CURRENT LITERATURE

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

General and Historical

Hale, W. A. Leprosy presenting as peripheral neuropathy. Am. Fam. Physician **37** (1988) 153–156.

Cases of leprosy are increasing in the United States because of immigration from countries where the disease is endemic. Infection may not become apparent for several years after immigration. Symptoms related to involvement of peripheral nervous tissue are often the presenting complaint. Prompt treatment can prevent the potentially severe sequelae of this disease. Current regimens utilize rifampin with dapsone to decrease the development of drug resistance.—Author's Abstract

Schubert, G. and Rogowitz, L. [Historical reflections on leprosy with regard to some military medical aspects.] Z. Gesamte Hyg. **33** (1987) 462–464. (in German)

Medicohistorical knowledge of leprosy can help us to better understand the present situation concerning this disease. Leprosy played an important role in many regions in the past. This disease is the cause for concern in some developing countries also today and, therefore, it is continuously and closely observed by the World Health Organization. Although leprosy probably spread as a consequence of campaigns, especially in the Mediterranean area, it had no substantial influence on the outcome and results of armed conflicts in the past. The social importance of leprosy in history is shown.—Authors' English Summary

Chemotherapy

Aschhoff, M., Irudaya Raj, P. P., Lilly, L. and Srinivasan, H. Secondary and primary dapsone resistant leprosy: an analysis of 199 patients from St. Thomas Hospital and Leprosy Project, Chettupattu, South India. Indian J. Lepr. **60** (1988) 34–46.

The occurrence of secondary and primary dapsone resistance in 199 patients in our control area and the influence of certain variables, such as age, initial bacteriological and morphological indices, duration of regular dapsone monotherapy, on the emergence of dapsone resistance was investigated. Ninety-one out of 122 patients and 29 out of 77 showed secondary (SDR) and primary (PDR) resistance to dapsone, respectively. Very low BI (BI = 2.5) group also showed both SDR (60%) and PDR (40%). Low or high MI group exhibited the same degree of resistance. Multiplication of *Mycobacterium leprae* was obtained even when the MI of the inocula was zero. Even in the group who had 1 to 5 years' duration of regular dapsone treatment, 85% of the patients showed SDR. The significance of such results are discussed in relation to chemotherapy. The overall minimum prevalence of SDR was found to be 5.6% and 21% in the case of PDR in our control area.—Authors' Abstract

Deenabandhu, A. and Kothandapani, V. G. Paucibacillary primary dapsone resistance—a case report. Indian J. Lepr. **60** (1988) 100–105.

A case of primary paucibacillary dapsone

resistance was presented. Its clinical suspicion and diagnosis are stressed. Emergence of dapsone resistance and its implications are shortly reviewed. A short note on its prevention is discussed. Literature is briefly reviewed.—Authors' Abstract

Douglas, J. T., Steven, L. M., Fajardo, T., Cellona, R. V., Madarang, M. G., Abalos, R. M. and Steenbergen, G. J. The effects of chemotherapy on antibody levels in lepromatous patients. Lepr. Rev. **59** (1988) 127–135.

We compare whole cell ELISA antigens (*Mycobacterium leprae*) and two specific antigens: PGL-I, phenolic glycolipid I of *M. leprae* and M-BGG, a synthetic antigen representing the terminal sugar of PGL-I, for their effectiveness in detecting antibody during chemotherapy. By the end of the first year of treatment, antibody levels to M-BGG had declined by 42% of the initial ELISA values, by the end of the second year by 61% and at the end of 3 years by 68%. Declines of similar magnitude were seen with the other antigens. We examined these sera by RID for changes in levels of IgG, IgM and IgA antibodies. The levels of IgG remained abnormally high throughout the 3 years of antimicrobial therapy. The serum levels of IgM and IgA antibodies remained at the upper limits of normal range. The decline seen with antibody to *M. leprae* antigens was not reflected by a similar decline of serum immunoglobulin levels. Thus, application of ELISA monitoring during the course of treatment may be valuable in measuring the effectiveness of chemotherapy.—Authors' Summary

Ellard, G. A., Kiran, K. U. and Stanley, J. N. A. Long-term prothionamide compliance: study carried out in India using a combined formulation containing prothionamide, dapsone and isoniazid. Lepr. Rev. **59** (1988) 163–175.

A comprehensive study of the self-administration of prothionamide is described in which over 2000 urine samples were collected from some 60 south Indian patients over a 2-year period. Prothionamide (350 mg) was prescribed for daily self-administration as the commercially available combined formulation "Isoprodian" that also contains dapsone and isoniazid. Drug ingestion was monitored by testing the samples qualitatively and quantitatively for the presence of the isoniazid metabolites acetylisoniazid and isonicotinic acid, and for dapsone together with its diazotizable metabolites.

About a third of the patients suffered from moderate or severe gastrointestinal side-effects attributed to prothionamide but no hepatic toxicity was encountered, whether or not treatment was supplemented with monthly supervised doses of rifampin. The results obtained using the different urine-test methods correlated well and it was concluded that overall just over half the prescribed doses had been ingested. Although enormous variations in individual patient compliance were demonstrated, there was a continuous spectrum of drug taking and patients could not be simply grouped into good or poor compliers.

Older patients took their prescribed treatment less regularly. The compliance of patients who suffered from severe gastrointestinal side-effects was markedly impaired and improved when daily thioamide treatment was replaced by dapsone. The proportion of positive urine tests among samples collected at the patients' monthly clinic visits was similar to those collected by means of surprise home visits.

It was concluded that if prothionamide is used as an alternative to clofazimine in the multidrug treatment of lepromatous leprosy its compliance should be monitored using an isoniazid-marked formulation.—Authors' Summary

Garg, S. K., Kumar, B., Shukla, V. K., Bakaya, V., Lal, R. and Kaur, S. Pharmacokinetics of aspirin and chloramphenicol in normal and leprotic patients before and after dapsone therapy. Int. J. Clin. Pharmacol. Ther. Toxicol. **26** (1988) 204–205.

The pharmacokinetics of aspirin and chloramphenicol was studied in 16 normal and 16 patients suffering from leprosy. A significant increase ($p < 0.05$) in the elimination half-life of chloramphenicol was observed before and after dapsone treatment

in leprotic patients as compared with the normal volunteers, while no significant difference was observed in any of the pharmacokinetic parameters with aspirin.—Authors' Abstract

George, J., Bhatia, V. N., and Balakrishnan, S. Microbiological assay versus spectrophotometry for determination of rifampicin in urine. Indian J. Lepr. **60** (1988) 47–52.

A comparative study on the microbiological and spectrophotometric methods for estimation of rifampin in urine was carried out in 15 individuals. The urinary levels of rifampin were determined on the 2nd, 8th and 15th days at 3-hour, 6-hour and 24-hour samples by the above methods after administration of 600 mg rifampin. The results suggest that the microbiological assay is more sensitive than the spectrophotometric method. The difference was highly significant in all the cases by the paired *t* test. It was also noticed that urinary excretion of rifampin was comparatively more on the 15th day.—Authors' Abstract

Grugni, A., Nadkarni, N. J. and Kini, M. S. Evaluation of two regimens of multidrug therapy in multibacillary leprosy (a preliminary report). Indian J. Dermatol. Venereol. Leprol. **54** (1988) 86–89.

A comparative evaluation of two regimens of multidrug therapy (IAL modification and the original WHO regimen) in multibacillary leprosy is presented. Patients were given MDT until the point of clinical and bacteriological inactivity. It was found that the IAL regimen confers a statistically significant advantage in patients with a higher initial BI (more than 2), as far as bacteriological inactivity is concerned. In patients with a lower initial BI, both regimens were equally effective. Side effects and lepra reactions were within reasonable limits with both the regimens. We feel that the IAL modification of the WHO regimen should be used in multibacillary leprosy, especially in cases with a high initial BI. The slight increase in the cost is compensated by the higher proportion of cases rendered negative.—Authors' Abstract

Jamet, P. and Robin, Y. [Quadruple twice monthly supervised chemotherapy for 72 paucibacillary patients in French Guyana.] Acta Leprol. **6** (1988) 35–44. (in French)

In French Guyana we have treated 72 paucibacillary leprosy patients with a combination of rifampin + clofazimine + ethionamide + dapsone given twice monthly under supervision for 6 months. Results have been satisfying and the side effects rare. The sequential character of treatment shows a substantial advantage on the operational side but may appear to be favorable for bacterial resistance.—Authors' English Summary

Lachant, N. A. and Tanaka, K. R. Case report: dapsone-associated Heinz body hemolytic anemia in a Cambodian woman with hemoglobin E trait. Am. J. Med. Sci. **294** (1987) 364–368.

A Cambodian woman with hemoglobin E trait (AE) and leprosy developed a Heinz body hemolytic anemia while taking a dose of dapsone (50 mg/day) not usually associated with clinical hemolysis. Her red blood cells (RBCs) had increased incubated Heinz body formation, decreased reduced glutathione (GSH), and decreased GSH stability. The pentose phosphate shunt activity of the dapsone-exposed AE RBCs was increased compared to normal RBCs. Although the AE RBCs from an individual not taking dapsone had increased incubated Heinz body formation, the GSH content and GSH stability were normal. The pentose phosphate shunt activity of the nondapsone-exposed AE RBCs was decreased compared to normal RBCs. Thus, AE RBCs appear to have an increased sensitivity to oxidant stress both *in vitro* and *in vivo,* since dapsone does not cause hemolytic anemia at this dose in hematologically normal individuals. Given the influx of Southeast Asians into the United States, oxidant medications should be used with caution, especially if an infection is present, in individuals of ethnic backgrounds who have an increased prevalence of hemoglobin E.—Authors' Abstract

Ma, B. [Pathologic changes in multibacillary leprosy after two years of treatment with MDT.] China Lepr. J. **4** (1988) 75–76. (in Chinese)

Fifty multibacillary leprosy patients have been taking rifampin, clofazimine and dapsone for 2 years and the biopsy of their skin before and after the treatment showed that all of the pathologic indices have declined and the efficiency of the treatment is also satisfactory even in dapsone-resistant cases.—Author's English Abstract

Patki, A. H., Jadhav, V. H. and Mehta, J. M. "Flu" syndrome on once monthly rifampicin. Indian J. Lepr. **60** (1988) 84–86.

Two cases of "flu" syndrome on once-monthly rifampin are reported. The symptoms were reproduced in one patient with the next supervised dose. In the second patient they did not recur probably because she was receiving systemic steroids for left ulnar neuritis.—Authors' Abstract

Pattyn, S. R., Groenen, G., Bourland, J., de Muynck, A., Grillone, S., Grossetete, G., Husser, J. A. and Janssens, L. The incubation time of relapses after treatment of multibacillary leprosy with rifampicin containing regimens. Eur. J. Epidemiol. **4** (1988) 231–234.

In order to determine the duration of follow-up needed to evaluate the efficacy of short-course bactericidal regimens for multibacillary leprosy, information is needed on the incubation time of relapses after stopping treatment. Several groups of patients, who had been on rifampin (RMP)-containing regimens, were followed up for periods ranging from 4 to 10 years. Two groups of relapses were observed: early relapses occurring within 3.5 years after stopping treatment, with a median incubation time of 1 year and 10 months (upper limit of 95% confidence interval: 2 years); and late relapses occurring more than 3.5 years after stopping treatment, with a median incubation of 5 years. Early relapses are probably due to insufficient treatment, and late relapses to persisting bacilli or to reinfection. It is concluded that the efficacy of short-course RMP-containing therapeutic regimens can be evaluated by observing the occurrence of early relapses, 50% of which occur before 2 years after the end of therapy.—Authors' Abstract

Singhal, S. K. Suicide with dapsone. Indian J. Lepr. **60** (1988) 87–89.

A case of suicide with dapsone is reported in a female medico. A chemical analysis report confirmed it to be death due to dapsone. Management in case of dapsone poisoning is also discussed.—Author's Abstract

Clinical Sciences

Bartel, P. R., Baker, M. K., Combrink, P., Robinson, E. and Van Der Meyden, C. H. Auditory brainstem evoked potentials in leprosy. S. Afr. Med. J. **73** (1988) 593–596.

An electrophysiological study of conduction in the auditory nerve and brainstem auditory pathways using the brainstem auditory evoked potential was undertaken in a group of 47 leprosy patients. There were no statistically significant differences between mean conduction times (interpeak latencies) in the leprosy and the control groups. Abnormal interpeak latencies were encountered in 3 leprosy patients, 1 of whom had a positive serological test for syphilis. In the remaining 2 patients, caudal pathway dysfunction (I-III interpeak latency abnormality) was indicated but specific auditory nerve involvement (an abnormally prolonged I-II interpeak latency) was not demonstrated. An explanation for these findings, other than the patients' disease, was not apparent.—Authors' Summary

Butov, Y. S., Lezvinskaya, E. M. and Ponomareva, E. I. A case of lepromatous leprosy. Vestn. Dermatol. Venereol. **3** (1988) 62–64. (in Russian)

The authors describe a female patient with lepromatous leprosy. The diagnosis has been confirmed bacteriologically and histologically. The patient has been examined immunologically. The authors emphasize that the disease has been diagnosed late and discuss the causes of this untimely diagnosis.—Authors' English Summary

Chattopadhyay, S. P. and Gupta, C. M. Primary hyperpigmented cutaneous lesions in tuberculoid leprosy. Indian J. Lepr. **60** (1988) 63–65.

Two cases of tuberculoid leprosy with primary hyperpigmented anesthetic lesions are reported and the subject is reviewed.—Authors' Abstract

Chaudhary, S. D., Gupta, V., Saini, A. S., Singh, V. and Lal, H. Adenosine deaminase activity in leprosy (a preliminary study). Indian J. Lepr. **60** (1988) 17–20.

Adenosine deaminase (ADA) activity was studied in 25 patients having different types of leprosy and 25 healthy volunteers as controls. There was a definite rise of ADA activity in BL (72.9 ± 6.85), LL (56.7 ± 3.35) and BT (39.1 ± 8.28) which was statistically significant when compared to ADA activity in healthy controls (9.7 ± 0.53).—Authors' Abstract

Chen, L., *et al.* [Clinical analysis of 70 cases of leprosy in children.] Chin. J. Clin. Dermatol. **17** (1988) 64–66. (in Chinese)

The article reports 70 cases of leprosy in children below 14 years old observed for 20 years. The ratio of boys and girls was 1.26:1, the mean age 12.4 years, and the mean duration of illness 18 months. The multibacillary type was found in 20% and paucibacillary type in 80%. The history of contact was documented in 58.6%. The primary lesions appeared as skin lesions in 55.8% and as numbness in 44.2% of cases and 40 cases were associated with deformities. Twenty-one patients were under follow-up observation. The prognosis was rather good.—Authors' English Abstract

Cree, I. A., Smith, W. C. S., Rees, R. J. W. and Swanson Beck, J. The influence of antimycobacterial chemotherapy on delayed hypersensitivity skin-test reactions in leprosy patients. Lepr. Rev. **59** (1988) 145–151.

Skin tests using purified protein derivative (PPD) and Rees' skin test antigen (RSTA), a soluble extract of *Mycobacterium leprae,* were performed in 53 treated leprosy patients, 52 newly diagnosed untreated leprosy patients, and 78 household contacts of untreated leprosy patients in northern Bangladesh. In addition, a small group of 20 leprosy hospital workers and a further group of 50 indigenous subjects with no known exposure to leprosy were studied.

Untreated paucibacillary and multibacillary patients showed significantly fewer positive reactions than comparable groups of treated patients to both PPD and RSTA. It appears from these results that treatment of leprosy patients is associated with enhanced ability to produce a delayed-type hypersensitivity response to mycobacterial antigens. The mechanisms underlying this phenomenon may include both general and specific suppression of antimycobacterial delayed-type hypersensitivity. The household contacts and indigenous subjects showed similar skin test responsiveness, but virtually all of the hospital workers responded to both PPD and RSTA. The implications of these results for studies of immunity in leprosy patients are discussed.—Authors' Summary

D'Souza, D. and Thomas, I. M. Chromosome aberrations and sister chromatid exchanges (SCEs) in peripheral blood lymphocyte cultures of untreated patients. Lepr. Rev. **59** (1988) 121–125.

The frequencies of various chromosome aberrations and sister chromatid exchanges (SCEs) were studied in blood lymphocyte cultures of untreated leprosy patients. The frequency of chromosome aberrations was significantly higher in lepromatous ($p < 0.001$) and tuberculoid ($p < 0.02$) groups in comparison with that of controls. The frequency of SCEs was found to be within normal range in the tuberculoid group whereas in lepromatous group, a significant ($p < 0.001$) increase was observed. The findings indicate a probable correlation be-

tween the form of leprosy and chromosome damage.—Authors' Summary

Giam, Y. C., Ong, B. H. and Tan, T. Erythema nodosum leprosum in Singapore. Ann. Acad. Med. Singapore **16** (1987) 658–662.

Erythema nodosum leprosum (ENL) or type 2 reaction is an immune complex syndrome seen in multibacillary leprosy. Twenty patients with histological confirmation of ENL in leprosy were studied from 1982 to 1986. These patients had a range of clinical signs, from fever, tender dusky nodules, bullae, ulcers to lymphadenopathy, arthralgia and neuritis. The four major histological patterns are: a) classical pattern showing heavy infiltrations of neutrophils in three cases; b) subepidermal bulla pattern with marked edema of the upper dermis, and collections of neutrophils in five cases; c) vasculitis pattern, affecting superficial and mid-dermal vessels, leading to epidermal necrosis, bulla formation and ulceration. Dilated vessels, congestion, lumenal fibrin clots and fibrinoid necrosis of vessels were seen. d) nonspecific picture in nine cases with mild edema, infiltration with neutrophils, and two cases with minimal reaction had chronic ENL with clinical vasculitis. All five cases with vasculitis showed C1q, C3 and fibrinogen in the vessels.

Comparing ENL reactions reported in Asia, our pattern is similar to that of Malaysians with the majority showing subepidermal edema. Vasculitis is more common in India. Edema with collagen necrosis was seen in acute ENL with iritis in New Guinea. Lucio's phenomenon was not seen in any of the countries in Asia.—Authors' Summary

Giam, Y. C. and Seow, C. S. Histoid leprosy in Singapore. Ann. Acad. Med. Singapore **16** (1987) 655–657.

Histoid leprosy is a rare variant of lepromatous leprosy. This is the first documented case of histoid leprosy in Singapore. The patient was diagnosed as borderline leprosy in 1973, remained untreated and progressed to lepromatous leprosy. The characteristic histoid lesions were firm pruriginous nodules on the dorsum of his feet. The histology showed a pseudocapsulated tumor with fibroblasts and histiocytes filled with lepra bacilli. Electron microscopy showed fibroblasts, macrophages with bacilli and plasmacytoid cells with active endoplasmic reticulum. He was found to be dapsone-resistant and the lesions cleared with clofazimine. Immunological defects were not detected.—Authors' Summary

Koranne, R. V. and Srivastava, G. Primary drug resistance to both rifampicin and dapsone in a paucibacillary leprosy patient. Indian J. Lepr. **60** (1988) 90–92.

A 31-year-old male patient was diagnosed and treated for a pure or better primary neuritic case of leprosy with dapsone (100 mg daily for 2 years) and rifampin (600 mg daily for 6 months). From the very outset, the patient did not show any improvement; on top of it, he subsequently developed a cutaneous patch which on histopathological examination revealed classical features of BT leprosy. Acid-fast bacilli were absent both in skin slit smear and histologic section. A primary resistance to both dapsone and rifampin, even in a paucibacillary patient, is speculated.—Authors' Abstract

Kuo, T.-T. and Chan, H.-L. Severe reactional state in lepromatous leprosy simulating Sweet's syndrome. Int. J. Dermatol. **26** (1987) 518–520.

A male patient with underlying lepromatous leprosy mimicked Sweet's syndrome clinically. He was believed to be in an atypical reactional state recognized as a variant form of erythema nodosum leprosum. In addition to the antileprosy treatment, steroid hormone was required to control the systemic symptoms.—Authors' Abstract

Latapi-Contreras, F., Caire-Loyer, P., Flores-Alonso, O. and Flores-Romero, R. M. [Fine needle aspiration of lymph nodes; study of 50 leprosy patients.] Acta Leprol. **6** (1988) 7–16. (in French)

Fine-needle aspiration of lymph nodes was performed in 50 leprosy patients and

was compared with usual techniques of bacillary smears taken from nasal mucosa, ear lobule and cutaneous lesions. We found that the former was more sensitive (30%) regarding bacteriologic and morphologic (34%) indices; moreover this proceeding was more sensitive (50%) in patients with type 2 leprosy reaction. After a 6-month multitherapy schedule in three patients, the morphologic index decreased 2 points (SFG) and bacteriologic index 1+ (mean value). It is concluded that fine-needle aspiration of lymph nodes is a useful method, because of its simplicity and low traumatic effects and its sensitivity to follow-up treatment and reactional phases.—Authors' English Summary

Mishra, B., Ramu, G., Chauhan, V. S., Kushwaha, S. S. and Dwivedi, M. P. Leprosy deformities. I. An epidemiological study in a rural area of Rajasthan. Indian J. Lepr. **60** (1988) 53–62.

Leprosy deformities have been the cause of dehabilitation, destitution and social ostracism. The present study was planned and conducted in a rural area situated in the eastern districts of Rajasthan. Out of 426 cases of leprosy, 90 cases were found suffering with deformities. The influences of various host factors and disease factors in the causation of deformities are discussed.—Authors' Abstract

Nigam, P., Mukhija, R. D., Kapoor, K. K., Kumar, A., Sarkari, N. B. S., Gupta, A. K. and Mishra, S. D. Male gonads in leprosy—a clinico-pathological study. Indian J. Lepr. **60** (1988) 77–83.

Sixty male leprosy patients (mean age 27.2 ± 5.04 years), selected at random, were studied for gonadal involvement with the mean duration of illness 4.17 ± 3.27 years. Only lepromatous and borderline leprosy cases developed testicular and epididymal changes. Testicular pain and/or swelling (lepromatous 62.5%, borderline 30%) was the main presenting feature. Altered sexual function was observed in 34 (56.6%) cases, and 11 patients revealed altered sexual hair pattern. Gynecomastia was seen in nine cases. Reduced testicular size along with its soft feeling was present in 25% of cases while no testicular sensation was felt in 8 (13.3%) cases, and impaired testicular sensation in 9 (15%) of them. Spermogram revealed azoospermia in 19 (35%) and oligospermia in 16 (26.6%) cases. Histopathology revealed evidences of leprous pathology irrespective of testicular size, semen picture and clinical manifestations. There was marked variation in histopathological findings in testes, hence it was difficult to categorize them into vascular, interstitial and obliterative phases.—Authors' Abstract

Ramu, G. and Desikan, K. V. A follow up study of borderline tuberculoid leprosy under sulphone monotherapy. Indian J. Lepr. **60** (1988) 26–33.

A retrospective study is presented herewith of 94 cases classified as BT and treated with sulfone monotherapy. A system of scoring based on the number and extent of lesions, and nerve involvement was followed. It was observed that cases with a clinical score of 2 or having more than 15 lesions or patients with extensive lesions covering 3 or more of 7 sectors of the body had a bad prognosis in respect of time taken for subsidence, occurrence of deformities and, most importantly, occurrence of relapses. Hence it is suggested that such cases should be considered as multibacillary and treated as such, despite bacteriological findings which may be either negative or a bacteriological positivity of less than 2 at any one site.—Authors' Abstract

Rao, K. N. and Saha, K. Undernutrition and lepromatous leprosy; serum vitamin A and E levels in leprosy spectrum. Indian J. Lepr. **60** (1988) 66–70.

Serum vitamins A and E were estimated by spectrophotocolorimetric methods in 67 leprosy patients comprising 9 BT, 10 BB, 15 BL, 27 LL, including 12 histoid cases. These findings were evaluated in comparison to 55 normal subjects serving as controls. Significant reductions in the mean serum levels of vitamins A and E were observed in the leprosy groups as compared to normal controls. These findings are of considerable importance and need to be taken note of in light of delineating these alterations to the cause or effect of the disease.

As far as we know, this is the first report describing serum levels of vitamins A and E in the leprosy spectrum.—Authors' Abstract

Ravindranathan, O. and Sarojini, P. A. Comparative study of lepromin reaction in indeterminate leprosy and controls. Indian J. Dermatol. Venereol. Leprol. **54** (1988) 24–26.

The lepromin test (LT) was done on 100 cases of indeterminate leprosy (IL) and in 100 age- and sex-matched controls. The LT was negative in 98% of IL, but positive in 80% of the controls. Lepromin-positive cases showed a tuberculoid picture histopathologically, although the clinical picture was that of IL. There was no correlation between the Fernandez reaction and the Mitsuda reaction.—Authors' Abstract

Sane, S. B. and Mehta, J. M. Malignant transformation in trophic ulcers in leprosy: a study of 12 cases. Indian J. Lepr. **60** (1988) 93–99.

Twelve cases of carcinomas arising in trophic ulcers of leprosy are presented. Out of these, 10 were on the plantar surface, more commonly on the proximal part of foot, one on lower leg and dorsum of foot, and one in an ulcer over the lateral malleolus. Almost all presented with infected growths and regional lymphadenopathy. Three cases presented with advanced disease with fungating inguinal nodes and were fatal. Nine cases underwent below-knee amputation under antibiotic cover as a definitive treatment and the lymph nodes were kept under observation. Histologically, all were low-grade squamous-cell carcinomas. In most cases lymph nodes regressed after removal of infected primary and in one case lymph nodes were positive for malignancy.—Authors' Abstract

Singh, J., Handa, F., Singh, A., Gupta, S. and Kalla, N. R. Assay of testosterone, FSH and LH in serum and spermogram in leprosy patients. Indian J. Dermatol. Venereol. Leprol. **54** (1988) 75–77.

Testicular functions in the form of testosterone, FSH and LH levels in serum by radioimmunoassays, complete semen examination and a few testicular biopsies were studied in 30 men with leprosy (LL-7, BL-6, BB-1, BT-12 and TT-4). Serum testosterone levels were lowered in all the groups. Serum FSH and LH levels were elevated in lepromatous and borderline lepromatous leprosy. Semen analysis showed oligospermia in the LL and BL groups. Lepra bacilli in smears of semen were present in two LL cases. Leprous changes were seen in the testicular biopsies.—Authors' Abstract

Tan, T. Leprosy in Singapore. Ann. Acad. Med. Singapore **16** (1987) 617–621.

The incidence of leprosy in Singapore is declining over the past 20 years. More than one third of new cases are now over 50 years of age, while no child under 5 years has been affected since 1970. Male to female ratio is 2:1. Indians are more significantly affected compared to the other races and a higher proportion has tuberculoid leprosy. Tuberculoid leprosy accounts for 50.4% of cases seen during the past decade. Case detection from household contacts is still worthwhile as it accounts for 3% to 13.5% of the yearly incidence of the disease. The first four cases of dapsone resistance were confirmed in 1969. Since then the yearly incidence of clinically diagnosed dapsone-resistant cases averaged 2.9 per thousand. Hence, various regimens of multiple drug therapy have been instituted.—Author's Summary

Tiwari, V. D., Tutakne, M. A., Singh, G. and Dutta, R. K. Multidrug therapy in hospitalised leprosy cases. Indian J. Lepr. **60** (1988) 71–76.

Fifty-eight cases including 44 paucibacillary (PB) and 14 multibacillary (MB) leprosy diagnosed at Command Hospital SC Pune, India, were hospitalized for the entire period of multidrug therapy (MDT); 76% of the cases belonged to high-endemic states of India. Reactions occurred in 13 cases during treatment, type 1 in 10 and type 2 in three. Seven MB cases experienced reaction; 69% of the reaction patients developed reaction within 2 months of starting MDT and all of them were multibacillary. Usually it took 3–6 months for the majority (61.5%) of the reactions to subside com-

pletely. In 65.5% of the PB patients, activity subsided within 12 months, however, 70.5% of the PB cases took more than 6 months to exhibit subsidence of activity. In 13 MB cases, activity subsided by 18 months although bacteriological negativity was obtained from 4 to 12 months.—Authors' Abstract

Immuno-Pathology

Alvarez-Mendoza, A., Escobar-Gutiérrez, A., Amezcua-Chavarria, M.-E., Lara-Padilla, E. and Salgado-Navarro, J. Demonstration of acid-fast bacilli in skin biopsies from indeterminate leprosy cases. Trans. R. Soc. Trop. Med. Hyg. **82** (1988) 492–494.

Because the correct diagnosis of indeterminate leprosy (IL) requires the finding of acid-fast bacilli in skin lesions from clinically and histopathologically suggestive cases, it is necessary to develop a reliable method for this purpose. This paper presents a simple procedure, available to every general laboratory, which consists in obtaining two suspensions: SI, by mincing and grinding the tissue in phosphate-buffered saline; and SII, after treating SI with NaOH solution and digesting with trypsin. In 22 IL skin biopsies, bacilli were directly observed in only three with the Ziehl-Neelsen (ZN) stain; and with the peroxidase-anti-peroxidase method it was impossible to differentiate between nonspecific precipitate and true positive reactions. In contrast, 18 positive results from the same 22 samples were obtained when both SI and SII were evaluated with ZN stain. The logarithmic bacterial index was also increased in at least seven cases.—Authors' Abstract

Anderson, D. C., Barry, M. E. and Buchanan, T. M. Exact definition of species-specific and cross-reactive epitopes of the 65-kilodalton protein of *Mycobacterium leprae* using synthetic peptides. J. Immunol. **141** (1988) 607–613.

With the use of solid-phase synthesis of peptides corresponding to major and minor peaks in a Hopp-Woods hydrophilicity plot, the epitopes for 10 of 14 known different monoclonal antibodies to the *Mycobacterium leprae* 65-kDa protein, a prominent T and B cell Ag of this bacillus, have been located in the primary structure. Five epitopes have been precisely mapped by using the synthetic peptides in inhibition ELISA experiments, and five others have been located on peptides of 22 amino acids or less in length. The epitope of an important species-specific antibody, IIIE9, which may be useful for the seriodiagnosis of leprosy, appears to be distinguished from the epitope of the antibody IVD2, widely crossreactive among mycobacteria, not by its sequence, but only by its critical residues. All epitopes studied appear continuous insofar as can be determined by this approach.—Authors' Abstract

Biggins, T., Narayanan, R. B., Ramu, G. and Desikan, K. V. T and B cells in borderline (BB) leprosy. Indian J. Lepr. **60** (1988) 21–25.

The response to standard Dharmendra lepromin and the circulating T, B cell numbers in the peripheral blood were quantitated in 15 patients with borderline (BB) leprosy. On the basis of lepromin response, the patients fall into three groups: a) negative, b) ± reaction, c) rarely positive. No significant difference in the numbers of E-rosette and EAC rosette-forming cells was observed in the BB patients in comparison to controls.—Authors' Abstract

Converse, P. J., Ottenhoff, T. H. M., Gebre, N., Ehrenberg, J. P. and Kiessling, R. Cellular, humoral, and gamma interferon responses to *Mycobacterium leprae* and BCG antigens in healthy individuals exposed to leprosy. Scand. J. Immunol. **27** (1988) 515–525.

Protective immunity against mycobacteria is dependent on antigen-specific T cells. The antibodies induced upon immunization with mycobacteria have no apparent role in host protection. Serological techniques have detected some antigens that are also recognized by human T cells but may fail to recognize others. Potentially, there may be differences in the epitopes seen by the T and B cell anti-mycobacterial antigen repertoires. We have screened the different components of sonicated BCG or *Mycobacterium leprae* that were separated according to their molecular weight (MW) by SDS-PAGE and then electroblotted on nitrocellulose paper. The blots were cut into squares and tested directly in a T-cell proliferation assay. Our results indicate that peripheral T cells of healthy leprosy patient contacts respond preferentially to the lower MW (<70,000) and not the higher MW fractions of *M. leprae* and BCG, in contrast to the humoral response of these same individuals. The most important fractions in inducing a lymphoproliferative response were in the regions of 11–16 kDa of BCG and *M. leprae* and to the 22–26 kDa region of *M. leprae*. These fractions appeared to represent molecular weight regions that were in some instances clearly distinct from previously defined antigens. It was further shown that lymphoproliferation in response to mycobacterial fractions correlated with the production of gamma interferon, a lymphokine required for macrophage activation and elimination of mycobacteria. These studies allow the direct assessment of antigens involved in protective T-cell-mediated immunity, and should be helpful in selecting relevant antigens for skin testing and immunization.—Authors' Abstract

Frey, F. L. P., Gottlieb, A. B. and Levis, W. R. A patient with lepromatous leprosy and anticytoskeletal antibodies. J. Am. Acad. Dermatol. **18** (1988) 1179–1184.

Sera from 34 patients with lepromatous leprosy were screened for the presence of autoantibodies by indirect immunofluorescence using two epithelial cell lines, PTK2 and HEp2, as substrates. Indirect immunofluorescence staining of both substrates with the serum of a patient with lepromatous leprosy revealed a cytoplasmic intermediate filament staining pattern. After exposure of PTK2 cells to colchicine, the filaments collapsed into thick perinuclear coils, confirming the presence of intermediate filament reactivity. Immunofluorescence of rat fibroblasts with the same serum also revealed an intermediate filamentous staining pattern. Human keratinocytes exposed to the patient's serum revealed a diffuse cytoplasmic staining pattern. Our study suggests the presence of autoantibodies to cytoskeletal intermediate filaments or to molecules associated with vimentin and possibly keratin subunit proteins in the serum of a patient with lepromatous leprosy.—Authors' Abstract

Gibbels, E., Henke-Lübke, U. and Klingmüller, G. Unmyelinated nerve fibres in leprosy. A qualitative and quantitative study of sural nerve biopsies in 2 cases of lepromatous leprosy. Lepr. Rev. **59** (1988) 153–162.

Since morphometric analysis of unmyelinated nerve fibers is lacking in leprosy literature, they were investigated in sural nerves of two lepromatous cases. Despite normal or even increased total numbers of unmyelinated axons, tentative differentiation in not-yet-myelinated axons and genuine unmyelinated fibers or their regenerates according to associated Schwann cells and fiber calibers revealed a mild to severe loss of genuine unmyelinated fibers. A predominant involvement, surpassing loss of genuine myelinated fibers, could not be stated in either case. Quantification of degenerating unmyelinated fibers, denervated Schwann cell complexes, and Schwann cell nuclei—both of the unmyelinated type—is also presented and discussed.—Authors' Summary

Gross, A., Weiss, E., Tapia, F. J., Aranzazu, N., Gallinoto, M. E. and Convit, J. Leukocyte subsets in the granulomatous response produced after inoculation with *Mycobacterium leprae*-BCG in lepromatous patients. Am. J. Trop. Med. Hyg. **38** (1988) 608–612.

Leukocyte subsets present in the granulomatous response produced after the in-

oculation of a mixture of *Mycobacterium leprae* and BCG in lepromatous leprosy patients were characterized *in situ* using monoclonal antibodies and an immunoperoxidase technique. The granuloma produced after *M. leprae*-BCG inoculation showed a distribution pattern similar to tuberculoid granulomas. T lymphocytes bearing the CD8 phenotype (T cytotoxic/suppressor) were sequestered to the periphery of the epithelioid tubercles and T helper-inducer CD4+ lymphocytes were distributed throughout the infiltrate. Langerhans' cells CD1+ were increased in the epidermis, and in dermis they were localized mainly in the mantle surrounding the granuloma. Most of the dermal infiltrate produced after the inoculation of *M. leprae*-BCG expresses the HLA-DR antigen. Similarly, most keratinocytes were also positive to this MHC antigen. The granulomatous response to BCG was similar to the inoculation of a mixture of *M. leprae*-BCG, however acid-fast bacilli were still present. The inoculation of *M. leprae* produced a macrophage granuloma with no clearing of the bacilli which resembles the lepromatous leprosy granuloma.—Authors' Abstract

Harris, D. P., Douglas Jones, A. G., Wade, S., Krahenbuhl, J. L., Gillis, T. P. and Watson, J. D. Genetic control of murine T cell proliferative responses to *Mycobacterium leprae*. V. Evidence for cross-reactivity between host antigens and *Mycobacterium leprae*. J. Immunol. **141** (1988) 1695–1700.

T-cell proliferative responses to *Mycobacterium leprae* were measured by immunization of mice at the base of the tail with Ag and challenging lymphocytes from draining lymph nodes in culture with *M. leprae*. C57BL/10J and B10.BR mice were identified as low-responder mice and the congenic strains B10.M, B10.Q, and B10.AKM as high responders; whereas F_1 (high × low) hybrid mice were found to be low responders. The cellular basis of low responsiveness did not appear to result from a defect in Ag-presenting cells or the activation of suppressor T cells by *M. leprae*. The influence of the environment in which T cells developed on responsiveness to *M. leprae* was analyzed in chimeric mice prepared by irradiating F_1 (C57BL/10J × B10.M) mice and reconstituting with bone marrow from C57BL/10J, B10.M, or F_1 donors. Six weeks later, chimeric mice were immunized with *M. leprae*, lymph node cells were subsequently prepared, and H-2 phenotyped and challenged in culture with *M. leprae* Ag. T-cell proliferative responses were found to be low in all cases, similar to those observed using lymph node cells from F_1 hybrid mice. These results suggested that high-responder B10.M lymphocytes developing in the irradiated F_1 mice became tolerized to antigenic determinants found on *M. leprae*. This implied crossreactive epitopes existed between some mouse strains and *M. leprae*. Low responsiveness to *M. leprae* in low-responder and F_1 hybrid mice may result from tolerance to H-2-encoded Ag that show crossreactivity with *M. leprae*.—Authors' Abstract

Holzer, T. J., Kizlaitis, L., Vachula, M., Weaver, C. W. and Andersen, B. R. Human phagocytic cell responses to *Mycobacterium leprae* and *Mycobacterium bovis* bacillus Calmette-Guérin; an *in vitro* comparison of leprosy vaccine components. J. Immunol. **141** (1988) 1701–1708.

Components of current vaccines for Hansen's disease include *Mycobacterium bovis* bacillus Calmette-Guérin (BCG) and killed *M. leprae*. BCG infections in humans are rare and most often occur in immune-compromised individuals. *M. leprae*, on the other hand, although not causing clinical disease in most exposed individuals, is capable of infecting and replicating within mononuclear phagocytes. Lymphocytes from patients with the lepromatous form of Hansen's disease exhibit defective lymphokine production when challenged *in vitro* with *M. leprae*. This may result in inefficient mononuclear phagocyte activation for oxidative killing. To study the ability of normal phagocytes to ingest and respond oxidatively to BCG and *M. leprae*, we measured phagocytic cell O_2^- release and fluorescent oxidative product formation and visually confirmed the ingestion of the organisms. BCG stimulated a vigorous O_2^-

generation in neutrophils and monocytes and flow cytometric oxidative product generation by neutrophils occurred in the majority of cells. *M. leprae* stimulated a weak but significant O_2^- release requiring a high concentration of organisms and long exposure. By flow cytometric analysis, most neutrophils were able to respond to both organisms with the generation of fluorescent oxidative products. Neutrophil oxidative responses to *M. leprae* were substantially less than responses seen from neutrophils exposed to BCG. By microscopic examination of neutrophils phagocytizing FITC-labeled bacteria, it was shown that both *M. leprae* and BCG were slowly ingested but that more BCG appeared to be associated with the cell membrane of more of the cells. When phagocytic cells were incubated with BCG and *M. leprae* for 30 min and subsequently examined by electron microscopy, few organisms were seen in either neutrophils or monocytes. This suggests that BCG are easily recognized and slowly ingested by normal phagocytic cells, the majority of which respond with a strong oxidative burst. *M. leprae* appeared to only weakly stimulate phagocyte oxidative responses and were also slowly phagocytized.—Authors' Abstract

Kaplan, G., Sheftel, G., Job, C. K., Mathur, N. K., Nath, I. and Cohn, Z. A. Efficacy of a cell-mediated reaction to purified protein derivative of tuberculin in the disposal of *Mycobacterium leprae* from human skin. Proc. Natl. Acad. Sci. U.S.A. **85** (1988) 5210–5214.

The purpose of this study was to evaluate the effects of a delayed-type, cell-mediated immune response to *Mycobacterium tuberculosis* antigen on the *M. leprae* load in the skin of leprosy patients. Twelve patients with the lepromatous form of leprosy have been injected intradermally with 5 units of the purified protein derivative of tuberculin (PPD). Ten individuals responded with areas of induration ranging from 12 to 21 mm in diameter, and two were unresponsive (<10 mm). Twenty-one days thereafter, the injected and control sites were biopsied, and the histology, number of acid-fast bacilli (AFB), nature and phenotype of the emigrant cells, and ultrastructural characteristics of the lesions were evaluated. Eight of the 10 responding patients showed reductions in the number of AFB by factors ranging from 5 to 10,000. Two responders and both nonresponders exhibited no discernible decline in the number of organisms. The reduction in bacillary load was correlated with an intense mononuclear cell infiltrate, the maintenance of a high CD4+ T-cell/CD8+ T-cell ratio, the formation of granulomas, and the extensive destruction of previously parasitized macrophages.—Authors' Abstract

Locniskar, M., Zumla, A., Mudd, D. W., Isenberg, D. A., Williams, W. and McAdam, K. P. W. J. Human monoclonal antibodies to phenolic glycolipid-I derived from patients with leprosy, and production of specific anti-idiotypes. Immunology **64** (1988) 245–251.

Human monoclonal antibodies (MABs) were produced by hybridomas derived from fusion of the GM4672 lymphoblastoid cell line and peripheral blood mononuclear cells from leprosy patients. Hybridoma supernatants were screened for immunoglobulin (Ig) secretion, binding to *Mycobacterium leprae,* phenolic glycolipid-I (PGL-I), the unique *M. leprae* glycolipid and single-stranded (ss) DNA by ELISA. On the basis of direct-binding ELISAs, two IgMk MABs (PR4 and TH3) were selected for characterization. PR4 and TH3 bound to *M. leprae,* PGL-I and ssDNA; PR4 also bound to *M. avium* and *M. kansasii,* and TH3 to *M. kansasii.* Inhibition assays demonstrated that these antibodies did not bind to the terminal disaccharide of PGL-I. In addition, both PR4 and TH3 bound to several autoantigens: ssDNA, double-stranded (ds) DNA and poly(ADP-ribose) but not RNA. PR4 and TH3 were used for preparation of rabbit anti-idiotype antisera. Inhibition studies demonstrated that the affinity-purified rabbit anti-idiotype antisera were specific for their respective idiotype and that both PGL-I and ssDNA inhibited binding of idiotype to its anti-idiotype. PR4, but not TH3, was found to be similar but not identical to the 16/6 idiotype originally identified on a human monoclonal anti-DNA antibody derived from a patient with systemic lupus erythematosus (SLE).—Authors' Summary

Matsubara, H. [Immunological analysis of leprosy.] Igaku Kenkyu **57** (1987) 1–9. (in Japanese)

Leprosy is an infectious disease caused by *Mycobacterium leprae* usually affecting only a few individuals among an exposed population. The extent of the bacillary invasion and the clinical symptoms of the disease depends on the ability of the exposed individuals to mount an efficient cell-mediated immune response. On the other hand, all patients with leprosy have more or less peripheral nerve damages. Some complications such as nerve damage are proposed to be due to immune reactions. For example, some of the microscopic findings of nerve damage in leprous patients showed the demyelination of peripheral nerve. Glycolipid is one of the constituents of peripheral nerve, and there is accumulating evidence that glycolipids may be involved in the process of demyelination. From this view, in the present work, I studied T-cell subsets defined by the surface marker using monoclonal antibodies against specific human T-cell subsets, antineutral glycolipid antibody against human peripheral nerve, immune complex, immunoglobulin and complement to clarify the protective immune mechanism in leprous patients.

The results showed that the percentage of OKT8-positive cells was significantly decreased in patients with lepromatous leprosy ($p < 0.005$), and the ratio of OKT8/OKT4-positive cells was also reduced significantly ($p < 0.05$), while they were normal in tuberculoid leprosy patients. In both lepromatous and tuberculoid leprosy, the percentages of OKT3-positive cells and OKT4-positive cells were normal. Antibody to neutral glycolipid was found in both lepromatous and tuberculoid leprosy patients, and an increased level of antineutral glycolipid antibody titer was found in lepromatous leprosy patients. Increased levels of γ-globulin, especially IgG and immune complex, and decreased levels of C3 and C4 were found in lepromatous leprosy patients, suggesting complement activation via the classical pathway. In conclusion, these results suggest that patients with lepromatous leprosy show decreased suppressor T cells and the tendency to produce the antibody against peripheral nerve. These may explain the clinical expression of lepromatous leprosy.—Author's Abstract

Mukherjee, A. and Misra, R. S. Comparative histology of skin and nerve granulomas in leprosy patients. Lepr. Rev. **59** (1988) 177–180.

Biopsies were taken from infiltrated lesions and thickened nerves in 23 patients with leprosy. The lesions were histologically graded and the histological features semiquantitated and compared at the two sites. No significant difference in the overall histological picture in the skin and the nerve was seen. Two features seen more in nerve granulomas were caseation and a higher granuloma fraction, neither of which was thought to have any significant bearing on the comparative immunohistological grading at the two sites.—Authors' Summary

Narayanan, R. B., Girdhar, B. K., Mishra, B., Lavania, R. K. and Sengupta, U. Effect of supernatants of dermal leprosy granulomas on lymphocyte morphology and function. Acta Leprol. **6** (1988) 18–27.

A comparison has been made of the characteristics of dermal granulomas of tuberculoid and lepromatous leprosy by culturing them *in vitro*. The granulomas were derived from lesions of untreated patients and their effect was assessed on the morphology and function of lymphocytes derived from peripheral blood of normal individuals. The concentration of proteins released in the supernatants was similar in both types of granulomas. However, the supernatants from the lepromatous granulomas markedly diminished the viability of lymphocytes when compared with supernatants derived from the tuberculoid granulomas. The supernatants from both the tuberculoid and lepromatous granulomas contained soluble factors which depressed the ^{14}C-leucine and ^{3}H-thymidine incorporation by lymphocytes. The depression in ^{3}H-thymidine uptake was more pronounced with the supernatants from the lepromatous granulomas while the diminution of ^{14}C-leucine incorporation was more marked with supernatants from the tuberculoid granulomas. The supernatants did not show any migratory inhibitory activity *in vitro*. When the cells

from the granulomas were dispersed and cultured *in vitro,* only a very low concentration of proteins was detectable.—Authors' Abstract

Narayanan, R. B., Natarajan, M., Katoch, K. and Bagga, A. K. CD1 positive epidermal Langerhans cells in indeterminate leprosy. Acta Leprol. **6** (1988) 29–34.

Langerhans' cells (LC) in the skin lesions of 10 untreated indeterminate leprosy patients were defined by indirect immunofluorescence using monoclonal antibodies. No difference was observed in the numbers and distribution of epidermal LC in the indeterminate lesions and controls. However, the infiltrates of these lesions contained CD1 + cells. Most cells in the infiltrates were positive for HLA DR antigens.—Authors' Abstract

Roberts, P. P., Dockrell, H. M. and McAdam, K. P. W. J. Evidence that the Mitsuda reaction to *Mycobacterium leprae* can be mediated by lymphocytes responsive to *Mycobacterium tuberculosis.* Clin. Exp. Immunol. **72** (1988) 390–393.

A positive Mitsuda skin test for delayed-type hypersensitivity to *Mycobacterium leprae* is associated with a high level of protection against lepromatous leprosy, while the value of tuberculin sensitivity in leprosy is less pronounced. Cutaneous lymphocytes, isolated from the Mitsuda reaction of a PPD-positive individual not previously exposed to *M. leprae*, were cloned with Dharmendra lepromin and analyzed for antigen specificity. Thirteen lepromin-responsive cell lines were derived, with greater than 95% certainty that the number of true clones was at least five and the number of functionally monoclonal lines at least seven. All lepromin-responsive clones proliferated in response to PPD as well, implying that PPD-responsive cells can fulfill the helper T-cell function required for the *in vivo* Mitsuda reaction.—Authors' Summary

Sarno, E. N., Alvarenga, F. B. F., Vieira, L. M. M. and Souza, P. R. C. de. [Characterization of mononuclear phagocytes in leprosy skin lesions: a monoclonal study.] Rev. Inst. Med. Trop. São Paulo **30** (1988) 45–50. (in Portuguese)

The skin lesions from 16 leprosy patients were studied by immunofluorescence technique using monoclonal antibodies against monocytes (OKM1 and Anti-Mo) and Ia-like antigen. Acid phosphatase activity was evaluated using naphthol AS-BI phosphate as substrate. The macrophages seem to be a heterogeneous population in concern with the antigens here studied as well as the enzymatic activity. Ia-like antigen was expressed in a great number of cells throughout the clinical spectrum.—Authors' English Summary

Sarno, E. N., Espinosa, M., Sampaio, E. P., Vieira, L. M. M., Figueiredo, A. A., Miranda, C. F., Esquenazi, D., Salgado, J. L. F. and Nogueira, N. Immunological responsiveness to *M. leprae* and BCG antigens in 98 leprosy patients and their household contacts. Braz. J. Med. Biol. Res. **21** (1988) 461–470.

The cellular immune response to *Mycobacterium leprae* and BCG antigens was evaluated in 98 leprosy patients and 143 household contacts lacking clinical manifestation of the disease. The proliferative responses and release of interferon-gamma by peripheral blood mononuclear cells were assessed, and both patients and contacts were classified as low or high responders to *M. leprae.* The high-responder contacts constituted 54.8% of the population analyzed, a three times higher proportion when compared to the controls, indicating the possible existence of active infection among them. The correlation coefficient between the immunological response to *M. leprae* and BCG was found to be higher within the contact group than in the patients, suggesting that crossreactivity defense mechanisms against mycobacteria exist even before the onset of clinically detectable disease.—Authors' Abstract

Sibley, L. D. and Krahenbuhl, J. L. Induction of unresponsiveness to gamma interferon in macrophages infected with *Mycobacterium leprae.* Infect. Immun. **56** (1988) 1912–1919.

We have previously demonstrated that *Mycobacterium leprae*-burdened granuloma macrophages isolated from infected nude mice are refractory to activation by

gamma interferon (IFN-γ). To explore further both the afferent and efferent functional capacity of *M. leprae*-infected macrophages, we examined the IFN-γ-mediated activation of resident mouse peritoneal macrophages infected *in vitro* with live or dead *M. leprae*. When IFN-γ was administered within 24 hr of *M. leprae* infection, macrophages were fully activated. However, defective activation was evident at 3 to 5 days postinfection in macrophages that were heavily burdened with viable *M. leprae*. This defect was evident by four parameters of activation in which IFN-γ failed to stimulate the enhancement of microbicidal activity, cytotoxicity for tumor target cells, O_2^- production, and surface Ia antigen expression. The development of defective activation closely followed an increase in macrophage production of prostaglandin F_2. Defective activation of *M. leprae*-burdened macrophages was reversible by indomethacin, and a similar block in IFN-γ activation was observed in three of these four parameters in normal macrophages treated with exogenous prostaglandin F_2. Thus, infection of mouse macrophages with *M. leprae* appears to restrict IFN-γ-mediated activation at least in part by induction of inhibitory levels of prostaglandin F_2.—Authors' Abstract

Tran Trao, V., Huong, P. L. T., Thuan, A. T., Long, H. T., Trach, D. D. and Wright, E. P. Responses to *Mycobacterium leprae* by lymphocytes from new and old leprosy: role of exogenous lymphokines. Ann. Inst. Pasteur Immunol. **139** (1988) 121–133.

Lepromatous leprosy patients generally have reduced response to *Mycobacterium leprae* antigens in an *in vitro* lymphocyte transformation test, which could be due to insufficient generation of reactions or to active suppression of any reaction generated. We could detect three types of lack of reactivity: one which could be restored by the addition of supernatants from healthy, PHA-stimulated lymphocyte cultures; one which could not thus be restored; and one in which the culture supernatant contained factors able to suppress mitogen responses of healthy cells. We compared responses of cells from untreated patients, patients treated for 12–20 months with multiple drug therapy, and patients with up to 20 years of dapsone treatment; all types of the disease were represented.

Untreated patients of all types had low responses which were not always reconstituted by lymphokine-rich supernatants, but they did not produce the nonspecific soluble suppressive factors. In most cases, including BL/LL types, after the initial months of treatment, antigen response improved and was further increased by the addition of supernatants containing lymphokines. Most of the long-term-treated, stable patients had a lymphokine-reconstitutable antigen response, and in most cases also produced nonspecific suppressive factor(s). The question as to why leprosy patients do not respond to *M. leprae* antigen is a complex one; our results suggest that it is related to the activity of the infection in each group of patients.—Authors' Summary

Young, D., Lathigra, R., Hendrix, R., Sweetser, D. and Young, R. A. Stress proteins are immune targets in leprosy and tuberculosis. Proc. Natl. Acad. Sci. U.S.A. **85** (1988) 4267–4270.

To understand the immune response to infection by tuberculosis and leprosy bacilli and to develop improved vaccines, the nature of antigens that are involved in humoral and cell-mediated immunity was investigated. We have determined that five immunodominant protein antigens under study are homologues of stress proteins. This finding and observations with other pathogens suggest that infectious agents may respond to the host environment by producing stress proteins and that these proteins can be important immune targets. We postulate that abundant and highly conserved stress proteins may have "immunoprophylactic" potential for a broad spectrum of human pathogens.—Authors' Abstract

Young, D. B. Immunoblotting and the immune response to leprosy. Biochem. Soc. Trans. **16** (1988) 143–144.

Immunoblotting has provided a powerful and effective approach to dissection of the immune response to mycobacterial antigens

in a situation in which the availability of isolated antigenic components is severely limited. The basic approach of blotting onto a solid-phase support has been used in combination with SDS/polyacrylamide-gel electrophoresis, thin-layer chromatography, recombinant DNA technology and T-cell cloning in order to carry out a comprehensive analysis of glycolipid and protein antigens involved in the immune response to mycobacterial infection.—Author's Summary

Zhu, W., *et al.* [Study of the pathologic changes of posterior tibial nerve in arrested leprosy patients: to compare the combined chemotherapy with DDS treatment.] Chin. J. Clin. Dermatol. **17** (1988) 114–119. (in Chinese)

This article reports the pathologic changes of the posterior tibial nerve in 26 arrested leprosy patients (LL = 4, BL = 3, BB = 1, BT = 18). Eighteen patients had received treatment with dapsone (DDS). The duration of treatment was from 10 to 26 years. Eight patients treated with DDS for 17–37 years had received combined chemotherapy for 7, 12, and 15 months (DDS 50–100 mg daily, rifampin 1200 mg monthly, clofazimine 300 mg monthly and 50 mg daily). The posterior tibial nerve of 5–10 cm in length was taken and cut continuously in 6–34 small pieces from the proximal to the distal end. The results showed that the pathological changes of the posterior tibial nerve were often asymmetric and patchy in distribution in leprosy patients. The specific pathologic changes associated with *Mycobacterium leprae* in the posterior tibial nerve were found in eight multibacillary (MB) patients and in 11 BT patients treated with DDS. There were fewer lymphocytes and epithelioid cells in the nerves of seven BT patients treated with combined chemotherapy than in the nerves of eight BT patients treated with DDS ($p < 0.01$). The numbers of foam cells or lepra cells in the posterior tibial nerves had no marked changes ($p > 0.05$) between two BL patients treated with DDS and one BL patient treated with combined chemotherapy for 12 months.—Authors' English Abstract

Microbiology

Bhatia, V. N., Cherian, E. and Harikrishnan, S. Auramine staining in detecting small number of bacilli in skin smears. Indian J. Lepr. **60** (1988) 13–16.

Auramine staining has been compared with Ziehl-Neelsen's staining of *Mycobacterium leprae* in skin-smear slide. The auramine method was found to be more sensitive than Ziehl-Neelsen's method and may be useful in detecting small number of *M. leprae* in skin smears. The interobserver variance was minimal with auramine staining.—Authors' Abstract

Daffé, M. and Lanéelle, M. A. Distribution of phthiocerol diester, phenolic mycosides and related compounds in mycobacteria. J. Gen. Microbiol. **134** (1988) 2049–2055.

Among 28 mycobacterial species studied, only *Mycobacterium tuberculosis, M. bovis, M. africanum, M. marinum, M. kansasii, M. gastri* and *M. ulcerans* produced waxes yielding long-chain β-diol components (called phthiocerol and companions) and polymethyl-branched fatty acids on saponification. The same mycobacterial species also produced diesters of phenol phthiocerol and companions. Fatty acids esterifying these fatty alcohols in *M. marinum* and *M. ulcerans* were found to belong to the phthioceranic series (dextrorotatory fatty acids), in contrast to those of the other species (laevorotatory fatty acids called mycocerosic acids), both groups having the same chain length and methyl-branched positions. *M. kansasii* and *M. gastri* contained the same waxes with identical structures, as did *M. tuberculosis, M. bovis* and *M. africanum.* Neither the type strain of *M. tuberculosis,* nor that of *M. bovis* or *M. marinum* accumulated the strain-specific phenolic glycolipids.—Authors' Abstract

de Wit, M. Y. L. and Klatser, P. R. Purification and characterization of a 36 kDa antigen of *Mycobacterium leprae.* J. Gen. Microbiol. **134** (1988) 1541–1548.

A 36 kDa antigen of *Mycobacterium leprae* was purified by phenol biphasic partition followed by preparative SDS-PAGE. The purified antigen appeared as a single band in SDS-PAGE and eluted as a single peak in ion-exchange chromatography. The antigen comprised epitopes which were crossreactive with *M. tuberculosis,* as well as a species-specific epitope (recognized by the monoclonal antibody F47-9). Different treatments of the 36 kDa antigen suggested it to be largely protein in nature; the amino acid composition of 81% of the antigen was determined. A majority of sera from leprosy patients contained antibodies recognizing the 36 kDa antigen.—Authors' Abstract

Dhople, A. M., Green, K. J. and Osborne, L. J. Limited *in vitro* multiplication of *Mycobacterium leprae.* Ann. Inst. Pasteur Microbiol. **139** (1988) 213–223.

The inability to cultivate *Mycobacterium leprae in vitro* has been a major bottleneck in leprosy research. There have been numerous reports on successful *in vitro* cultivation of this organism, but these reports could not be confirmed by others in the field. Hence, *in vitro* multiplication of *M. leprae* was evaluated in various culture media. Only two media supported limited multiplication of *M. leprae.* One medium was used previously by one of the authors (AMD) for *in vitro* growth of *M. lepraemurium* and the other was a conditioned medium used for growth of mouse dorsal root ganglion. Growth was evaluated by three biochemical parameters: bacterial ATP, DNA, and ^{3}H-thymidine uptake. All three measurements revealed a 4–6-fold increase in cell biomass after 16 weeks of incubation at 34°C. The harvested bacilli demonstrated a few of the important properties of *M. leprae,* including growth in mouse foot pads. However, subcultures of these *in vitro*-grown cells in the respective media could not be achieved. By the end of 12 weeks, the bacilli lost all intracellular ATP and the ability to incorporate ^{3}H-thymidine; they also failed to multiply in mouse foot pads.—Authors' Summary

Estrada-G., I. C. E., Lamb, F. I., Colston, M. J. and Cox, R. A. Partial nucleotide sequences of 16S ribosomal RNA isolated from armadillo-grown *Mycobacterium leprae.* J. Gen. Microbiol. **134** (1988) 1449–1453.

Ribosomal RNA (rRNA) was isolated from *Mycobacterium leprae* recovered from the infected tissue of the nine-banded armadillo, and nucleotide sequences near the 3′ end of the 16S species were determined by primer extension in the presence of dideoxynucleotides. Previously published data for bacterial 16S rRNAs show a pattern of conserved and non-conserved sequences that fit a common secondary structure. Our data for *M. leprae* fit this general pattern.—Authors' Abstract

Franzblau, S. G. and Harris, E. B. Biophysical optima for metabolism of *Mycobacterium leprae.* J. Clin. Microbiol. **26** (1988) 1124–1129.

The metabolic response of freshly harvested, nude-mouse-derived *Mycobacterium leprae* to biophysical parameters was studied to facilitate an understanding of axenic culture requirements. Quantitation of intracellular ATP and the rate of [U-^{14}C]palmitic acid incorporation into phenolic glycolipid I (PGL-I) were used as metabolic indicators after axenic incubation in modified Dubos medium under various biophysical conditions. PGL-I synthesis was optimal at 33°C; whereas ATP was optimally maintained at ≤33°C. Both metabolic indices showed sharp reductions at 37°C. After 5 days of incubation, PGL-I synthesis and ATP maintenance showed pH optima of 5.1 to 5.6, with the higher value appearing optimal for ATP maintenance after extended incubation. Metabolic activity was negatively affected by strong reducing agents, and ATP maintenance was optimal when the gaseous environment was maintained at 2.5% to 10% oxygen. The results may partially explain the failure to cultivate the leprosy bacillus *in vitro.*—Authors' Abstract

Katoch, V. M., Katoch, K., Ramu, G., Sharma, V. D., Datta, A. K., Shivannavar, C. T. and Desikan, K. V. *In vitro* methods for determination of viability of mycobacteria: comparison of ATP content, morphological index and FDA-EB fluorescent staining in *Mycobacterium leprae*. Lepr. Rev. **59** (1988) 137–143.

Bacilli were purified from the 23 cases of multibacillary type leprosy. The ATP content of these bacilli was assayed by a firefly bioluminescent technique which is capable of detecting a very small number of cultivable mycobacteria as assessed by colony counts. The ATP content was compared with morphological index (MI) and FDA-EB staining of bacilli from the same specimens. It was observed that when MI was 1% or more, the ATP content/solid bacillus was fairly constant in 15 cases studied. It ranged from 2.02×10^{-15} g to 5.60×10^{-15} g/solid bacillus (mean 3.46×10^{-15} g) and was in the same range as ATP content of viable cultivable mycobacteria. In the same 15 cases, when the green-staining bacilli were considered as "supposedly viable bacilli," ATP content/green-staining bacillus varied up to ninefold (0.22×10^{-15} g to 1.98×10^{-15} g/green-staining bacillus) and this did not correlate. The percentage of green-staining bacilli (FDA-EB) and solid-staining bacilli (MI) was different in all the cases. In two cases with 0% MI in which ATP levels were also zero, 7.5% and 21.5% green-staining bacilli were present, which implies that the enzymes responsible for green-staining character may persist for some time after death. Three cases with 0% MI had also 0% green-staining bacilli and zero ATP levels; whereas in another three cases with zero MI significantly high levels of ATP were detected. It is inferred that solid-staining bacilli may be the viable bacilli but when MI is 0% (1% or less) a sampling error or clumping may be responsible for missing the solid bacilli in some cases. It is concluded that the ATP content of *Mycobacterium leprae* appears to be an easy, rapid and sensitive tool for determining the viability for monitoring the therapy. On the other hand MI and FDA-EB staining appear to have their limitations.—Authors' Summary

Venkatesan, K., Singh, H., Bharadwaj, V. P. and Ramu, G. Isolation, purification and quantification of phenolic glycolipid-1 from human leprosy skin tissues. Trans. R. Soc. Trop. Med. Hyg. **82** (1988) 321–323.

Phenolic glycolipid-I, a marker lipid of *Mycobacterium leprae*, was isolated from skin biopsies obtained from untreated lepromatous leprosy patients by silicic acid and florisil column chromatography and purified by thin-layer chromatography. Tissues with varying bacillary loads were analyzed for their phenolic glycolipid content. A good correlation was observed between the bacillary population of the tissues and the phenolic glycolipid content.—Authors' Abstract

Wheeler, P. R. and Ratledge, C. Use of carbon sources for lipid biosynthesis of *Mycobacterium leprae*: a comparison with other pathogenic mycobacteria. J. Gen. Microbiol. **134** (1988) 2111–2121.

Carbon from glycerol and palmitate, but not significantly from five other carbon sources tested, was incorporated into lipids by suspensions of nongrowing *Mycobacterium leprae* organisms. However, of the five other substrates three—citrate, glucose and pyruvate—were taken up. Nongrowing *M. microti* and *M. avium* incorporated carbon into lipids from most simple carbon sources tested unless they were obtained from growth media including palmitate or from experimentally infected animals, when incorporation of carbon into lipids from carbon sources except palmitate occurred up to 20 times more slowly. Thus, utilization of simple carbon appeared to be repressible while utilization of the one fatty acid tested, palmitate, appeared constitutive. In *M. leprae*, carbon from glycerol was incorporated into the glycerol moiety of acylglycerols but not into the fatty acid moieties or into free fatty acids. *M. microti* and *M. avium* incorporated carbon from simple carbon sources into fatty acids, even (though very slowly) when these organisms were obtained from host tissue. Isocitrate lyase, malate synthase and acetate kinase were detected in *M. leprae*. However acetyl-CoA synthetase was not detectable and phosphoacetylase was deficient; thus, *M. leprae* may be incapable of making acetyl-CoA from acetate. Phosphotransacetylase was readily detected in both

host-grown *M. avium* and *M. microti.*—Authors' Abstract

Young, D. B. Stress-induced proteins and the immune response to leprosy. Microbiol. Sci. **5** (1988) 143–146.

Characterization of antigens recognized during the immune response to mycobacterial infection has revealed an unexpected relationship to proteins involved in stress-induced responses. Among the hypotheses that can be proposed to account for the apparent immunodominance of these proteins is an attractive speculation that the process of intracellular infection may involve induction of the synthesis of stress proteins and that detailed analysis of the regulation of the stress response may provide basic information of importance in the design of future vaccines to combat mycobacterial diseases. The highly conserved nature of stress proteins suggests that they could play a complex role in the immune response, with the possible induction of tolerance or of autoimmune pathology.—Author's Conclusions

Experimental Infections

Resnick, M., Ben-Ishay, Z., Mor, N., Levy, L. and Bercovier, H. Haemophagocytosis and other haematological aspects of *Mycobacterium lepraemurium* disease of mice. J. Comp. Pathol. **99** (1988) 65–75.

CBA mice inoculated intravenously with 2×10^8 viable *Mycobacterium lepraemurium* (MLM) were observed at intervals for 5 months. In the bone marrow, hematopoietic cells were progressively displaced by MLM-laden phagocytes; depletion of erythroid cells began earlier and was more pronounced than that of myeloid cells. Transiently, mild anemia and profound leukopenia were noted. The spleen was enlarged and the site of increasing histiocytosis and extramedullary hematopoiesis which was accompanied by displacement of splenic parenchyma. The liver was enlarged and its parenchyma contained scattered islands of hematopoietic elements. Lymph node cells had been largely replaced by MLM-laden macrophages by the end of the process. Thus, MLM infection exerts important effects on hematopoiesis of susceptible mice and is accompanied by active extramedullary hematopoiesis. In addition, the hemophagocytosis observed most commonly in immunocompromised patients infected with certain viral or mycobacterial pathogens was observed late in the course of MLM disease of mice.—Authors' Summary

Epidemiology and Prevention

Abel, L. and Demenais, F. Detection of major genes for susceptibility to leprosy and its subtypes in a Caribbean island: Desirade Island. Am. J. Hum. Genet. **42** (1988) 256–266.

To determine the nature of the genetic component controlling susceptibility to leprosy and its subtypes, complex segregation analysis, by means of the POINTER strategy, was performed on 27 multigenerational pedigrees from Desirade, a Caribbean island where leprosy is highly prevalent. The results are consistent with the presence of a recessive or codominant major gene controlling susceptibility to leprosy per se and nonlepromatous leprosy, respectively. Under the major-gene model, tests of homogeneity to check for internal consistency of the sample and to compare subsamples according to an epidemiological criterion, the place of residence of the probands, were conducted; results of none of these tests were significant. However, we have noted that

information on three generations (nuclear families with a pointer to the sibship) is of major importance for detecting major gene(s). In addition, the discrepancy in the results obtained in separate analyses of the family subsamples defined by the place of residence of the probands is discussed in terms of possible genetic and/or environmental differences. Referring to experimental data and previous studies, we suggest that the gene for susceptibility to leprosy per se and that for susceptibility to nonlepromatous leprosy might be different, acting at successive stages of the immune response to infection with *Mycobacterium leprae.*—Authors' Summary

Chaturvedi, R. M. Epidemiological study of leprosy in Malwani suburb of Bombay. Lepr. Rev. **59** (1988) 113–120.

The present investigation was undertaken to study the epidemiology of leprosy in Malwani, a western suburb of Bombay, which has a population of 63,321. A total of 691 cases were detected in a 4-year follow-up period between April 1979 and April 1983. The prevalence rate in schoolchildren was 13.88% and the peak incidence occurred in the age group 10–19 years. In this study, the females predominated, the male to female ratio being 1:1.33. The disease was found to be more prevalent in the low socioeconomic group and in overcrowded families. Extremities were most commonly affected. A large number of cases occurred in contacts of infectious lepromatous patients. The exact reasons for this could not be ascertained from this rather small sample. It could be related to droplet infections or skin contact.—Author's Summary

Pearson, M. What does distance matter? Leprosy control in West Nepal. Soc. Sci. Med. **26** (1988) 25–36.

One of the major planks of leprosy control strategies is that distance from established treatment centers deters leprosy cases from seeking treatment. The integration of leprosy care with locally available primary health care services is therefore a common feature of leprosy control programs. Within these guidelines, a National Leprosy Control Programme was established in Nepal in 1975, with intensive case-finding surveys and the provision of leprosy care in government basic health posts.

A study of one district, Lamjung, in West Nepal suggests that far from being a deterrent, distance afforded welcome anonymity for leprosy cases anxious to disguise their diagnosis and thereby avoid the social ostracism which could result. Cases from ethnic groups in which the stigma of leprosy was high traveled farther for treatment. Gender differences in distance traveled suggest that women's mobility was restricted, but the local availability of care did not increase attendance for regular treatment. It is suggested that this was more the result of poor quality of care than fear of being known locally as a leprosy case.—Author's Abstract

Ponnighaus, J. M., Fine, P. E. M., Maine, N., Bliss, L., Kalambo, M. and Ponnighaus, I. The Lepra Evaluation Project (LEP), an epidemiological study of leprosy in north Malawi. II. Prevalence rates. Lepr. Rev. **59** (1988) 97–112.

Prevalence data obtained during a population survey carried out by the Lepra Evaluation Project (LEP) in Karonga District in northern Malawi (Central Africa) are presented and analyzed. Three different prevalence measures are presented: of individuals with current clinical leprosy who are likely to benefit from (further) antileprosy treatment (the "clinical" prevalence rate), of individuals with either current clinical leprosy or residual signs only (the "visible" prevalence rate), and of individuals with any physical or historical evidence of present or past leprosy (the "cumulative" prevalence rate). Effects of past treatment and leprosy control efforts come to light in the difference between the "visible" rate and the "cumulative" rate and indicate that about 61% of the leprosy patients in this area who have received antileprosy treatment in the past, from the Lepra Control Project, are now without remaining signs of clinical leprosy. Past BCG vaccination campaigns and active case finding through school surveys appear to have affected the current age and sex patterns of the disease. Prevalence rates are higher among females than males in the older age groups. The paper

demonstrates how the observed pattern and extent of leprosy are a function of the prevalence measure used.—Authors' Summary

Wagener, D. K., Schauf, V., Nelson, K. E., Scollard, D., Brown, A. and Smith, T. Segregation analysis of leprosy in families of northern Thailand. Genet. Epidemiol. **5** (1988) 95–105.

Sixty-three families with multiple instances of leprosy were identified through a major leprosy treatment center in northern Thailand. Complex segregation analyses for single major genes or polygenic inheritance were performed using the maximum-likelihood routine POINTER to determine the most likely etiologic model of genetic susceptibility. Liability differences between men and women were considered in these models. When individuals were considered to be affected because they had any form of leprosy, a generalized major gene model with nearly dominant parameters on the liability scale, but additive penetrances, was found to be the most likely. When only those individuals who had tuberculoid forms of leprosy were considered to be affected, a recessive model was found to be the most likely; however, the discrimination between various models was poor. Further analyses are necessary to delineate genetic mechanisms to explain these apparently divergent results. In particular, methods of testing two locus models should be considered.—Authors' Abstract

Walsh, G. P., Meyers, W. M., Binford, C. H., Gormus, B. J., Baskin, G. B., Wolf, R. H. and Gerone, P. J. Leprosy as a zoonosis: an update. Acta Leprol. (Genève) **6** (1988) 51–60.

Naturally acquired leprosy has been reported in nine-banded armadillos captured in the southern United States, a chimpanzee from Sierra Leone, and in two "sooty" mangabey monkeys from Nigeria. A significant prevalence of leprosy in wild armadillos establishes this animal as a reservoir of *Mycobacterium leprae,* and exposure to armadillos has been implicated as a source of leprosy in humans. Current evidence suggests that leprosy is a zoonosis in certain nonhuman primate species. Control and eradication programs for leprosy should take into consideration the possible influence of extrahuman sources of *M. leprae,* especially zoonotic leprosy.—Authors' Summary

Rehabilitation

Amritmahal, A. and Mehta, J. M. Common Vocational Training Project for the Handicapped (CVTPH). Int. J. Rehab. Res. **10** (1987) 285–292.

CVTPH is a special project imparting vocational training to leprosy patients as well as other categories of the handicapped under the same roof, in order to combat the leprosy stigma which is the major obstacle in all leprosy work and to aid rehabilitation by making the trainees economically self-sufficient. The project, which offers training in the industrial sector to leprosy patients, orthopedically handicapped individuals and able-bodied but socioeconomically disadvantaged individuals, began in a small way in 1977, but has grown considerably since then, thus demonstrating the effectiveness of the concept. There have been several problems—chief among which are the leprosy stigma and the reluctance of the trainees themselves to move out from a sheltered environment into the world outside—but these are slowly being overcome by the formation of cooperative societies controlled by the handicapped. This project hopes to serve as a model for similar vocational training programs.—Authors' Abstract

Horibe, S., Tada, K. and Nagano, J. Neuroarthropathy of the foot in leprosy. J. Bone Joint Surg. [Br.] **70-B** (1988) 481–485.

Among 449 patients with leprosy, 40 had clinical and radiographic evidence of neuroarthropathy in 50 feet. These changes were classified into four types according to the joints first involved by major lesions: ankle

(25 feet), midtarsal (15 feet), tarsometatarsal (7 feet), and subtalar (3 feet). The progression of joint destruction was different in each type, but despite the severe destructive changes seen in radiographs, the patients had relatively few complaints. The muscles innervated by the peroneal nerve were severely paralyzed in ankle and midtarsal types, and it seems that, over a long term, repeated trauma and/or abnormal stress may lead to these types of neuroarthropathy. Neuropathy was less severe in the tarsometatarsal type of joint degeneration; the pathogenesis in this type seemed to be mainly direct trauma to the forefoot.—Authors' Abstract

Kadir, A. H. A. Correction of claw fingers in leprosy by the Brand four-tailed tendon graft operation. Med. J. Malaysia **41** (1986) 264–268.

Many operations have been described for the correction of claw hands following involvement in leprosy, from Sir Harold Stiles (1922) of Edinburgh, through Bunnell, Brand and many others in India and the U.S.A. Some of these procedures are classified "static" and attempt mainly to correct hyperextension at the metacarpo-phalangeal joint, while the "dynamic" procedures employ a variety of tendon graft operations to restore the function of the paralyzed lumbrical muscles. This study is an analysis of the four-tailed tendon graft operation of Paul Brand, carried out in the National Leprosy Control Centre, Sungei Buloh, Selangor, during the period 1965–1975, by a host of surgeons, mainly by Dr. M. K. Bhojwani, MRCP, FRCSEd, the Director of the Centre at that time. The analysis carried out during November–December 1976, was made on 36 hands in 33 patients; it revealed an average improvement in the metacarpo-phalangeal joint flexion of nearly 90% and in the proximal interphalangeal joint extension in nearly 80%, and an improvement in the grafted lumbrical voluntary motor tone of nearly 70%.—Author's Summary

Other Mycobacterial Diseases and Related Entities

Belyakova, O. I., Kharakter, Z. Z., Sibirnaya, R. I. and Snitinskaya, O. S. [Experimental study on effect of antituberculosis drugs and certain pathogenetic agents on host immunological reactions.] Probl. Tuberk. **4** (1988) 65–68. (in Russian)

Complex studies on 310 guinea pigs and 357 inbred mice revealed characteristic features of immunological shifts in tuberculosis treated according to different schemes. In addition to rifampin and isoniazid the animals of some groups were treated with drugs of immunological and metabolic profiles such as sodium succinate, sodium malate, RNA-ase, sodium nucleate and levamisol. In the *in vitro* and *in vivo* experiments there were stated general features and differences in the effect of the above drugs and criteria for their use were grounded. The best results were achieved in the group of the animals treated with rifampin, isoniazid and sodium succinate.—Authors' English Abstract

Dolzhansky, V. M. [Use of biseptol for preventing rifampin resistance development in tubercle bacilli.] Probl. Tuberk. **4** (1988) 54–56. (in Russian)

It was shown *in vitro* that biseptol (bactrim, oribact) had no effect on rifampin resistant strains of *Mycobacterium tuberculosis* and did not lower the level of the initial drug resistance. On contact of high-density microbial populations with various concentrations of rifampin biseptol could prevent the development of rifampin resistance or lower it.—Author's English Abstract

Fortier, A. H., Mock, B. A., Meltzer, M. S. and Nacy, C. A. *Mycobacterium bovis* BCG-induced protection against cutaneous and systemic *Leishmania major*

infections in mice. Infect. Immun. **55** (1987) 1707–1714.

[The authors] examined the protective effects of *Mycobacterium bovis* bacillus Calmette-Guérin (BCG) administration on *Leishmania major* infections of BALB/c and P/J mice. There were two treatment protocols. In the first, the foot pads of naive animals were inoculated with mixtures of *L. major* and BCG (viable or heat killed) or the soluble mycobacterial antigen, purified protein derivative. Viable BCG, but not heat-killed BCG or purified protein derivative, inoculated with *L. major* amastigotes into the foot pads of naive BALB/c or P/J mice protected these animals from the metastatic spread of parasites to the viscera and from ensuing lethal systemic infection. This treatment also induced cures of the cutaneous lesions of P/J mice but not of BALB/c mice. In the second protocol, [the authors] induced an immune response to BCG before inoculation of *L. major*. BCG given intraperitoneally 10 days before infection of foot pads with leishmania offered protection against the metastatic spread of amastigotes in both P/J and BALB/c mice, regardless of intralesional treatment, and modulated the severity of cutaneous infection by 30% to 50%. Inoculation of a mixture of viable BCG and *L. major* amastigotes into BCG-immune mice completely protected both BALB/c and P/J strains from cutaneous disease; [the authors] recovered no parasites from the inoculated foot pads of these animals. Furthermore, each of the nonspecifically protected mice of both the BALB/c and P/J strains developed immunity to rechallenge with viable *L. major*. Injection of amastigotes at a site remote from the original lesion, the contralateral foot pad, resulted in the complete clearance of parasites with no evidence of either cutaneous or systemic disease over an extended observation period.—(AS/R.S. Bray *from* Trop. Dis. Bull.)

Gimenez, M. F., Gimenez, M. M., Resoagli, E. H. and de Millan, S. G. [Langerhans' cells in the armadillo.] Rev. Argent. Dermatol. **69** (1988) 153–155. (in Spanish)

Langerhans' cells (LC) have been identified in a variety of stratified epithelia in normal and pathologic conditions. They are known to be antigen-presenting cells for T lymphocytes. We investigated the intraepithelial density of LC in 11 wild armadillos. The study was performed using adenosine triphosphatase staining of epidermal sheets (Wolff-Winkelman). Shave biopsy specimens obtained from uninvolved nonsun-exposed skin of the upper part of the legs were stored in citrate buffer. In all the samples, the ATPase activity was found in the dendritic cells. There was no significant difference between the seven- and nine-banded armadillo. Morphological differences of these cells were noted when we compared them with the Langerhans' cells in guinea pigs and control population.—Authors' English Summary

Lockwood, D. N. J., McManus, I. C., Stanford, J. L., Thomas, A. and Abeyagunawardana, D. V. P. Three types of response to mycobacterial antigens. Eur. J. Respir. Dis. **71** (1987) 348–355.

Responses to pathogenic and environmental mycobacteria were assessed in 2680 children in India and Sri Lanka using quadruple skin testing with new tuberculins. Statistical analysis of the results, by fitting a log-linear mixture model, confirmed the presence of three different categories of response: category 2 nonresponders (about 55%) did not react to any component of the mycobacteria; category 3 responders (about 40%) were sensitive to the species-specific group *iv* antigens; and category 1 responders (about 5%) were sensitive to the group *i* antigens which are common to all mycobacteria. The proportions of the three response categories vary with age and with BCG status. BCG vaccination and increasing age act independently to decrease the proportion of category 2 nonresponders and increase the proportion of category 3 individuals. BCG vaccination and increasing age interact to increase the proportion of category 1 responders.—(AS *from* Trop. Dis. Bull.)

Mor, N., Goren, M. B. and Pabst, M. J. *Mycobacterium lepraemurium* activates macrophages but fails to trigger release of superoxide anion. J. Immunol. **140** (1988) 3956–3961.

Mycobacterium lepraemurium failed to stimulate a normal respiratory burst when presented to mouse-peritoneal or bone-marrow macrophages. By comparison, *M. bovis* (strain bacillus Calmette-Guérin) or *Saccharomyces cerevisiae,* as expected, stimulated macrophages to release a large amount of superoxide anion (O_2^-). *M. lepraemurium* did not interfere with the response to yeast when both microbes were added together to macrophages. The low release of O_2^- induced by *M. lepraemurium* was not due to failure of *M. lepraemurium* to activate or prime macrophages, because exposure of macrophages to *M. lepraemurium* caused the expected enhancement of O_2^- release when the macrophages were stimulated by PMA. Similarly, macrophages taken from mice infected with *M. lepraemurium* were activated, as indicated by high PMA-stimulated O_2^- release. Macrophages primed *in vitro* by exposure to *Escherichia coli* LPS for 24 hr did show a moderate O_2^- response when stimulated by *M. lepraemurium,* but macrophages primed by exposure to IFN-γ muramyl dipeptide or *M. lepraemurium* showed a weak response when subsequently challenged with *M. lepraemurium.* The priming effect of *M. lepraemurium* or LPS decreased substantially after macrophages were cultured in fresh medium for 24 hr. Heat killing or opsonization of *M. lepraemurium* caused the *M. lepraemurium* to stimulate a high amount of O_2^- release from LPS-primed macrophages, but heat killing or opsonization of *M. lepraemurium* had no effect on release of O_2^- from unprimed macrophages. The results suggest that *M. lepraemurium* is taken into macrophages by a mechanism that bypasses the FcR and other receptors that are capable of triggering the production of O_2^-.—Authors' Abstract

Mowszowicz, M., de Anda, G., Vignale, R. A., Turak, V., Errico, F., Gezuele, E. and Calegari, L. [Cutaneous granuloma due to *Mycobacterium vaccae.*] Rev. Argent. Dermatol. **69** (1988) 192–195. (in Spanish)

We report the first case of cutaneous granuloma due to *Mycobacterium vaccae,* formerly considered a nonpathogenic mycobacterium (group IV, Runyon).

It is a female patient, 58 years old, with two lesions localized on the knee with an evolution of 5 months developing after minimal local trauma. The diagnosis was established by finding acid-fast bacilli on microscopic examination, their isolation on special culture and the experimental reproduction of lesions in the foot pad of golden hamsters. The patient's lesions regressed following thermotherapy.—Authors' English Summary

Orme, I. M. Evidence for a biphasic memory T-cell response to high dose BCG vaccination in mice. Tubercle **69** (1988) 125–131.

Memory immunity in mice to BCG vaccination is mediated by Thy-1.2+ L3T4+ Lyt-2− cyclophosphamide-resistant T lymphocytes. The time required for the emergence of acquired memory immunity was inversely proportional to the BCG inoculum size, although the level of memory expressed, once established, was equivalent regardless of the original dose of BCG administered. In mice given a high intravenous dose (10^8) of BCG, an apparently biphasic memory response was observed, initially peaking on day 15–20, then declining for 10 days or so before increasing again to maximal levels between day 30 and 60 of the infection. This trough in resistance was not due to an active immunosuppressive mechanism; instead, it is suggested that it represents an initial loss or consumption of memory T cells generated early during the infection which are stimulated to give rise to a state of active immunity as a result of the persisting high mycobacterial load.—Author's Summary

Pabst, M. J., Gross, J. M., Brozna, J. P. and Goren, M. B. Inhibition of macrophage priming by sulfatide from *Mycobacterium tuberculosis.* J. Immunol. **140** (1988) 634–640.

Sulfatide from the outer surface of *Mycobacterium tuberculosis* blocked priming in cultured human monocytes. Monocytes were primed *in vitro* with either lipopolysaccharide (LPS) or interferon-γ. Primed monocytes released increased amounts of superoxide anion (O_2^-) when stimulated with

formyl-methionyl-leucyl-phenylalanine or with phorbol myristate acetate. Primed monocytes also showed increased phagocytosis of sheep erythrocytes and increased release of interleukin 1. When primed monocytes were treated with 10 μg/ml of sulfatide, these enhanced functions, characteristic of primed monocytes, returned to levels found in unprimed monocytes. (With respect to these functions and others, monocytes or macrophages primed *in vitro* by exposure to LPS or interferon-γ resemble macrophages activated *in vivo* by infection. *In vivo,* activated macrophages provide nonspecific resistance to infection.) Inhibition of priming by sulfatide could be detected within 10 min but maximum effect of sulfatide required 3 to 5 hr. Sulfatide had no effect on O_2^- release, if it was added after the cells had been stimulated by PMA, suggesting that sulfatide did not inhibit enzymes involved in formation of O_2^-, but rather that sulfatide inhibited priming. Increasing the amounts of LPS or interferon-γ did not counteract the effects of sulfatide. Sulfatide did cause monocytes to release some prostaglandin E_2 (<1 nM), but the amount was not sufficient to inhibit monocyte functions. The effect of sulfatide was not blocked by indomethacin. Other sulfated compounds and other products of mycobacteria did not produce the sulfatide effect. We conclude that *M. tuberculosis* has on its outer surface a chemical that directly interferes with monocyte priming. *In vivo, M. tuberculosis* might use sulfatide to block macrophage activation and thereby resist being killed by macrophages.—Authors' Abstract

Portaels, F. [AIDS and atypical mycobacteria.] Ann. Soc. Belg. Med. Trop. **67** (1987) 93–116. (in French)

Infections due to atypical mycobacteria occupy an important place among the opportunistic infections which develop in AIDS patients. In industrialized countries, about half of the patients develop a mycobacteriosis, caused predominantly by *Mycobacterium avium-intracellulare* (90% of the cases). Conversely, in developing countries tuberculosis represents the predominant mycobacterial infection. Even though a few cases of atypical mycobacteriosis have been described in patients originating from developing countries who were treated in industrialized countries, the frequency of atypical mycobacteriosis in developing countries is still unclear. Several studies tied in with AIDS and mycobacteria seem necessary. The possible role as cofactor played by certain mycobacteria in the multiplication of the HIV virus should be analyzed. Research should be undertaken in an effort to explain the high frequency of *M. avium-intracellulare* infections as compared to other atypical mycobacteria. The different factors intervening in the pathogenicity of strains isolated from AIDS patients also call for more ample study. The preparation of DNA probes permitting the recognition of virulent strains deserve particular attention. Furthermore, the possibilities of early diagnosis and the use of new anti-mycobacterial drugs should be studied to enhance the chances of therapeutic success. Finally, the possibility that infections due to atypical mycobacteria can also play an important role in HIV-infected patients from developing countries is worth looking into.—(*Translated from* Author's Conclusions)

Raheman, S. F., Wagner, S., Mauch, H., Vasudeva, N. D. and Ingole, D. L. Evaluation of a dual-antigen ELISA test for the serodiagnosis of tuberculosis. Bull. WHO **66** (1988) 203–209.

Two antigen preparations from *Mycobacterium tuberculosis* and *M. bovis,* respectively, were used in an enzyme-linked immunosorbent assay (ELISA) to quantitate the level of IgG antibodies in samples of 169 sera obtained in India from 75 patients with pulmonary tuberculosis and from 94 controls. The results of the two ELISA tests were integrated using defined criteria. All the controls were correctly classified by this dual-ELISA approach and only two patients were categorized as false-negatives. The method has a specificity of 1.00 and a sensitivity of 0.974, while the gain in the certainty of diagnosis was 1.974, only slightly less than the ideal value of 2.00.—Authors' Abstract

Zarco Olivo, C., Manrique Martinez, P., Onate Cuchet, J. M., Dauden Tello, E. and Vanaclocha Sebastian, F. [Sporotri-

coid infection due to *Mycobacterium chelonei.*] Actas Dermosifiliogr. **79** (1988) 104–108. (in Spanish)

A 57-year-old woman, with no known antecedents of previous local injury or injection, presented with a verrucous nodule persisting from 7 years ago on her right knee and, subsequently, developed similar lesions on her right thigh resembling the morphological pattern of sporotrichosis. A Löwenstein-Jensen culture from biopsy material yielded growth of an atypical mycobacterium, later identified as *Mycobacterium chelonei.* We believe this is the third case of sporotricoid cutaneous infection due to *M. chelonei* reported in the literature. The biopsy revealed acid-fast bacilli in large clumps forming amorphous granules surrounded by eosinophilic halos within a granulomatous infiltrate with abscess formation; granules like those usually seen in a heterogeneous group of infections; mycobacteriosis had never before been included among them. The lesions regressed over 4 months with oral erythromycin treatment.—Authors' English Summary