, was successful. In both prophylactic and therapeutic administration, animals did not develop GVHD after drug cessation. Animals were shown to be stable chimeras by acceptance of donor strain skin grafts and mixed lymphocyte cultures (no response to donor or recipient strain while responding to third party strain). Treatment of chronic GVHD in this model has shown thalidomide to be better tolerated and more successful than cyclosporine (CSA) or prednisone plus azathioprine. The mechanism of action of thalidomide has been explored using a fluorescent thalidomide derivative. These studies have shown striking similarities between thalidomide and CSA. Both drugs appear to allow the development of antigen-specific suppressor cells while inhibiting the development of precursor cytotoxic cells. Because of these encouraging results, we have begun a phase I/II trial of thalidomide in refractory GVHD. The preliminary results are encouraging.—Authors' Summary

Wong, C. S., Palmer, G. S. and Cynamon, M. H. *In-vitro* susceptibility of *Mycobacterium tuberculosis, Mycobacterium bovis* and *Mycobacterium kansasii* to amoxycillin and ticarcillin in combination with clavulanic acid. J. Antimicrob. Chemother. **22** (1988) 863–866.

The *in-vitro* susceptibility of *Mycobacterium tuberculosis, M. bovis,* and *M. kansasii* to amoxycillin alone and in combination with 2 mg/l of clavulanic acid was evaluated by broth dilution. The MIC_{90} of amoxycillin plus clavulanic acid was 4 mg/l compared with > 32 mg/l for amoxycillin alone when tested against *M. tuberculosis* (n = 27). *M. bovis* (n = 8) was the most susceptible species with an MIC_{90} of amoxycillin 8 mg/l, compared with 0.5 mg/l for the combination. *M. kansasii* (n = 6), with an MIC_{90} of 16 mg/l for amoxycillin plus clavulanic acid, was more resistant than either *M. tuberculosis* or *M. bovis*. Ticarcillin plus clavulanic acid with an MIC_{90} of 32 mg/l was less active against *M. tuberculosis*

(n = 28) than amoxycillin plus clavulanic acid. The addition of clavulanic acid to amoxycillin greatly improves its *in-vitro* activity against *M. tuberculosis* and *M. bovis*.—Authors' Abstract

Yangco, B. G., Lackman-Smith, C., Espinoza, C. G., Solomon, D. A. and Deresinski, S. C. The hamster model of chronic *Mycobacterium avium* complex infection. J. Infect. Dis. **159** (1989) 556–561.

Male golden Syrian hamsters were evaluated as a model for the pathogenesis of human infection with *Mycobacterium avium* complex. Intratracheal inoculation produced a chronic, nonfatal, pulmonary and disseminated infection (overall rate, 86%). The frequency of infection in hamsters that received 5×10^8 versus 1×10^8 colony-forming units (cfu) was not significantly different (87% and 92%, respectively), but 1×10^7 cfu produced infection in only 78% of inoculated animals ($p = 0.034$). The percentage of animals developing pulmonary infection with *M. avium* complex did not differ between inoculum groups (77%–80%). Disseminated infection occurred significantly less frequently in the 1×10^7 group (46%) compared with the 5×10^8 (79%) and 1×10^8 (68%) groups ($p = 0.001$ and 0.056, respectively). After 7 weeks, partial clearance of *M. avium* complex from the lungs coincided with an increased number of animals with splenic involvement. The hamster may be a useful model for human infection with *M. avium* complex.—Authors' Abstract

Youle, M., Clarbour, J., Farthing, C., Connolly, M., Hawkins, D., Staughton, R. and Gazzard, B. Treatment of resistant aphthous ulceration with thalidomide in patients positive for HIV antibody. Br. Med. J. **298** (1989) 432.

Mouth ulceration is common in patients infected with HIV and is mainly due to malignancy, herpes simplex virus, or fungal infection. Some patients positive for HIV antibody have recurrent mouth ulcers that are not caused by obvious infection but are histologically similar to the giant aphthous ulcers seen in Behcet's syndrome.

We studied seven patients positive for HIV antibody who had had recurrent mouth ulcers for more than 2 months. A biopsy specimen taken from one patient showed histological changes suggestive of aphthous ulceration. Swabs of ulcers were taken from all seven patients and cultured for herpes simplex virus and fungi with negative results. The patients were treated with acyclovir 200 mg five times daily for at least 10 days and also used steroid-based creams or lozenges without benefit. They all received courses of antibiotics, and five of them used tropical tetracycline, without healing of the ulcers. Thalidomide 100 mg was given at night for 2 weeks, and thereafter a maintenance regimen of 100 mg every fifth day was followed. The mouth ulcers healed rapidly in all seven patients.—(*From the* Article)

Zeis, B. M., Shulz, E. J., Anderson, R. and Kleeberg, H. H. Mononuclear leucocyte function in patients with lichen planus and cutaneous lupus erythematosus during chemotherapy with clofazimine. S. Afr. Med. J. **75** (1989) 161–162.

Mitogen-induced transformation and the production of reactive oxidants by mononuclear leukocytes (MNLs) from patients with chronic dermatological disorders were investigated *in vitro* before and during the administration of the antimycobacterial/immunosuppressive agent clofazimine (200 mg 3 times weekly). Seven patients, 4 with lichen planus and 3 with cutaneous lupus erythematosus, were included in the study. Clofazimine administration did not influence the mitogen-induced proliferative responses of patients' MNLs. However, chemotherapy with this drug stimulated the production of reactive oxidants by MNLs. Since reactive oxidants are immunosuppressive, it is possible that these effects may be involved in the pharmacotherapeutic activity of clofazimine.—Authors' Summary