CURRENT LITERATURE

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

General and Historical

Godal, T. [Leprosy research in Norway.] Nord. Med. **100** (1985) 324–325. (in Norwegian)

Leprosy research has made great strides in the last 15–20 years. The establishment of the Armauer Hansen Research Institute in Addis Ababa and the special program for diseases of tropical medicine has been of great importance. The breakthroughs which have occurred in the last few years in basic immunology and molecular biology have paved the way for the advances in leprosy research, including such as clearly have practical potential, e.g., new diagnostic methods, recombinant vaccines and immune therapy with recombinantly produced interleukins, primarily interleukin-2 and γ-interferon.—Author's English Abstract

Guillet, G., Tillard, J.-P., Hélenon, R., Quisi, D. and Relouzat, M. [Leprosy in young children; report of 2 cases at 3 years of age.] Ann. Dermatol. Venereol. **112** (1985) 353–357. (in French)

Two children (age 3 years) presented with leprosy in an endemic area: one was type T (tuberculoid paucibacillary); the other was type BL (borderline lepromatous) considering a very fast evolution, and was treated as a multibacillary leprosy. The family of the second child reported that the onset of the disease was consecutive to an insect bite at 5½ months of age. Such observations remind us that leprosy must be suspected or thought about very early, since the incubation period is likely to be shorter than previously proclaimed.—Authors' English Summary

Kumar, A., Thangavel, N., Durgambal, K. and Sirumban, P. Medical care delivery through leprosy clinics—consumer's perception, experiences and suggestions. Indian J. Lepr. **57** (1985) 845–861.

Randomly selected 500 adult leprosy patients, registered for treatment with six sectors of a leprosy control unit in Chingleput District of Tamil Nadu (India), were interviewed to study their perception and experiences with medical care being delivered to them through leprosy clinic(s), and their suggestions to improve the system.

About 14% of the patients did not perceive their disease as leprosy, and 8% of the total patients were taking treatment outside their sector leprosy clinics. The services like physiotherapy, rehabilitation, health education, etc., were known to only 3–8% of the patients, perhaps on account of their nonavailability and or nonpractice. On an average, a patient had to cover a distance of 2.1 $\pm$ 2.5 km (one side) in 24 $\pm$ 49 min to reach clinic spot, mostly by walking (83.2%), and spent 58.9 $\pm$ 32.2 min at clinic, two thirds of which in waiting for service(s). Each patient had consulted 1.23 $\pm$ 0.55 medical agencies for treatment of leprosy. The average man-day and wage losses to a patient, due to monthly clinic attendance, were estimated to be 0.48 $\pm$ 0.49 days and Rs. 2.28 $\pm$ 3.06, respectively. Only 10.6% of the 500 patients got admitted 1.55 $\pm$ 0.89 times in leprosy hospital for a duration of 63 $\pm$ 69.30 days and lost wages of Rs. 126.4 $\pm$ 85.64 per month of stay in hospital.

Availability and efficient delivery of comprehensive medical care through well-organized and regularly conducted leprosy

clinics by considerate and sympathetic staff was much emphasized by patients. Various factors influencing medical care delivery and its utilization by patients are discussed in this communication.—Authors' Abstract

Lechat, M. F. [Leprosy control in the Third World.] Bull. Mem. Acad. R. Med. Belg. **140** (1985) 274–282. (in French)

Leprosy affects today more than 10 million patients. Leprosy control has been characterized in the past by a number of delusions and pitfalls. Examples are the lack of basic research, the unavailability of *in vitro* and animal models, misconception regarding therapeutic regimens. Present difficulties are not fewer: integration into inappropriate health systems or services, emergence of resistant strains of *Mycobacterium leprae* requiring multiple drug therapy, development of a vaccine whose trial and widescale application raise major yet unsolved problems.—Authors' English Summary

Chemotherapy

Almeida, J. G. and Chacko, C. J. G. Computerized mathematical model of *M. leprae* population dynamics during multiple drug therapy. Indian J. Lepr. **57** (1985) 780–789.

A computerized mathematical model of *Mycobacterium leprae* populations during multiple drug therapy (MDT) was constructed. Relevant published information available to date was fed into it, and reasoned assumptions were made. From the model, it seems likely that MDT steadily selects bacteria resistant to the most powerful of the three drugs used unless the individual bactericidal potencies of the drugs balance one another. If the drugs used have differing potencies, cure probably hinges on treatment being continued until all metabolically active bacteria are killed. Withdrawal of treatment before that could lead to relapse with bacteria resistant to the most powerful of the drugs used.—Authors' Abstract

Anderson, R. Enhancement by clofazimine and inhibition by dapsone of production of prostaglandin E_2 by human polymorphonuclear leukocytes *in vitro*. Antimicrob. Agents Chemother. **27** (1985) 257–262.

The effects of the antileprosy agents clofazimine and dapsone (1 to 10 μg/ml) on the spontaneous and stimulated release of prostaglandin E_2 (PG E_2) by human polymorphonuclear leukocytes (PMNL) *in vitro* have been investigated. PMNL were obtained from normal adult volunteers and 3 patients with leprosy (2 borderline lepromatous and 1 subpolar lepromatous leprosy). The synthetic chemotactic tripeptide *N*-formyl-L-methionyl-L-leucyl-L-phenylalanine (FMLP) at a concentration of 10^{-7} M was used as the stimulant of PG E_2 synthesis. None of the test agents at the concentrations used inhibited the binding of radiolabeled FMLP to PMNL. However, dapsone at 5 and 10 μg/ml inhibited the spontaneous and FMLP-induced release of PG E_2 by PMNL. Clofazimine, on the other hand, significantly increased both the spontaneous and the FMLP-induced synthesis of PG E_2 by PMNL. The enhancing effects of clofazimine on FMLP-mediated synthesis of PG E_2 were particularly striking and were observed at concentrations of 1 to 10 μg of the drug per ml. Measurements of PMNL spontaneous and FMLP-induced synthesis of PG E_2 in the presence of both clofazimine and dapsone (5 μg/ml) indicated that the two drugs are mutually antagonistic. PMNL from both normal control subjects and patients with leprosy were equally sensitive to these effects of clofazimine and dapsone. The immunostimulatory and immunosuppressive properties of dapsone and clofazimine, respectively, may be related to the opposite effects of these agents on PG E_2

synthesis in human leukocytes.—Author's Abstract

Banerjee, D. K. Ciprofloxacin (4-quinolone) and *Mycobacterium leprae.* Lepr. Rev. **57** (1986) 159–162.

A new synthetic antimicrobial agent, ciprofloxacin (4-quinolone compound), active against a wide variety of bacteria including *Mycobacterium tuberculosis,* was tested in the mouse foot pad system against *M. leprae.* At doses tested, ciprofloxacin was found to be ineffective in suppressing the growth of *M. leprae.*—Author's Summary

Becx-Bleumink, M. Implementation of multidrug therapy in the ALERT Leprosy Programme in the Shoa Region of Ethiopia. First results with paucibacillary patients. Lepr. Rev. **57** (1986) 111–119.

Multidrug therapy (MDT) was introduced in the ALERT Leprosy Control Programme in January 1983, using the regimens recommended by the World Health Organization (WHO). During the period 1 January–30 June 1983, 1684 paucibacillary patients started their course of MDT in two districts in the northeastern part of the Shoa Region; 1501 patients (89.1%) completed their 6-month course of treatment within a period of 9 months. Although there are some communication problems in the area, the implementation of MDT with a once-monthly supervised component has proved to be feasible; in only 1 of the 65 clinics which were involved did less than 70% of the patients complete their course of MDT. This paper discusses the results of implementation of MDT for paucibacillary patients.—Author's Summary

Chen, J., *et al.* [Modification of multidrug therapy regimen for leprosy; decreasing the side effect of the treatment.] China Lepr. J. **1** (1985) 18–20. (in Chinese)

Twenty-two cases of multibacillary leprosy were randomly divided into two groups (each 11 cases). One group was treated according to the multidrug therapeutic regimen recommended by the WHO Expert Committee on Leprosy for multibacillary leprosy. The other group was treated by the modified regimen in which patients did not take prothionamide on the day that they took rifampin. The therapeutic effects of the two groups were similar, but in the group with the WHO regimen the elevation in GPT was 45.45% while in those with the modified regimen it was 9.09%. The results suggest if rifampin and prothionamide were not taken on the same day it might decrease the drug's side effect.—Authors' English Abstract

Easmon, C. S. F. and Crane, J. P. Comparative uptake of rifampicin and rifapentine (DL473) by human neutrophils. J. Antimicrob. Chemother. **13** (1984) 585–591.

Rifapentine, a new cyclopentyl rifamycin, was weight-for-weight less active than rifampin against *Staphylococcus aureus.* It was, however, equally effective at reducing the survival of *S. aureus* within human neutrophils even at concentrations below the conventionally determined MIC. The intracellular survival of antibiotic-resistant *S. aureus* was affected by neither agent. The bactericidal activity of neutrophil sonicates after exposure to both antibiotics showed that rifapentine was concentrated threefold more than rifampin. Uptake was temperature dependent and rapidly reached a plateau within 10 min. Uptake of rifampin was unaffected by pH; whereas that of rifapentine was reduced when the pH was lowered from 7.3 to 5. Studies with the metabolic inhibitors, sodium cyanide and potassium fluoride, suggested a minor role for both oxidative and glycolytic metabolism in this process. However, neither inhibitor had any demonstrable effect on the intracellular killing of *S. aureus* by either rifapentine or rifampin.—Authors' Abstract

Ganapati, R., Naik, S. S., Revankar, C. R., Vartak, R. B., Desai, A. P., Panvalkar, N. A. and Despande, S. S. Supervised administration of multidrug therapy in leprosy colonies through volunteers—a bacteriological assessment. Indian J. Lepr. **58** (1986) 86–90.

Multidrug therapy can be introduced successfully, even in difficult terrains such as leprosy colonies, without much operational

difficulty through trained student volunteers. The drug delivery can be entrusted to motivated college students as this procedure reduced operational cost of the program. Rapid clinical regression and novelty of three-drug regimen helped to gain the patients' confidence and better cooperation in drug compliance. Reduction in bacteriological indices with multidrug therapy was faster than compared to available data with DDS monotherapy.—Authors' Conclusion

Hess, C. W., Hunziker, T., Küpfer, A. and Ludin, H. P. Thalidomide-induced peripheral neuropathy; a prospective clinical, neurophysiological and pharmacogenetic evaluation. J. Neurol. **233** (1986) 83–89.

Prospective clinical and electrophysiological follow up was performed on nine patients under thalidomide treatment in order to detect the very beginning of possible drug-induced peripheral neuropathy. For neurophysiological assessment, nerve conduction measurements of the median, peroneal and sural nerves (seven conduction parameters) and needle EMG examination of the anterior tibial muscle were performed. The results of a first control after about 3 months of treatment were compared with the starting point examination, and the patients were then classified as "affected" or "not affected" according to clinical and neurophysiological criteria. At this point, three patients showed clinical and electrophysiological, and another two only electrophysiological alterations suggesting early neuropathy. This classification did not change after further clinical and electrophysiological controls. Without starting-point values, the early detection of neuropathy would not have been possible in all patients. No single reliable neurophysiological parameter for detection of thalidomide-induced neuropathy could be found. Pharmacogenetic classification with regard to hydroxylation and acetylation phenotypes was then performed in some patients and interpreted with relation to thalidomide neurotoxicity. A possible relationship between slow acetylators and development of thalidomide-induced neuropathy was found.—Authors' Summary

Huikeshoven, H. A simple urine spot test for monitoring dapsone self-administration in leprosy treatment. Bull. WHO **64** (1986) 279–281.

A simple urine spot test for monitoring patient compliance to dapsone self-administration in leprosy therapy was recommended by WHO but later abandoned. The present article describes some important improvements to the test, which is characterized by its validity and straightforwardness.—Author's Abstract

Irani, S., Mukherjee, R., Jagannathan, R. and Antia, N. H. *In vitro* study of the effect of dapsone on the components of the peripheral nerve in organised nerve culture model. Indian J. Med. Res. **83** (1986) 449–452.

Diaminodiphenyl sulfone (DDS) was added to the growth medium of dorsal root ganglion cultures of newborn mice at graded doses for extended periods of three weeks to study the direct action of this antileprosy drug *in vitro* on the Schwann cell and neuronal components of the peripheral nerves. No evidence was seen of rounding or sloughing of the cultured cells. Light microscopic appearance of the neurons and axons was normal. Migratory behavior and proliferative capacity of the Schwann cells and Schwann cell-axon interaction remained unaffected.—Authors' Abstract

Jagannathan, R. and Mahadevan, P. R. Minimum inhibitory concentration of drugs against *Mycobacterium leprae* as determined by *in vitro* assay. J. Biosci. **10** (1986) 137–144.

The observations that live *Mycobacterium leprae* after entry into cultured peritoneal macrophages from mice, reduced the EA rosetting macrophages, have been exploited to determine the minimum inhibitory concentration of diaminodiphenylsulfone and rifampin. Diaminodiphenylsulfone showed a minimum inhibitory concentration of 0.028 μg/ml and rifampin 0.11 μg/ml when given externally. However, there was accumulation of diamino-

diphenylsulfone inside the macrophages. At an external concentration of 0.028 μg/ml the concentration inside the macrophage was 0.5 μg/ml. The minimum inhibitory concentration for diaminodiphenylsulfone in this assay system is higher by several fold and that for rifampin is slightly lower than what is reported earlier with mice foot pad experiments. The minimum inhibitory concentration reported in this assay system is quite close to what is observed for *in vitro* inhibition of *M. lufu* with both the drugs.—Authors' Abstract

Kulkarni, V. M. and Mishra, D. S. Chemical drug delivery systems: I. Preparation and evaluation of prodrugs of dapsone. Indian J. Lepr. **57** (1985) 756–762.

Several prodrugs of dapsone have been prepared and evaluated *in vivo* for the release of parent drug. The prodrug: 4,4'-dibutyrylaminodiphenylsulfone gave blood levels above 0.5 μg/ml of DDS for about 34 days in rabbits injected intragluteally. The results have been compared with DDS and DADDS.—Authors' Abstract

Millan, J. and Bodian, M. [The fight against leprosy in an urban African setting: Dakar.] Acta Leprol. **4** (1986) 5–17. (in French)

The authors first explain the main epidemiological parameters of leprosy in Dakar, their evolution, and their differences with those of the rest of the country. The second part deals with case finding and reveals the essential importance of voluntary detection which appears as rather early: 3.5% of second-degree physical disabilities; 37% of monomacular lesions with paucibacillary. The third part explains the problems encountered in leprosy control with the study of a cohort of 241 patients: 64% were missing in 4 years and half of them during the first year. At the end of 4 to 6 years, only 19% of the patients had a regular attendance at treatment. The defects are significantly more frequent with male patients and with people who have been residing in Dakar for less than two years. In the suggested solutions, the authors insist on the necessity to adopt short multidrug protocols and to make health education for patients so that they care about case finding with their contacts.—Authors' English Summary

Millan, J., Bodian, M., Naudin, J.-C., Diouf, B., Boucher, P., Ndoye, B., Grosset, J., *et al.* [A multidrug trial in the Dakar region. First observations on the acceptability of the protocols used.] Acta Leprol. **4** (1986) 19–35. (in French)

Since 1982, in Dakar, a controlled trial tests the suitability of several short protocols of multidrug therapy (MDT), some of them being close to those advised by the WHO, others showing a starter stage of a 2-month daily MDT. In 3 years, 198 paucibacillars and 123 multibacillars have been treated. The short duration of these treatments leads to an important decrease in the load of the department. The total rate of those who have not attended for treatment is 15.2%; whereas it was 52% with DDS monotherapy for a similar treatment duration. Those who gave up do not seem to live in Dakar. To judge by the assiduity of the patients, the compliance seems excellent even for the protocols requiring a daily dose of ethionamide: 95% of paucibacillars, 76% of multibacillars have a top assiduity.

The authors think that any MDT program must be preceded by a retraining of staffs; must give a priority to the health education of the patients; must involve a home patient search system.—Authors' English Summary

Mishra, B. and Girdhar, B. K. Limitation of clofazimine in the treatment of lepra reactions. Indian J. Lepr. **58** (1986) 73–78.

Eight out of 30 cases of borderline lepromatous and lepromatous leprosy suffering with chronic recurrent lepra reactions failed to respond to clofazimine therapy. Three of the eight were steroid dependent. All eight patients are doing well after weaning off the clofazimine. Lymphadenitis in postclofazimine reactional status was the presenting feature in present retrospective study.—Authors' Abstract

Revankar, C. R., Ganapati, R. and Naik, D. D. Multidrug therapy for paucibacillary leprosy: experience in Bombay. Indian J. Lepr. **57** (1985) 773–779.

This study showed that such short-term therapy could be practiced successfully under field conditions prevailing in Bombay under the supervision of paramedical workers and field assistants. Addition of rifampin on pulse therapy basis increased compliance rate significantly (91%) as compared to dapsone attendance rate (64%). This also hastens clinical regression, especially in single-lesion tuberculoid patients. However, long-term studies are essential to study the relapse rate for judging efficacy of such short-term therapy.—Authors' Conclusion

Sharma, V. K., Kumar, B., Kaur, I., Singh, M. and Kaur, S. Colchicine in the treatment of type 2 lepra reaction. Indian J. Lepr. **58** (1986) 43–47.

Fifteen patients of lepromatous leprosy having type 2 lepra reaction were treated with colchicine. Seven had moderate, five mild, and three had severe ENL. Colchicine was found effective in all mild, six moderate and one case of pustular ENL.—Authors' Abstract

Tahan, S. R., Diamond, J. R., Blank, J. M. and Horan, R. F. Acute hemolysis and renal failure with rifampicin-dependent antibodies after discontinuous administration. Transfusion **25** (1985) 124–127.

Acute hemolysis as a reaction to rifampin is extremely rare; case reports number less than 15. We recently evaluated a 65-year-old Cambodian refugee who self-regulated the use of rifampin and isoniazid for pulmonary tuberculosis. Fifteen minutes after a single discontinuous oral dose, he developed flank pain, chills, rigors, vomiting, diarrhea, fever, and brown turbid urine. Laboratory tests at presentation showed acute intravascular hemolysis. Nonoliguric renal failure ensued, and he was transferred to our institution 2 days later. The patient was group A, Rh (D) positive, P_1 negative with a cold autoantibody and cold anti-P_1 alloantibody. The direct antiglobulin test was negative at the time of transfer. To evaluate the hemolysis, studies were done to test for rifampin- or isoniazid-dependent antibodies. Rifampin-dependent antibodies were detected in the antiglobulin phase with broad spectrum antihuman globulin, monospecific anti-gamma chain, and anti-complement antisera. Agglutination titers did not change after dithiothreitol reduction of the patient's serum. We conclude that this patient developed rifampin-dependent IgG antibodies with complement-fixing capability. The presence of rifampin-dependent antibodies should be suspected in a patient with hemolysis and/or renal failure taking rifampin.—Authors' Abstract

van Asbeck-Raat, A.-M. and Becx-Bleumink, M. Monitoring dapsone self-administration in a multidrug therapy programme. Lepr. Rev. **57** (1986) 121–127.

In the ALERT Leprosy Control Programme implementation of multidrug therapy (MDT) started in January 1983. The majority of the patients had received dapsone monotherapy prior to MDT. To assess the intake of dapsone in the MDT program the urine spot test is done in all the paucibacillary patients during the 4th and 6th supervised treatment day; with the multibacillary patients during the 4th, 6th, 12th, 18th and 24th supervised treatment. Results of the 4th and 6th treatment round are presented and discussed.

Of the 721 patients tested the overall percentage of patients with a positive test was 90.9%. Patients with a previous duration of treatment of more than 3 years were found to be significantly less compliant than others. Determinants like age, sex, disability grade or having a leprosy contact in the family did not influence compliance in a significant way.—Authors' Summary

Wang, H., *et al.* [Preliminary observation on the bactericidal effect of R-77-3.] Chin. J. Clin. Dermatol. **15** (1986) 121–123. (in Chinese)

R-77-3 [3-(4-cyclo-pentyl-1-piperazinyl) imino methyl rifamycin Sv] was studied by

mouse foot pad infection of *Mycobacterium leprae* using the kinetic method. The bactericidal effect was compared with rifampin (RMP). The antileprosy action of R-77-3 was also observed in four cases of multibacillary leprosy patients with a single dose of 400 or 600 mg under the supervision of authors. The preliminary results indicated that the antileprosy action of R-77-3 was better than that of RMP.—Authors' English Abstract

Wang, H., *et al.* [Survey of primary dapsone resistance in leprosy.] China Lepr. J. **1** (1985) 6–8. (in Chinese)

A primary dapsone-resistance survey was performed in the seven counties of Jiangsu Province during 1979–1984. A total of 28 untreated previously multibacillary leprosy patients was randomly selected. The results showed that the 6 strains of dapsone-resistant *Mycobacterium leprae* were isolated, 5 of them were of low degree resistance and only 1 was high degree. The prevalence of primary dapsone resistant leprosy is 24%. In all of the strains, three failed to infect the mice.—Authors' English Abstract

Waters, M. F. R., Rees, R. J. W., Laing, A. B. G., Khoo Kah Fah, Meade, T. W., Parikshak, N. and North, W. R. S. The rate of relapse in lepromatous leprosy following completion of twenty years of supervised sulphone therapy. Lepr. Rev. **57** (1986) 101–109.

In July 1970, 362 leprosy patients, all long-term residents of Sungei Buloh Leprosarium, who had been classified as lepromatous (LL and BL according to the Ridley-Jopling classification), and who had commenced treatment with sulfones as inpatients during the years 1948–1951, were "released from control." During a period of follow-up observation extending over 8–9 years, 25 of these patients relapsed clinically, giving an overall relapse rate of 8.6% and an average risk of relapse of 1.04 per 100 patient-years of observation. This risk did not change significantly from year to year during the period of observation. Of eight strains of *Mycobacterium leprae* isolated from patients in relapse, five were found to exhibit some level of dapsone resistance in mice. That the risk of relapse of lepromatous leprosy after long-term monotherapy with dapsone is so small is surprising, considering the deficient immune response to *M. leprae* characteristically displayed by these patients. Despite the small risk of relapse, it is recommended that smear-negative lepromatous patients who have received long-term monotherapy with dapsone receive a course of multidrug therapy before release from control.—Authors' Summary

Williams, S. E., Wardman, A. G., Taylor, G. A., Peacock, M. and Cooke, N. J. Long term study of the effect of rifampicin and isoniazid on vitamin D metabolism. Tubercle **66** (1985) 49–54.

Eight patients with tuberculosis were studied before, during, and after 9 months' treatment with rifampin and isoniazid to assess the overall effect on vitamin D metabolism. No significant uniform change in either $1,25(OH)_2D$ or 25 OH D nor in any of the other biochemistry measured occurred during the study. It seems unlikely that the combined effects of these drugs cause clinically significant derangement of vitamin D metabolism in patients treated over a 9-month period for tuberculosis.—Authors' Summary

Clinical Sciences

Anilkumar, G. and Patil, S. D. Squamous cell carcinoma developing in trophic ulcer in leprosy—a case report. Indian J. Lepr. **57** (1985) 879–882.

Development of malignancy in the trophic ulcer in leprosy is not previously believed rare. In India, less than a dozen cases are reported until now. We present a case of squamous cell carcinoma in trophic ulcer in leprosy patient because of its paucity in literature. Etiopathogenesis of malignancy is discussed briefly.—Authors' Abstract

Balybin, E. S. [Iodine metabolism in leprosy patients (examination with a method of total body radiometry).] Med. Radiol. (Mosk.) **31** (1986) 36–39. (in Russian)

A method of total body radiometry was used to study iodine metabolism in 47 patients with lepromatous leprosy. Disorders were found in one third of the cases. The level of organic iodine in the body was the most informative of all iodine metabolism indices. In the active stage of leprosy it was twice as low, on an average, as the normal one; in the stage of incomplete and stable regression it rose, not reaching, however, the values of healthy persons. The lowest mean value of an organic iodine level in the body was observed in patients with noticeable specific polyneuritis. The content of iodine in the thyroid of leprosy patients showed a tendency to a rise, starting from the active stage. However, it was only in the stages of incomplete and stable regression that it significantly exceeded the normal level. The data obtained should be considered during therapy of leprosy patients to predict and control an unfavorable complication like specific polyneuritis.—Author's English Summary

Bumb, R. A., Busar, R. P., Kothari, A., Singhi, M. K. and Jain, S. Dermatoglyphics in leprosy. Indian J. Lepr. **57** (1985) 834–840.

In the present study, dermatoglyphic parameters were analyzed in the handprints of 25 LL/BL, 25 TT/BT, and 25 healthy persons, by printer's ink method. Frequency of loops were more on right hand and whorls were more on left hand in LL patients as compared to normal healthy controls. In TT the whorls were less frequent than in controls. The a-b ridge count in LL patients has shown insignificant difference from control while the same in TT was significantly decreased ($p < 0.05$). Distance between distal wrist crease and axial triradius was significantly decreased in LL as compared to normal ($p < 0.05$); whereas no such decrease was observed in TT patients.—Authors' Abstract

Cavett, J. R., III, McAfee, R. and Ramzy, I. Hansen's disease (leprosy); diagnosis by aspiration biopsy of lymph nodes. Acta Cytol. (Baltimore) **30** (1986) 189–194.

A 61-year-old male native of Mexico presented with generalized enlargement of lymph nodes. Fine needle aspiration (FNA) biopsy established lepromatous leprosy as the cause of the lymphadenopathy. The cytologic findings included abundant, frequently multinucleated histiocytes (globus cells), the cytoplasm of which showed multiple vacuoles; cytoplasmic membrane-bound vacuoles were seen free in the background. The vacuoles contained large numbers of acid-fast bacilli. Globus cells, while characteristic, are not specific for *Mycobacterium leprae* infection are seen in certain atypical mycobacterioses in immunodeficient patients. This appears to be the first report of lymphadenopathy due to lepromatous leprosy in which the diagnosis was made by FNA biopsy. The immunologic spectrum of leprosy is correlated with clinical and pathologic findings, and the need to remember infectious processes in evaluating lymphadenopathy and the value of reserving air-dried and alcohol-fixed smears for special stains are emphasized.—Authors' Abstract

Chaturvedi, V. N., Rathi, S. S., Raizada, R. M. and Jain, S. K. T. Olfaction in leprosy. Indian J. Lepr. **57** (1985) 814–819.

Olfactory tests were carried out in 225 cases of Hansen's disease with 75 cases each

of lepromatous leprosy (LL), borderline leprosy (BL) and tuberculoid leprosy (T). Impairment of olfaction was found in 94 (41.7%) cases. It was seen in 69.33% cases of LL, 33.33% cases of BL and 22.6% cases of T. Total anosmia was present in 5 (6.61%) cases of LL only. Males were more affected than the females. Impairment of olfaction was related to the duration of the disease, severity of the nasal condition, and ENL reaction. It was not related to the type of antileprosy drug used.—Authors' Abstract

Deshpande, S. V., Zawar, P. B., Chawhan, R. N., Sengupta, S. R. and Mehta, M. C. Alpha-1-antitrypsin in leprosy. Indian J. Lepr. **57** (1985) 767–772.

Estimation of alpha-1-antitrypsin (AAT) levels was carried out in 52 patients of various types of leprosy. Fifty age- and sex-matched healthy individuals served as controls. The mean level of AAT in controls was 290.12 ± 59.56 mg/dl. In patients with tuberculoid leprosy (TT), borderline tuberculoid leprosy (BT) and borderline leprosy (BB), the AAT levels were found to be 284 ± 47.03, 314.37 ± 31.56 and 324.44 ± 32.05 mg/dl, respectively. These were statistically insignificantly raised when compared with controls. In borderline lepromatous leprosy (BL), lepromatous leprosy without erythema nodosum leprosum (LL without ENL) and in LL with ENL there was a statistically significant rise in AAT levels. The maximum levels of AAT were observed in patients of LL with ENL (mean 500.8 ± 93.44 mg/dl, $p < 0.001$).—Authors' Abstract

Duncan, M. E. and Pearson, J. M. H. The message of "rheumatism": a symptom of leprosy in pregnancy and lactation. Ethiop. Med. J. **23** (1985) 49–58.

In a prospective study of 108 Ethiopian women with leprosy (113 pregnancies) and 32 healthy controls (35 pregnancies) throughout pregnancy and lactation, "rheumatism" as a symptom was recorded and correlated to relapse, reaction, neuritis and new nerve enlargement, lymphadenopathy and paresthesias. Rheumatism was experienced by 35% of "cured" tuberculoid (TT) and borderline tuberculoid (BT) patients, and by 50% of women with TT and BT, borderline lepromatous and lepromatous leprosy receiving treatment; in contrast, only two healthy controls complained of rheumatism, and one of these developed overt leprosy shortly afterwards. In the "rheumatism group," relapse was seen more than twice as frequently as in the nonrheumatism patients; reaction (erythema nodosum leprosum) and reversal reaction were 5 times as common; new nerve enlargement was seen 4 times as often; neuritis 7 times as often; and lymphadenopathy and paresthesiae were found 5 times as often. A particularly sinister triad for the lactating mother was rheumatism, new nerve enlargement and silent neuritis. It was rare for rheumatism to occur without some objective evidence of nerve damage or relapse.—Authors' Abstract

Furukawa, F., Kashihara, M., Imamura, S., Ohsio, G. and Hamashima, Y. Evaluation of anti-cardiolipin antibody and its cross-reactivity in sera of patients with lepromatous leprosy. Arch. Dermatol. Res. **278** (1986) 317–319.

Using a sensitive and modified solid-phase radioimmunoassay for detecting anticardiolipin antibodies, sera of 45 patients with lepromatous leprosy were examined. Nine of the 45 (20%) showed positive levels of anticardiolipin antibodies. Inhibition tests revealed that these antibodies significantly crossreacted with double-stranded (ds) DNA, but not with single-stranded (ss) DNA or extractable nuclear antigens (ENA). We describe the unique pattern of antibody crossreactivity with cardiolipin and dsDNA in sera of patients with lepromatous leprosy.—Authors' Summary

Ghei, S. K., Girdhar, B. K., Ramu, G., Katoch, K., Ramanathan, U., Sengupta, U. and Desikan, K. V. Dermatoglyphics in leprosy (II. Metric analysis of palms). Indian J. Lepr. **57** (1985) 826–833.

A group of 100 leprosy patients consisting of 50 lepromatous (BL/LL) and 50 tuberculoid (BT/TT) were investigated for metric analysis of the patterns present on their palms. One hundred normal persons were also selected from the families of patients

to serve as controls. BT/TT patients and controls did not show any significant difference in their palmar patterns. On the other hand, significant differences were observed in the patterns between BL/LL patients and controls.—Authors' Abstract

Gupta, C. M., Tutakne, M. A. and Tiwari, V. D. Study of finger print patterns in leprosy. Indian J. Lepr. **58** (1986) 79–85.

Fingerprint patterns of 150 male leprosy patients (100 paucibacillary and 50 multibacillary leprosy) were compared with 50 matched controls. Significant differences were found in fingerprint patterns of multibacillary leprosy patients and controls. No differences in dermatoglyphic patterns were observed between paucibacillary leprosy and controls. The total finger ridge count in both types of leprosy was slightly lower than controls. A significant difference in individual finger ridge count on digit 1 of the right hand was noted in paucibacillary leprosy cases as compared to controls.—Authors' Abstract

Joseph, M. S. von Recklinghausen's disease associated with diffuse lepromatous leprosy—a case report. Indian J. Lepr. **57** (1985) 872–875.

Both leprosy and von Recklinghausen's disease (neurofibromatosis) are diseases affecting the Schwann cells of the peripheral nerves, although both are quite different entities. Lesions of neurofibromatosis may be mistaken for nodules of lepromatous leprosy and vice versa, but when they occur simultaneously in the same patient, this may pose difficulty in the diagnosis of leprosy. Their coexistence is only a casual one. One such case of multiple neurofibromatosis (VRHD) associated with diffuse LL is reported here.—Author's Abstract

Kumar, B., Narang, A. P. S. and Kaur, S. Gamma-glutamyl transpeptidase (GGT) in leprosy. Indian J. Lepr. **57** (1985) 763–766.

Activity of the enzyme gamma-glutamyl transpeptidase (GGT) was measured in 21 patients of BL or LL disease and 10 age-matched healthy controls. None of the patients had any systemic or hepatic diseases. Mean values in the patients (53.67 ± 9.67 U/L) were significantly higher ($p < 0.05$) compared to that of controls (34.2 ± 5.69 U/L).—Authors' Abstract

Murray, P. I., Muir, M. G. K. and Rahi, A. H. S. Immunopathogenesis of acute lepromatous uveitis: a case report. Lepr. Rev. **57** (1986) 163–168.

Various immunological parameters were examined in a patient with acute anterior uveitis who was also suffering from lepromatous leprosy. The most significant abnormality detected was a reduction in a subpopulation of T-lymphocytes known as suppressor cells, which occurred only during the acute attack and returned to normal once the attack subsided. This finding leads to the speculation that acute anterior uveitis in lepromatous leprosy may be regarded as an intraocular component of erythema nodosum leprosum, precipitated by an imbalance of T lymphocytes and probably mediated through immune-complex deposition in the uveal vasculature.—Authors' Summary

Naik, R. P. C., Srinivas, C. R. and Rao, R. V. Thickening of peripheral nerves in neurofibromatosis. Indian J. Lepr. **57** (1985) 876–878.

A rare case of multiple neurofibromatosis (von Recklinghausen's disease) with bilateral, uniform and gross enlargement of peripheral nerves simulating nerve thickening in leprosy is reported. The case also showed characteristic palmar melanotic macules.—Authors' Abstract

Nickless, S. J. Flow charts for use in leprosy control programmes. Lepr. Rev. **57** (1986) 169–176.

These charts were developed as a personal exercise during a visit to Green Pastures Leprosy Hospital, Pokhara, Nepal. They are an attempt to summarize in a readily accessible format the clinical and administrative "standing orders" which govern the work of leprosy control project paramedical workers in remote clinics. They could be modified and translated for use in other settings.—(*From* the Article)

Parikh, D. A., Oberai, C. and Ganapati, R. Involvement of scalp in leprosy—a case report. Indian J. Lepr. **57** (1985) 883–886.

Involvement of the hairy area of the scalp in leprosy is considered to be infrequent. Jopling is of the opinion that such involvement of scalp is rare. At the most, it could be demonstrated in those lepromatous patients who have their hair shaved off. We report a case of borderline tuberculoid leprosy with involvement of the hairy area of the scalp.—(*From* the Article)

Park, J. Y., Kim, K. W., Kim, S. J. and Kim, J. D. Circulating immune complexes in patients with leprosy. Yonsei Med. J. **25** (1984) 18–26.

The occurrence of immune complexes in the serum from rats infected with *M. lepraemurium* and 38 patients with leprosy were studied by the polyethylene glycol precipitation complement consumption (PEG-CC) test and the results were compared in the various forms of the disease. Circulating immune complexes (CIC) were significantly increased in the sera from rats infected with *M. lepraemurium* compared to normal control rats ($p < 0.005$). There were no significant differences between the level of CIC in the sera from lepromatous leprosy patients and that from tuberculoid leprosy patients, but in the sera from patients with erythema nodosum leprosum (ENL) the level of CIC was significantly increased ($p < 0.005$). And although we could not find a correlation between the level of CIC and bacterial indices in lepromatous leprosy patients, CIC tends to decrease after negative conversion of their bacterial indices.

These findings suggested that the detection of CIC can be of some practical interest in the early diagnosis of ENL and can be a valuable assessment in following the therapy after negative conversion of their bacterial indices.—Authors' Abstract

Ravisse, P. and Rollier, R. [Reflections on the histopathology of leprosy; study of more than 2300 biopsies.] Bull. Soc. Pathol. Exot. Filiales **79** (1986) 172–179. (in French)

Biopsies (2326) on Moroccan subjects suffering from leprosy had been studied in 4 years. After a critical study of histopathologic diagnosis and the classifications, the authors studied especially the lepromatous granuloma, its evolution during treatment and the lepromatous reactions. Defining histologically a reactional background, they make a certain generalization among all the types of reactions observed in lepromatous patients.—Authors' English Summary

Samuel, N. M. Acid-fast bacilli in the fingers and toes of long treated lepromatous leprosy. Asian Med. J. **28** (1985) 568–579.

This paper from Kathmandu in Nepal essentially confirms previous studies on the value of examining the fingers and toes for the presence of leprosy bacilli, using the standard slit-skin techniques. The patients were not in fact from Nepal: 32 were from three different states in India and eight were from a small group attending the Hospital for Tropical Diseases in London. Smears were taken from the nose, earlobes, fingers and toes (it was planned to take smears from lesions at other body sites but for reasons beyond the author's control this was not possible in this study). The patients from India had all received dapsone monotherapy. The results of slit-skin smear examination at the various sites are recorded in full in four tables, using both bacteriological and solid–fragmented–granular indices. The periods of drug treatment in India ranged from 2 to 38 years. The patients from London received various combinations of dapsone, clofazimine and rifampin, and the period of treatment ranged from 4 to 32 years. The author summarizes the most important findings with regard to fingers and toes as follows: (1) bacilli were present in extremities and yielded "significant bacillary counts" at these sites, (2) 21 of 32 bare-foot patients showed solid bacilli in toes, (3) nonbare-foot patients did not reveal appreciable numbers of bacilli in their toes, (4) no significant difference was noted between bacilli in fingers and toes of patients from India, (5) 12 patients who had received treatment for extended periods of time "tended to show high concentrations of bacilli in their extremities."—A. C. McDougall (Trop. Dis. Bull.)

Sehgal, V. N., Koranne, R. V., Sehgal, S., Beoher, P. C. and Sharma, V. K. Correlation of morphological, bacteriological, histopathological and immunological feature of leprosy—a double-blind study. J. Dermatol. **12** (1985) 243–250.

Fifty untreated and uncomplicated leprosy patients, 3 with TT, 26 with BT, 10 with BB, 4 with BL, and 7 with LL, formed the subject material for the study. They were subjected to detailed morphological, bacteriological, histopathological, and immunological investigations. Four investigators undertook the study, and each one independently investigated one parameter according to a preconceived standard set. The data were pooled and analyzed after breaking the code. A good correlation among all four parameters was seen only in 44%. A striking variation in three other parameters was found in 56%, primarily in the borderline groups, suggesting subclinical bacteriological, histopathological and immunological instability, either in the form of upgrading or downgrading. Similarly, the separation of five indeterminate cases from those of BT group was intriguing.—Authors' Abstract

Sharma, V. K., Kaur, S., Kumar, B. and Singh, M. Dapsone syndrome in India. Indian J. Lepr. **57** (1985) 807–813.

Three cases of "dapsone syndrome" that occurred between 1981 to 1984 are described and relevent literature reviewed.—Authors' Abstract

Sharma, V. K., Kumar, B., Kaur, S. and Dutta, B. N. Involvement of tongue in leprosy. Indian J. Lepr. **57** (1985) 841–844.

Two cases of leproma of the tongue were detected among 200 cases of lepromatous leprosy. The details are discussed.—Authors' Abstract

Singh, G., Tutakne, M. A., Tiwari, V. D. and Dutta, R. K. Quantification of thermal sensory loss in follow up of progress in leprosy. Indian J. Lepr. **57** (1985) 790–795.

Thermal sensory perception quantitatively was studied in follow up of 10 lesions (4 TT, 3 BT and 1 indeterminate case) of cases put on polytherapy as per WHO regime for 6 months. Significant thermal sensory improvements were noticed in four lesions after 4 months of therapy. Within 2 months of therapy, three cases showed improved perception of heat sensation but one showed deterioration. Recovery of sensations did not correspond to other clinical parameters of improvement in all the cases. The utility of quantitative evaluation of thermal sensory perception in follow up of leprosy cases is discussed.—Authors' Abstract

Singh, G., Tutakne, M. A., Tiwari, V. D. and Dutta, R. K. Inoculation leprosy developing after tattooing—a case report. Indian J. Lepr. **57** (1985) 887–888.

A case of inoculation leprosy following tattooing in a soldier is being reported. Escape of infection in one tattoo and occurrence of disease in another when tattooing was done simultaneously is of interest. Possible mechanism for such occurrence is discussed.—Authors' Abstract

Singh, I. P., Mehta, S. R., Gupta, C. M. and Bhate, R. C. Cardiovascular system in leprosy. Indian J. Lepr. **58** (1986) 69–72.

Involvement of cardiovascular system (CVS) in 50 multibacillary (MB) and 20 paucibacillary (PB) cases of leprosy was evaluated; 20 age- and sex-matched controls were also studied. In addition to detailed clinical examination and resting electrocardiogram, Master's two-step exercise test (DMT) was also carried out to find out the occult and asymptomatic cardiac involvement. We have not found any significant symptomatic or electrocardiographic evidence of CVS involvement in various groups of leprosy.—Authors' Abstract

Singh, K., Dawar, R. and Ramesh, V. Lymphocytic infiltration of skin of Jessner-Kanof masquerading as borderline leprosy. Indian J. Lepr. **57** (1985) 804–806.

A case of pseudolymphoma from India is being reported which had been masquerading for quite some time as a case of borderline leprosy. The patient has been having

for the past 16 years recurrent, occasionally pruritic, multiple, bilateral, erythematous papules and plaques, which on casual examination elsewhere had suggested leprosy.—Authors' Abstract

Singh, M., Kumar, B., Ayagiri, A. and Kaur, S. Natural tetanus immunity in lepromatous leprosy patients. Indian J. Lepr. **58** (1986) 91–95.

Thirty-five lepromatous leprosy patients with recurrent trophic ulcers were analyzed for tetanus antitoxin levels by the passive hemagglutination test (PHA); 42.85% patients and 32% controls had protective levels of antitoxin in their serum (≥ 0.1). All the patients (100%) demonstrated measurable antitoxin levels. The findings indicate immunological protection from tetanus and support the clinical impression of its rarity in leprosy patients.—Authors' Abstract

Singh, P. K., Nigam, P. K. and Singh, G. Terry's nails in a case of leprosy. Indian J. Lepr. **58** (1986) 107–109.

First case of Terry's nails following onset of borderline tuberculoid leprosy without any other involvement in a 40-year-old male is reported. This condition is, however, well known in cirrhosis of liver.—Authors' Abstract

Swamy, S., Durai, V., Oommen, P. K. and Rao, K. S. Cauliflower growths in trophic ulcers of leprosy—a 10 year study. Indian J. Lepr. **58** (1986) 44–52.

A 10-year study of cauliflower growths in trophic ulcers of leprosy patients was done; 75 cases were seen, out of which 72 were in foot and 3 in hand. Even though appearance was like that of malignancy, malignant change was seen only in four cases and in the other 71 cases it was pseudoepitheliomatous hyperplasia. Various surgical procedures were done. Wide excision appears to be the procedure of choice where feasible as per our studies.—Authors' Abstract

Zhang, W., *et al.* [Investigation of leprosy eye diseases in 1080 leprosy cases in Guangdong Province.] China Lepr. J. **1** (1985) 9–14. (in Chinese)

In 1984 and 1985, 1080 leprosy patients were examined. In 980 cases the authors found leprosy eye disease for an incidence of 90.74%. The cured patients were found with a higher rate than those with present illness, the latter mostly belong to L type. The longer the disease, the more severe the leprosy reactions are and the higher the incidence rate of eye diseases. Nevertheless, some patients with a clinical history of 16–31 years, in spite of loss of eyebrow and trichiasis, still retain their normal vision due to early treatment. Therefore, in the prevention and treatment of leprosy reaction, special attention should be paid to the pathological eye changes. The inflictions occur mostly in the anterior portion of the eye; 43 cases were found in which the winking phenomena appeared less and 61 cases had Grafe's disease; 28 cases have spotted pigment deposit on the fundus. Vision of less than 0.05 occurred in 132 eyes of 93 people; 39 people were blind in both eyes and 54 in a single eye, the causal rate is 9.49%, in which L type is more. Leprosy lagophthalmos and eyelid ectropion and their sequelae caused 80% of the blindness, irido-cyclitis and its sequelae 20%. To prevent leprosy eye blindness, one should chiefly aim at correcting lagophthalmos and eyelid ectropion. The examination of the conjunctival scraping of 244 uncured patients revealed *Mycobacterium leprae* only in eight cases. Besides using 0.1% rifampin, the eyelid ectropion, lagophthalmos, cataract, occlusion of pupil, etc., were treated with corrective measures, rehabilitation of the vision being successful in 85 eyes of 74 cases. The use of the nylon thread correction technique for eyelid lagophthalmos can protect corneas in severe cases and completely close the eyelids in mild cases and keeping patients' facial beauty. The ophthalmologist should take part in preventing leprosy diseases of the eye.—Authors' English Abstract

Zhang, X., *et al.* [Eyebrow implantation by single hairs for 27 cases.] China Lepr. J. **1** (1985) 42–43. (in Chinese)

The recovery of eyebrows in leprosy is a problem of concern to both patients and physicians, and it is one of the important problems of rehabilitation in leprosy. Present work introduces eyebrow implantation

by single hairs for 27 leprosy patients without eyebrows. Survival rates of 70% have been obtained in a single operation. In addition, this method is heartily accepted by patients because it is simple, convenient to get the hairs, no scar, and easy to make up individually. Therefore, it is available and worth being popularized.—Authors' English Abstract

Zhao, X., *et al.* [The methods of examining swelling of the peripheral nerves in leprosy.] China Lepr. J. **1** (1985) 29–32. (in Chinese)

The swelling of the peripheral nerve trunks is a valuable sign for diagnosing leprosy. But due to the differences in the thickness of the nerves between individuals, if only regarding their thickness, it is sometimes very difficult to judge correctly whether there is swelling. If the thickness, hardness, surface evenness, roundness, or flatness in shape and tenderness of the nerve trunks are examined and the comparison of the nerves on the opposite side are made, it might be much easier to judge whether the nerves are swollen. The nature of the neurotropism of *Mycobacterium leprae* determines its selective affection to the superficial nerve trunks. Because leprosy is a disease affecting all of the body and the nerves affected are not uniformly distributed, therefore, not only the *n. auricularis magnus, n. ulnaris* and *n. peroneus communis,* but other superficial nerve trunks should also be routinely examined. The examination methods and the superficial nerves to be examined are discussed in the article.—Authors' English Abstract

Immuno-Pathology

Agarwal, S., Vemuri, N. and Mahadevan, P. R. Macrophage membrane alterations in leprosy as determined by change in sialic acid level. J. Clin. Lab. Immunol. **19** (1986) 119–122.

The level of sialic acid removable by neuraminidase from macrophages of bacteriologically positive lepromatous leprosy (B(+)LL) patient is extremely low, compared to macrophages from tuberculoid leprosy patients or normal individuals. On the other hand, macrophages from long-term treated bacteriologically negative lepromatous leprosy (B(−)LL) patients show a much higher level of sialic acid. This higher level is drastically reduced when these macrophages from (B(−)LL) patients are allowed to phagocytose *Mycobacterium leprae.* This modulation could be host- and pathogen-specific. It is demonstrated that *M. leprae* infection brings out membrane changes in the macrophages leading to alteration in the surface molecules. Such membrane changes may cause hindrance in the ability of macrophages to participate successfully in the immune process.—Authors' Summary

Aubry, P., Barabe, P. and Darie, H. [Visceral manifestations in leprosy.] Med. Afr. Noire **32** (1985) 345–349. (in French)

Visceral involvement with leprosy has been evidenced in autopsies, while clinical manifestations are rare with the exception of cases with lepromatous leprosy and with leprous reactions. In multibacillary forms, the Hansen bacillus may invade the majority of the deep viscera, the liver, the lymph glands, the spleen, the testicles and the suprarenal glands. The bone marrow may also be affected. The most frequent clinical manifestations are adenopathy, splenomegaly and orchitis. The Hansen bacillus is not directly responsible for the visceral damage, which represents the expression at different levels of the host's immunological reaction. In the liver and ganglion, the histopathological lesions take the form of a leprous granuloma, the structure of which may dif-

fer depending on the type of leprosy involved. Type 2 reactions are characterized by secondary vasculitis followed by a type of Arthus' reaction induced by circulating immune complexes. Although they are diffuse, these lesions are especially found in the kidney and they may be life threatening, even more so in the presence of amyloidosis. Some authors have reported an increased incidence of electrocardiographic anomalies and a lower incidence of arterial hypertension. In practice, the diagnosis of visceral involvement does not pose any problems in patients with cutaneous and or nervous lesions. In rare cases the onset of the condition is characterized by fever, arthralgia, myalgia, sometimes adenopathy, splenomegaly with septicemia, malignant hemopathy and disseminated tuberculosis. The diagnosis may be delayed without carrying out a systematic bacilloscopic examination of the skin (which is always positive in multibacillary forms) which will reveal any intercurrent modification in the host's immune system.—English Abstract from Excerpta Medica

Bahr, G. M., Stanford, J. L., Rook, G. A. W., Rees, R. J. W., Abdelnoor, A. M. and Frayha, G. J. Two potential improvements to BCG and their effect on skin test reactivity in The Lebanon. Tubercle **67** (1986) 205–218.

An account of an ongoing project to assess the possible benefits of two additives to BCG vaccine is presented. These additives are suspensions of irradiation killed *Mycobacterium vaccae* in one case, and *M. leprae* in the other. Groups of children aged 7–17 living in Zgharta and Akkar districts of north Lebanon have received vaccination with BCG alone or with either of the two additives since 1980. This region was chosen since contact with environmental mycobacteria is small, but both leprosy and tuberculosis occur there. So far the effects of the additives have been assessed by annual skin testing of volunteers with tuberculin, leprosin A, vaccin and scrofulin, and by measuring the size of the vaccine scars. Some children have now been followed up on four occasions, and special attention is paid to them.

No complications have been encountered in the 1740 children who have entered the study (by our observation, or by local report on those who have not attended for follow up) and the mean scar sizes after vaccines with the additives are no larger than those after BCG alone. There is no evidence that the additives have prevented development of tuberculin positivity after vaccination, or have changed the nature of reaction to it. Incorporation of *M. leprae* significantly increased leprosin A positivity and both additives increased vaccin positivity in comparison with the effects of BCG alone. The results are fitted to a model of the theoretical expectations of the study and may be beginning to show the advantages expected of the additives. The only unexpected finding was a reduction in scrofulin positivity especially associated with the additives.

The very low contact with environmental mycobacteria experienced in the study area has allowed the pattern of postvaccination decay of skin test positivity to be studied with greater precision than has been reported before, and differences have been detected between the two districts where the study was conducted. Confirmation of the possible advantage of the additives will rest with data to be obtained in longer term follow ups and in studies being carried out in other countries.—Authors' Summary

Bahr, G. M., Stanford, J. L., Rook, G. A. W., Rees, R. J. W., Frayha, G. J. and Abdelnoor, A. M. Skin sensitization to mycobacteria amongst school children prior to a study of BCG vaccination in north Lebanon. Tubercle **67** (1986) 197–203.

One thousand eight hundred eighty-eight school children aged between 7 and 17 years, living in 13 villages in two districts of north Lebanon, were skin tested with four new tuberculins as the initial step in a study of BCG vaccination. The great majority of children were tested with tuberculin, leprosin A, vaccin and scrofulin. In comparison with other countries where similar studies have been carried out, extremely low levels of sensitization were discovered, indicating very little contact with mycobacteria. There was, however, a statistically significant increase in positivity with increasing age.

The results obtained for the villages of

each district were significantly different from each other, positivity being greatest in Akkar district for each reagent. The 8 villages of Zgharta district could be separated into a lowland group of 4 villages, a mountain group of 3 villages, and 1 anomalous mountain village. There was significantly more positivity in the lowland than in the mountain villages. In Akkar district, where leprosy has a low prevalence, positivity to leprosin A was 8% among the children (leaving out an anomalous village). In Zgharta district where the disease does not occur, positivity was 3.4% to leprosin A for the lowland villages and 0.9% for the group of three mountain villages. The two anomalous villages were the only ones in which tuberculosis cases were known to have occurred recently, and they were the only two villages in which tuberculin positivity exceeded 10%.—Authors' Summary

Band, H. Interleukin-1—a possible mediator of neural fibrosis in leprosy. Med. Hypotheses **20** (1986) 143–150.

Neural fibrosis in leprosy, the disease caused by the obligate intracellular bacterium *Mycobacterium leprae,* is closely related to the cell-mediated immune response to this microorganism. The fibrosis appears to be due to soluble mediators released by the immune effector cells. Interleukin-1, a macrophage product that stimulates fibroblast migration, proliferation and synthetic activity, possesses the requisite properties to qualify for such a mediator.—Author's Abstract

Beck, J. S., Morley, S. M., Gibbs, J. H., Potts, R. C., Ilias, M. I., Kardjito, T., Grange, J. M., Stanford, J. and Brown, R. A. The cellular responses of tuberculosis and leprosy patients and of healthy controls in skin tests to "New Tuberculin" and Leprosin A. Clin. Exp. Immunol. **64** (1986) 484–494.

The density and distribution of T4 and T8 lymphocytes and of monocyte/macrophages at the site of skin tests with mycobacterial antigens was studied in pulmonary tuberculosis and leprosy patients and in healthy controls. Most of the inflammatory cells were located in perivascular and periappendicular foci in the dermis: the percentage of the dermis occupied by focal infiltrate was unrelated to the clinical measurement of the area of induration. There was a less intense diffuse infiltrate in the dermis between the foci, most marked in the papillary dermis and lessening progressively in deeper layers. In patients, diffusely infiltrating lymphocytes were more numerous (mainly due to an excess of T8 cells) in relation to extracts of the pathogen causing their disease than to extracts of the other organism: T8 cells were particularly numerous in reactions to leprosin A in 3 of 4 partly treated leprosy patients who had been classified as tuberculoid at the time of diagnosis. The density of diffusely infiltrating macrophages showed a similar density gradient and selective concentration in response to active disease pathogens. However, these cells were less numerous in partly treated leprosy patients than in controls and most frequent in untreated pulmonary tuberculosis patients. Selective migration of monocyte/macrophages and, to a lesser extent T8 cells, appears to be a prominent feature in the reaction of patient with active mycobacterial disease to antigens derived from the causative organisms; this suggests that it might become possible to distinguish direct reactions from crossreactions in human delayed hypersensitivity reactions by identification of these histological features.—Authors' Summary

Birdi, T. J., Salgame, P. R., Bharucha, H. and Antia, N. H. *In vitro* tests for screening of immuno-modulating mycobacterial strains in leprosy. J. Biosci. **10** (1986) 127–135.

There is an urgent need for the development of an *in vitro* assay for the initial screening of a large number of organisms from which potential candidates as vaccines can be identified. Our previous studies have demonstrated a crucial defect in the lepromatous macrophage. In this study, by monitoring this defective macrophage response we have screened various mycobacteria for their ability to reverse the alterations induced by *Mycobacterium leprae.* Among the limited mycobacteria tested *M. vaccae* appears to be the most promising as an im-

munomodulator. Our results also indicate the need for caution in using the mouse model for this purpose.—Authors' Abstract

Castellanos-Barba, C., Islas-Rodriguez, A., Morales, R., Gonzalez-Mendoza, A., Zambrano-Villa, S. and Ortiz-Ortiz, L. [Lepromatous leprosy: study of some subpopulations of lymphocytes and its functional analysis.] Arch. Invest. Med. (Mex.) **16** (1985) 217–224. (in English and Spanish)

Total T-lymphocyte levels were investigated in a group of patients with lepromatous leprosy and in another one made up by clinically healthy individuals, by the capacity to form E rosettes together with Fc-gamma suppressor T lymphocytes and blastoid transformation capacity of the lymphoid cells, when stimulated with concanavalin A. The determination of T lymphocytes by E rosettes showed patients had decreased levels when compared to normal control subjects. The determination of Fc-gamma suppressor T lymphocytes evaluated by rosette formation with chicken erythrocytes sensitized with IgG showed significantly increased levels of such lymphocytes. In the culture of peripheral blood lymphocytes, blastoid transformation induced by concanavalin A and mediated by tritiated thymidine revealed low levels in leprosy patients.—Authors' Abstract

Chatterjee, D., Douglas, J. T., Cho, S.-N., Rea, T. H., Gelber, R. H., Aspinall, G. O. and Brennan, P. J. Synthesis of neoglycoproteins containing the 3,6-di-*O*-methyl-β-D-glucopyranosyl epitope and their use in serodiagnosis of leprosy. Glycoconjugate J. **2** (1985) 187–208.

A stratagem for the synthesis of *neo*glycoproteins suitable for the selective serodiagnosis of leprosy is described in which synthetic 3,6-di-*O*-methyl-β-D-glucopyranose, the epitope of phenolic glycolipid-I from *Mycobacterium leprae,* was used. Condensation of 8-methoxycarbonyloctanol with the acetobromo derivative of 3,6-di-*O*-methyl-glucose gave 8-methoxycarbonyloctyl 2,4-di-*O*-acetyl-3,6-di-*O*-methyl-β-D-glucopyranoside in 65% yield, and with absolute stereospecificity for the β anomer. The deacylated product was converted to the crystalline hydrazide and coupled to bovine gamma globulin, bovine serum albumin and poly-D-lysine via intermediate acyl azide formation to produce the 8-carbonyloctyl 3,6-di-*O*-methyl-β-D-glucopyranosyl polypeptides. The *neo*glycoproteins were highly sensitive in ELISA and emulated the specificity of the native glycolipid in analysis of sera from patients throughout the spectrum of leprosy and from different geographical regions. The 8-carbonyloctyl 3,6-di-*O*-methyl-α-D-glucopyranoside-bovine serum albumin was also synthesized and shown to have about one half the activity of the β-linked *neo*glycoprotein. A different synthetic approach produced the 8-carbonyloctyl 4-*O*-(3′,6′-di-*O*-methyl-β-D-glucopyranosyl)-α-L-rhamnopyranoside-bovine serum albumin which was also highly sensitive and specific for the serodiagnosis of leprosy. The presence of the second sugar unit, similar to that in the native glycolipid but for the absence of *O*-methyl groups, seemed to provide a probe with greater felicity for the serological detection of tuberculoid leprosy. Thus, the results indicate that highly sensitive and specific antigen probes for the serodiagnosis of leprosy can be constructed based only on the terminal one or two sugars of phenolic glycolipid-I, and the synthetic approach leads to the formation of haptens with absolute stereospecificity.—Authors' Abstract

Chen, Z., *et al.* [Study on the immunopathomorphology of lymph nodes in leprosy; light and electron microscopic observations.] China Lepr. J. **1** (1985) 33–36. (in Chinese)

Lymph nodes from 26 cases of leprosy, biopsied or autopsied, were immunopathomorphologically studied with light and electron microscopes, revealing that in LL and BL leprosy the cellular immunologic function was decreased or lost.

ANAE method showed that active esterase granules were decreased or lost, and this explained that the defect of nonspecific cellular immunity is incomplete. The esterase granules of type TT were clearly seen and this appearance is in accordance with their

highly cellular immunologic function.—Authors' English Abstract

Engers, H. D., Bloom, B. R. and Godal, T. Monoclonal antibodies against mycobacterial antigens. Immunol. Today **6** (1985) 347–348.

This article gives a summary of the properties of some 55 murine monoclonal antibodies that have been raised against *Mycobacterium leprae* or *M. tuberculosis* and submitted to the IMMLEP and IMMTUB monoclonal antibody banks.—(Trop. Dis. Bull.)

Eustis-Turf, E. P., Benjamins, J. A. and Lefford, M. J. Characterization of the antineural antibodies in the sera of leprosy patients. J. Neuroimmunol. **10** (1986) 313–330.

Sera from 43 leprosy patients were tested for antibodies that bound to normal human nerve. Thirty-eight percent showed positive staining as demonstrated by indirect immunofluorescence. Only 1 out of 30 control sera tested displayed similar staining. Western blots of myelin and neural intermediate filament (IF) proteins were tested with patient sera. Two of the antineural antibody (ANeAb)-positive leprosy sera bound to the P_0 protein of PNS myelin. All 17 ANeAb-positive leprosy sera displayed two or more bands in the molecular weight range of M_r 45,000–55,000, when tested against IF proteins.

One explanation for these findings is that leprosy patients produce antibodies to intermediate filament (IF) proteins released subsequent to the bacterial invasion of the peripheral nerves. The importance of these autoantibodies in the pathogenesis of leprosy is discussed.—Authors' Summary

Gill, H. K. and Godal, T. Deficiency of cell mediated immunity in leprosy. Prog. Allergy **37** (1986) 377–390.

Leprosy manifests itself in a range of clinical forms which have been systematically gathered into a spectrum. At one end of this spectrum is the high-resistant, pancibacillary tuberculoid leprosy while at the other end is the low-resistant, multibacillary lepromatous leprosy. Lepromatous leprosy is a systemic form of the disease in which the patient does not possess the ability to mount a cell-mediated immune response against *Mycobacterium leprae*. This immunological deficiency is specifically related to *M. leprae* antigens. LL individuals exhibit an unimpaired immune response to such closely related antigens as BCG and PPD.

Recent studies have shown that LL lymphocytes fail to produce IL-2 in response to *M. leprae*, and that their proliferative response to this antigen may be restored by IL-2. This, and the evidence that LL macrophages function normally, would appear to indicate that the immunological deficiency in lepromatous leprosy is due to a defect in the T-cell population. Data have been presented which show that such a deficiency may be brought about by suppressor T cells which have been induced by antigens specific to *M. leprae*.—Authors' Summary

Gill, H. K., Mustafa, A. S. and Godal, T. Induction of delayed-type hypersensitivity in human volunteers immunized with a candidate leprosy vaccine consisting of killed *Mycobacterium leprae*. Bull. WHO **64** (1986) 121–126.

A killed armadillo-derived *Mycobacterium leprae* vaccine was examined for its ability to induce a delayed-type hypersensitivity (DTH) response in purified protein derivative (PPD)-positive human volunteers living in a leprosy nonendemic country. Four groups of individuals aged between 23 and 28 years were given 1.5×10^7, 5×10^7, 1.5×10^8, and 5×10^8 *M. leprae* intradermally. A marked increase in reactivity to the *M. leprae*-derived skin test antigen was observed in the vaccinated groups receiving the three highest doses of vaccine, while there was very little change observed in their PPD reactivity. No unacceptable side effects attributable to the vaccine were observed. The killed armadillo-derived *M. leprae* vaccine thus appears to be able to induce a DTH response in man at doses which do not cause unacceptable side effects.—Authors' Abstract

Imaeda, T. and Imaeda, H. Electron microscopy of *Mycobacterium leprae* in cutaneous nerve components. Cutis **37** (1986) 59–61.

Cutaneous nerves in lepromatous lesions from 96 patients were observed by electron microscopy. The regenerative process of myelinated fibers was evident within lepromatous tissues. Intact or degenerative forms of *Mycobacterium leprae* were surrounded by the electron transparent substance within the axoplasm and Schwann cell cytoplasm. In contrast, the microenvironment of *M. leprae* in macrophages was characterized with fusing lysosomes and foamy structures. These results suggest that the electron transparent substance may be derived from bacterial metabolites and also that the foamy structure may originate from lysosomal substance.—Authors' Abstract

Ivanyi, J., Morris, J. A. and Keen, M. Studies with monoclonal antibodies to mycobacteria. In: *Monoclonal Antibodies Against Bacteria.* London: Academic Press, Inc., 1985, vol. 1, chapter 3.

This chapter presents an interim review of the basic characteristics of monoclonal antibodies and of the corresponding antigens of *Mycobacterium tuberculosis, M. leprae,* and *M. bovis.* Several of the described antibodies defined quasi species-specific determinants on protein antigens. A combination of antibodies of a narrow crossreactivity spectrum will be suitable for the serotyping of multiple mycobacterial species. The potential for the serological definition of strain variants has also been indicated. The molecular weights of antigens were determined by the SDS–gel electrophoresis–immunoblot technique. The study of the mutual topographical relationship of epitopes on molecules or on their soluble complexes has been approached by antibody competition and immunoradiometric assays. Partial purification of two *M. leprae*-specific antigens [MY1 (12K) and MY2 (35K)] has been achieved by affinity chromatography. The results of pilot studies on the application of monoclonal antibodies for the serological diagnosis of tuberculosis and leprosy have been briefly reviewed.—Authors' Summary

Jones, R. L. and Ryan, T. J. Demonstration of leprosy bacilli in the eyes of experimentally infected armadillos: a comparison of five melanin bleaching methods. Med. Lab. Sci. **43** (1986) 211–214.

While leprosy bacilli are known to invade the eyes of experimentally infected armadillos, the presence of overlying melanin can hinder full interpretation of bacillary numbers and morphology. Five melanin bleaching methods have each been combined with a modified Fite-Faraco stain for leprosy bacilli. Only two of these successfully decolorized the melanin although none of the methods adversely affected the quality of staining of *Mycobacterium leprae.* The successful bleaching methods clearly revealed many more bacilli within the choroid, ciliary body and iris.—Authors' Abstract

Kaplan, G., Nathan, C. F., Gandhi, R., Horwitz, M. A., Levis, W. R. and Cohn, Z. A. Effect of recombinant interferon-γ on hydrogen peroxide-releasing capacity of monocyte-derived macrophages from patients with lepromatous leprosy. J. Immunol. **137** (1986) 983–987.

Monocyte-derived macrophages from 14 patients with lepromatous leprosy respond to rIFN-γ with an enhanced secretion of H_2O_2 in a fashion similar to that of cells obtained from normal donors. The activation is not dependent on the cutaneous bacterial index, the length of treatment, or the stage and activity of the disease. H_2O_2 release can be triggered in these cells both by phorbol myristate acetate and by intact irradiated *Mycobacterium leprae.* Uptake of *M. leprae* by both normal donors' and patients' macrophages is proportional to the number of bacilli added. Prior ingestion of *M. leprae* does not interfere with the ability of macrophages to respond to IFN-γ by the production of oxygen intermediates. We conclude that the immune defect in lepromatous leprosy probably results from a lack of response to *M. leprae* by the patients' T cells rather than an inability of mononuclear phagocytes to respond to IFN-γ.—Authors' Abstract

Kingston, A. E., Stagg, A. J. and Colston, M. J. Investigation of antigen cross-reactivity of *Mycobacterium leprae*-reactive murine T-cell lines and clones. Immunology **58** (1986) 217–223.

Inguinal lymph node lymphocytes from BALB/c mice immunized intradermally with 10^8 ^{60}Co-irradiated *Mycobacterium leprae* were cloned by limiting dilution culture. In general, cloned T-cell lines exhibited helper-type activity producing interleukin-2, macrophage activation factor and γ-interferon and lines were further characterized in terms of their crossreactivities with other species of mycobacteria. *M. leprae* clones derived after a period of *in vitro* restimulation were found to crossreact with other species of mycobacteria probably recognizing nonspecific or closely related common cell-wall associated mycobacterial determinants. On the other hand, lines established by cloning directly from immune mice appeared more *M. leprae*-specific, exhibiting antigen-dependent lymphokine production and proliferation *in vitro*.—Authors' Summary

Levis, W. R., Meeker, H. C., Schuller-Levis, G., Sersen, E. and Schwerer, B. IgM and IgG antibodies to phenolic glycolipid I from *Mycobacterium leprae* in leprosy: insight into patient monitoring, erythema nodosum leprosum, and bacillary persistence. J. Invest. Dermatol. **86** (1986) 529–534.

Serum IgM and IgG antibodies against *Mycobacterium leprae*-derived phenolic glycolipid-I (PG) were determined in leprosy patients, contacts, and controls by enzyme-linked immunosorbent assay (ELISA). Anti-PG IgM levels increased from the tuberculoid (TT) to the lepromatous (LL) pole of the disease spectrum. There was a positive linear correlation between anti-PG IgM and bacillary index (BI). Patients with erythema nodosum leprosum (ENL) had lower levels of serum anti-PG IgM than non-ENL patients of comparable BI, suggesting that anti-PG IgM is involved in the pathogenesis of ENL. Initial observations indicate that high anti-PG IgM levels in bacillary-negative patients might reflect bacillary persistence. A study of two different substrate reagents in the ELISA [2,2′-azino-di-(3-ethyl-benzthiazoline-6-sulfonic acid) (ABTS), 0.1 mM H_2O_2, serum diluted 1:20, and *o*-phenylenediamine (OPD), 5 mM H_2O_2, serum diluted 1:300] showed generally good correlation in detection of anti-PG IgM. However, the OPD system detected more paucibacillary disease (BT), while the ABTS system detected the significant effect of ENL on the relationship between BI and anti-PG IgM. Anti-PG IgM was clearly dominant over anti-PG IgG. However, certain patients, including several patients who had upgraded from LL and borderline lepromatous leprosy (BL), showed high levels of anti-PG IgG. Since studies have shown that LL patients are selectively deficient in cell-mediated immunity, T-cell products may be required for the IgM to IgG isotype switch. We conclude that anti-PG IgM is useful for monitoring the bacillary load in individual patients and should prove useful for leprosy control strategies.—Authors' Abstract

Luo, J., *et al.* [A practical observation of spectral classification for leprosy in dermatohistopathology.] China Lepr. J. **1** (1985) 37–41. (in Chinese)

In this article, 126 cases of leprosy were classified by Ridley-Jopling classification spectrum. The results indicated that the skin lesions could be classified exactly with Ridley-Jopling classification only in the untreated cases with sufficiently developed lesions. The coincidented rate of diagnoses between clinic and histopathology was 59%. The variation mainly occurred between neighboring types. Fifty of the 126 cases were examined with lymphocyte transformation test (LTT) with *Mycobacterium leprae* as antigen. The results indicated that the same types showed remarkable variation in LTT reaction. When the LTT was strongly positive, the histopathologic pictures of lesions might show significant inflammation of delayed hypersensitivity. Mean value of LTT reactions in all types did not show immunological spectral characteristics. Strength of LTT reactions had no obvious relation with the amount of infiltrate with lymphocytes in lesions.—Authors' English Abstract

Miller, R. A., Collier, A. C., Buchanan, T. M. and Handsfield, H. H. Seroepidemiologic screening for antibodies to LAV/HTLV-III in Sri Lanka, 1980–1982. (Letter) N. Engl. J. Med. **313** (1985) 1352–1353.

An additional finding in our study was the absence of serologic false-positive results among the patients with leprosy. The intense polyclonal B-cell stimulation present in multibacillary leprosy frequently results in false-positive tests for syphilis or in the production of autoantibodies. Since the prevalence of leprosy exceeds 1% in regions of many developing countries in Asia and central Africa, the clinical utility of the assay for LAV/HTLV-III would be compromised in these settings if crossreacting antibodies were frequently present in patients with leprosy. Fortunately, the specificity of commercial ELISA kits does not appear to be adversely affected by infection with *Mycobacterium leprae.*—(*From* the Letter)

Mistry, N. F., Birdi, T. J. and Antia, N. H. *M. leprae* phagocytosis and its association with membrane changes in macrophages from leprosy patients. Parasite Immunol. **8** (1986) 129–138.

Abnormal phagocytosis of *Mycobacterium leprae* by macrophages of lepromatous patients was demonstrated under various conditions. The largest proportion of macrophages with an excessive bacterial load belonged to the lepromatous group of patients. Lepromatous macrophages treated with cytochalasin B, an inhibitor of phagocytosis, exhibited a significantly lower degree of ingestion of heat-killed organisms; whereas uptake of "viable" organisms was not affected to the same extent. Regulation of phagocytosis was studied by noting the rate of phagocytosis of *M. leprae* after the ingestion of a primary particle, i.e., carbonyl iron. Solely in lepromatous macrophages, phagocytosis of carbonyl iron did not result in a decreased uptake of *M. leprae,* implying aberrant phagocytic activity. Lastly, excessive phagocytosis was always noted in macrophages of familial contacts of leprosy patients who displayed decreased Fc receptor expression after *M. leprae* ingestion. This is of interest since phagocytosis, like Fc receptor expression, is a membrane-dependent event and other membrane-associated defects have been recognized by us earlier in lepromatous macrophages.—Authors' Summary

Modlin, R. L., Kato, H., Mehra, V., Nelson, E. E., Fan, X., Rea, T. H., Pattengale, P. K. and Bloom, B. R. Genetically restricted suppressor T-cell clones derived from lepromatous leprosy lesions. (Letter) Nature **322** (1986) 459–460.

Leprosy is a spectral disease in which immune responses to *Mycobacterium leprae* correlate with the clinical, bacteriological and histopathological manifestations of disease, so study of its pathology provides insights into immunoregulatory mechanisms in man. At the tuberculoid pole, patients have few lesions in the skin which contain rare organisms and are able to mount strong cell-mediated immune responses to *M. leprae* antigens. In contrast, at the lepromatous pole, patients have disseminated skin lesions containing large numbers of acid-fast bacilli and are selectively unresponsive to antigens of *M. leprae. M. leprae*-induced suppressor cells derived from peripheral blood have been reported to be active *in vitro,* yet their *in vivo* significance has remained unclear. Because the focal point of the immune response to *M. leprae* is the skin lesion consisting of lymphocytes and macrophages, we have recently developed methods for isolating lymphocytes from skin biopsies of leprosy patients. We report here that two T8 clones derived from lepromatous leprosy skin biopsies, in the presence of lepromin, suppress concanavalin A (ConA) responses both of peripheral blood mononuclear cells and of T4 clones in an HLA-D (HLA, histocompatibility locus antigen)-restricted manner. Moreover, these T8 clones suppressed responses of HLA-D-matched, but not HLA-D-mismatched antigen-responsive T4 clones to *M. leprae* antigens, indicating that T-cell suppression is major histocompatibility complex (MHC)-restricted at some level in man.—Authors' Abstract

Murphy, G. F., Sanchez, N. P., Flynn, T. C., Sanchez, J. L., Mihm, M. C., Jr. and Soter, N. A. Erythema nodosum leprosum: nature and extent of the cutaneous microvascular alterations. Am. Acad. Dermatol. **14** (1986) 59–69.

Skin biopsy specimens from four patients with erythema nodosum leprosum (ENL),

when examined as Epon-embedded, 1-μm sections, exhibited a necrotizing vasculitis involving capillaries, venules, and small-to-medium arteries and veins. In the superficial dermis, affected venules and capillaries showed endothelial cell enlargement and focal necrosis associated with perivascular infiltrates of lymphocytes. In the deep dermis and subcutaneous tissue, affected venules, arterioles, and arteries exhibited endothelial cell necrosis and matted fibrin in the vessel walls associated with perivascular infiltrates of neutrophils. Throughout the dermis, mononuclear phagocytes with vacuoles containing numerous fragmented organisms were observed. By electron microscopy, electron-dense material resembling immune complexes was observed in the walls of these vessels. These observations support the concept that ENL is an immune complex-mediated necrotizing vasculitis involving capillaries, arterioles, arteries, venules, and veins.—Authors' Abstract

Nathan, C. F., Kaplan, G., Levis, W. R., Nusrat, A., Witmer, M. D., Sherwin, S. A., Job, C. K., Horowitz, C. R., Steinman, R. M. and Cohn, Z. A. Local and systemic effects of intradermal recombinant interferon-γ in patients with lepromatous leprosy. N. Engl. J. Med. **315** (1986) 6–15.

Evidence that interferon-γ may be a physiologic macrophage-activating factor, and that macrophage activation may be defective in lepromatous leprosy, led us to test the effects of intradermal injection of low doses of recombinant interferon-γ in six patients with this disease.

Interferon-γ, 1 or 10 μg, was administered daily by jet gun for 3 days into a single cutaneous lesion. A biopsy specimen was taken from the injection site on the sixth study day and compared with specimens obtained previously from a site where no injection had been made or where excipient alone had been injected in the same way as the interferon. Interferon-γ elicited local effects similar to certain features of delayed-type hypersensitivity reactions or tuberculoid leprosy, including induration, T-cell and monocyte infiltration, keratinocyte proliferation, diminution of epidermal Langerhans' cells, and dermal and epidermal cell HLA-DR (Ia) antigen expression. At some of the sites of interferon-γ injection, there was also an apparent decrease in acid-fast bacilli. Before treatment, monocytes from patients with lepromatous leprosy released 48% as much hydrogen peroxide as did monocytes from controls in response to phorbol myristate acetate, and 36% as much as those from controls in response to *Mycobacterium leprae.* When recombinant interferon-γ was injected, these responses became normal. No toxic effects were observed.

These observations suggest that interferon-γ can mediate certain manifestations of delayed-type hypersensitivity or cell-mediated immunity *in vivo,* and that recombinant interferon-γ should be tested for possible therapeutic effects in certain nonviral infectious diseases.—Authors' Abstract

Nye, P. M., Stanford, J. L., Rook, G. A. W., Lawton, P., MacGregor, M., Reily, C., Humber, D., Orege, P., Revankar, C. R., Terencio de las Aguas, J. and Torres, P. Suppressor determinants of mycobacteria and their potential relevance to leprosy. Lepr. Rev. **57** (1986) 147–157.

This paper extends our studies of the local and distant suppressions of skin-test responses to mixed mycobacterial reagents previously demonstrated in Nepal and Bombay. Several new mixtures were prepared, which included DEAE-separated fractions of a sonicate of *Mycobacterium vaccae* (vaccin). Local suppression was a major feature of the results in all the centers except Kopri in Bombay. All of the vaccin fractions were capable of inducing local suppression. Distant suppression associated with all the fractions was observed at one of the Bombay centers, but not the other ($p < 0.00001$). In Kenya distant suppression also occurred at only one of the centers ($p < 0.00003$), but at this center it was associated significantly with only 2 of the 5 fractions tested ($p < 0.001$ in each case).

Our results may well depend on geographical differences probably associated with the quantity and quality of sensitization by fast-growing environmental mycobacteria. The possibly essential part played by suppressor determinants within the fractions described in the initial infection with

M. leprae and in the pathogenesis of multibacillary disease is discussed.—Authors' Summary

Ottenhoff, T. H. M., Elferink, D. G., Klatser, P. R. and de Vries, R. R. P. Cloned suppressor T cells from a lepromatous leprosy patient suppress *Mycobacterium leprae* reactive helper T cells. (Letter) Nature **322** (1986) 462–464.

Leprosy is a chronic infectious disease caused by *Mycobacterium leprae.* A characteristic feature of the disease is its remarkable spectrum of clinical symptoms correlating with the cellular immune responsiveness of the patient. At one pole of this spectrum are tuberculoid patients displaying both acquired cell-mediated immunity and delayed-type hypersensitivity against the bacillus. At the other pole are lepromatous patients who show a specific T-cell unresponsiveness against *M. leprae.* In between those two poles variable degrees of tuberculoid and lepromatous features may be seen in borderline leprosy patients. Thus far, studies on the mechanism of the antigen-specific unresponsiveness in lepromatous leprosy have been contradictory and difficult to interpret, probably because of the use of heterogeneous cell populations in those experiments. We have now succeeded in cloning *M. leprae* stimulated T-helper (Th) as well as T-suppressor (Ts) cells from a borderline lepromatous patient. The Ts clones of this patient specifically suppress responses of peripheral Th cells as well as Th clones induced by both *M. leprae* and other mycobacteria, but not unrelated antigen or mitogen. These Ts cells also completely suppress Th cell responses against a *M. leprae*-specific protein with a relative molecular mass of 36,000 (36K), suggesting the presence of a suppression inducing determinant on this 36K *M. leprae* protein.—Authors' Abstract

Patil, S. A., Sinha, S. and Sengupta, U. Detection of mycobacterial antigens in leprosy serum immune complex. J. Clin. Microbiol. **24** (1986) 169–171.

The antigens from immune complexes of sera from patients with mycobacterial diseases were released by sodium dodecyl sulfate. The antigenic activity of the released proteins was tested by agar gel diffusion and immunoelectrophoresis. This simple method provided direct evidence for the presence of mycobacterial antigens in the immune complexes of sera from patients with leprosy and tuberculosis.—Authors' Abstract

Rea, T. H., Shen, J.-Y. and Modlin, R. L. Epidermal keratinocyte Ia expression, Langerhans cell hyperplasia and lymphocytic infiltration in skin lesions of leprosy. Clin. Exp. Immunol. **65** (1986) 253–259.

Epidermal changes, Ia expression on keratinocytes, Langerhans' cell hyperplasia, and lymphocyte infiltration were sought in skin lesions of leprosy: 15 borderline tuberculoid (BT), 6 borderline lepromatous (BL), 17 lepromatous (LL), 13 erythema nodosum leprosum (ENL), 6 Lucio reactions and 9 reversal reactions. All three changes were well developed in BT and reversal reactions. ENL showed well-developed keratinocyte Ia and Langerhans' cell hyperplasia, but little lymphocytic infiltration. LL and Lucio tissues had some Langerhans' cell hyperplasia but little or no keratinocyte Ia or lymphocytic infiltration. BL tissues were so diverse as to suggest two distinct subgroups. These findings are consistent with the hypothesis that keratinocyte Ia expression is an immunohistological sign of a cell-mediated immune (CMI) response. However, the Ia keratinocyte expression found in BL and ENL tissues appears contrary to the undifferentiated macrophages and numerous bacilli found in the lesions. Thus, if a sign of CMI, keratinocyte Ia expression is not a measure of the effectiveness of the response.—Authors' Summary

Ridel, P.-R., Jamet, P., Robin, Y. and Bach, M.-A. Interleukin-1 released by blood-monocyte-derived macrophages from patients with leprosy. Infect. Immun. **52** (1986) 303–308.

In highly purified blood-monocyte-derived macrophages collected from patients with leprosy and from healthy individuals and cultured *in vitro* with mycobacterial antigens such as *Mycobacterium bovis* BCG or *M. leprae,* we nonspecifically induced the

synthesis of interleukin-1. Normally, all supernatants from cultured macrophages of all subjects tested produced similar amounts of interleukin-1. However, only in patients with lepromatous leprosy, *M. leprae,* but not BCG, induced high-level synthesis of prostaglandin E_2, which acted as a suppressor factor in the mouse thymocyte proliferative assay used to measure the interleukin-1 content of the supernatants. Normal interleukin-1 content of those supernatants was demonstrated by blocking the prostaglandin E_2 synthesis by the addition of indomethacin to the medium throughout the experimental procedure. We also tested the efficiency of a combination of BCG and *M. leprae* in reducing the prostaglandin E_2 synthesis, but with the methodology used, we did not observe any beneficial effect of such a combination. These results demonstrate the possible role of *M. leprae* in the induction of at least one of the suppressive monokines and are additional arguments for the involvement of macrophages in the suppression of the specific cell-mediated immunity to *M. leprae* observed in lepromatous leprosy.—Authors' Abstract

Roy, A. Serological study of leprosy employing ELISA with arabinogalactan of *Mycobacterium smegmatis* as antigen. Lepr. Rev. **57** (1986) 137–145.

An ELISA has been developed for detecting circulating antibodies in leprosy sera using arabinogalactan, a cell-wall polysaccharide of *Mycobacterium smegmatis* as the antigen. In normal sera, arabinogalactan-specific IgM is higher than IgG; whereas in untreated leprosy sera anti-arabinogalactan (AG) IgG is more than the corresponding IgM. With long-term treatment of the disease, IgM level goes up compared to IgG.—Author's Summary

Shankar, P., Agis, F., Wallach, D., Flageul, B., Cottenot, F., Augier, J. and Bach, M.-A. *M. leprae* and PPD-triggered T cell lines in tuberculoid and lepromatous leprosy. J. Immunol. **136** (1986) 4255–4263.

Proliferative responses of peripheral blood mononuclear cells (PBMC) to *Mycobacterium leprae* and bacillus Calmette Guèrin-derived purified protein derivative (PPD) were studied in the presence or absence of interleukin-2 (IL-2) in high *M. leprae* responders (tuberculoid leprosy patients and healthy subjects) and low *M. leprae* responders (lepromatous leprosy patients). High responders in most cases developed a strong proliferative response to both antigens in the absence of IL-2. Additional IL-2 and restimulation with antigen plus autologous antigen-presenting cells (APC) allowed the derivation of antigen-specific T-cell lines. The lines were assayed for proliferative responses to several mycobacterial antigens. Both PPD and *M. leprae*-triggered T-cell lines exhibited a good proliferative response to either antigen and showed in addition a broad crossreactivity with other mycobacteria, suggesting a preferential T-cell response to epitopes shared by several mycobacterial species. Within the lepromatous group, 50% of the patients studied could mount a proliferative response to PPD antigen in the absence of IL-2, but none of them was able to do so with *M. leprae* antigen. The addition of IL-2 increased the number of positive responders to PPD in this group, and in some patients IL-2 was able to restore *M. leprae* reactivity as well, suggesting that IL-2 had overcome a suppressor mechanism. PPD and *M. leprae*-triggered T-cell lines were obtained from these subjects (with IL-2 added from the beginning of the culture when required). *M. leprae* lines exhibited variable and unstable patterns of specificity, most lines exhibiting, at least transiently, a crossreactive response to other mycobacteria, but some displaying only *M. leprae*-specific response. In contrast, PPD lines from these subjects consistently exhibited a good response to PPD, a lesser response to various other mycobacteria and no response to *M. leprae,* a pattern differing from that obtained with PPD lines of high *M. leprae* responders. Co-cultures of irradiated lepromatous PPD triggered T-cell lines with fresh autologous PBMC nonspecifically reduced the proliferative response of the latter to PPD, as well as to unrelated antigens. A similar suppression was also observed when PPD lines from one of the tuberculoid patients were assayed. PPD and *M. leprae* T-cell lines from both high and low responders initially exhibited the same $CD4^+$ $CD8^-$ phenotype. In all

cases, antigenic specificity declined and could not be maintained after 5 to 8 wk of continuous culture, a change associated with the progressive appearance of $CD8^+$ and Leu-8^+ cells.—Authors' Abstract

Shi, Y., *et al.* [Observation of skin lesions of leprosy with DIF technique.] China Lepr. J. **1** (1985) 26–28. (in Chinese)

In this paper, immunopathologic features in skin lesions of 27 patients with leprosy were observed with DIF technique. The results were: band-like deposits of IgG and IgM were present at BMZ in two BT patients, and IgM deposits at BMZ in one BL patient. In most cases from BT to BL, IgM and C3 deposits were found in the dermal vascular walls. No deposit was found in skin lesions of two I and three TT patients, and no deposits of IgA were shown in skin lesions of any of the patients. These findings might be significant for further study on pathogenesis of leprosy.—Authors' English Abstract

Wu, Q., *et al.* [Preliminary study on serological activity of phenolic glycolipid and its applications in diagnosis of leprosy.] China Lepr. J. **1** (1985) 1–5. (in Chinese)

In this article, we conducted: a) a study on comparisons of serological activity between phenolic glycolipid (PGl) and its terminal sugar which is a synthetic antigen conjugated to bovine gamma globulin. The sera for comparison were collected from leprosy patients (182 cases), tuberculosis patients (20 cases), and normal persons (108 cases in nonendemic areas of leprosy). The results indicated that there are highly significant positive correlation (rBGG = 0.9953, $p < 0.0005$) between them, and their MOD values in sera from normal persons are similar to those of sera from tuberculosis patients. These suggested that PGl–ELISA and BGG–ELISA are highly specific for detection of infection with *Mycobacterium leprae* (ML). When comparison of PGl–ELISA with ML–ELISA was performed, the similar sensitivity of two tests to sera from leprosy patients was found. These suggested that PGl–ELISA and BGG–ELISA are as highly sensitive as ML–ELISA to sera from leprosy patients. For these reasons, either PGl–ELISA or BGG–ELISA is highly sensitive and specific for detection of infection with *M. leprae.* b) A study on correlation of PGl–ELISA with ML–ELISA and FLA-ABS. T. The results indicated that they are also of highly significant positive correlation (rFLA–ABS. T = 0.945, $p < 0.01$; rML–ELISA = 0.972, $p < 0.005$). c) A study on blocking nonspecific binding. The results indicated that conventional BSA and GS can be replaced with EA. The efficiency of EA is not only equal to BSA and GS, but also facile, cheaper, and easier to get. Therefore, the authors suggest popularizing the application of EA for blocking nonspecific binding in ML–ELISA and PGl–ELISA or BGG–ELISA.—Authors' English Abstract

Microbiology

Bloom, B. R., Mehra, V. and Young, R. A. Genes for the protein antigens of the tuberculosis and leprosy bacilli. Biosci. Rep. **5** (1985) 835–846.

The λgt11 expression vector permitted us to survey protein antigens of *Mycobacterium leprae* and *M. tuberculosis* expressed in *Escherichia coli.* Using monoclonal antibodies, recombinant clones were detected producing three major antigens of *M. tuberculosis* and five major protein antigens of *M. leprae.* These recombinant antigens produced in *E. coli* should prove useful for diagnosis, epidemiology and possibly the development of recombinant mycobacterial vaccines.—Authors' Abstract

Brett, S. J., Payne, S. N., Gigg, J., Burgess, P. and Gigg, R. Use of synthetic glycoconjugates containing the *Mycobacterium*

leprae specific and immunodominant epitope of phenolic glycolipid I in the serology of leprosy. Clin. Exp. Immunol. **64** (1986) 476–483.

The high specificity of phenolic glycolipid I (PG-I) in the identifying individuals with leprosy appears to be attributable to the species-specific trisaccharide region of the molecule. Synthetic glycoconjugates were produced by coupling the corresponding terminal mono- or disaccharide to bovine serum albumin by reductive amination. Conjugates which contained only the terminal sugar maintained in its pyranose form, the terminal disaccharide with only the terminal sugar in its pyranose form and the terminal disaccharide with both the 3,6,di-*o*-Me-glucose and 2,3,di-*o*-Me-rhamnose sugars in their pyranose forms, were all highly active in the enzyme-linked immunosorbent assay (ELISA) and showed good concordance with native PG-I in analysis of sera from leprosy patients. The antibody levels to the glycoconjugates in tuberculosis patients and patients with other mycobacterial infections were not significantly different from the levels in normal healthy control subjects. A few of the leprosy sera showed much stronger binding to conjugates which contained the disaccharide with both sugars in the pyranose form than to conjugates with only the terminal sugar in its pyranose form. Therefore, a synthetic conjugate which contains the intact disaccharide region of PG-I may provide the most sensitive antigen for the large scale serodiagnosis of leprosy.—Authors' Summary

Chatterjee, B. R. and Roy, R. D. Growth of *Mycobacterium leprae* in a redox system: II. Further improvements in the system and growth efficiency. Indian J. Lepr. **57** (1985) 739–749.

Improvement of the redox system for growth of *Mycobacterium leprae* as brought about by modification in the concentration and mode of preparation of individual media constituents, and by addition of newer substances, is being reported. A structural modification in the construction of the Thunberg's tubes and flasks that are used as culture vessels has been introduced for ease of handling. Vitamin E (α-tocopherol) has been found to be useful. Concentrations of liposomes and gelatin in the medium could be reduced by at least fivefold, considerably easing thereby smearing and harvesting of cultures. Dimercaptopropanol (British anti-lewisite or BAL) has been used, but its usefulness or otherwise is yet to be determined conclusively. The basis of intracellular parasitism of *M. leprae* has been discussed.—Authors' Abstract

Fujiwara, T., Hunter, S. W. and Brennan, P. J. Chemical synthesis of disaccharides of the specific phenolic glycolipid antigens from *Mycobacterium leprae* and of related sugars. Carbohydrate Res. **148** (1986) 287–298.

O-(3,6-Di-*O*-methyl-β-D-glucopyranosyl)-(1→4)-2,3-di-*O*-methyl-L-rhamnopyranose, which is the nonreducing disaccharide of the haptenic trisaccharide of the *Mycobacterium leprae*-specific, phenolic glycolipid-I, *O*-(6-*O*-methyl-β-D-glucopyranosyl)-(1→4)-2,3-di-*O*-methyl-L-rhamnopyranose, the nonreducing end of the specific, phenolic glycolipid-III, and the nonhaptenic *O*-β-(D-glucopyranosyl)-(1→4)-2,3-di-*O*-methyl-L-rhamnopyranose, were synthesized in relatively good yield from 3-*O*-methyl-D-glucose, or D-glucose, and L-rhamnose via Koenigs-Knorr reactions. These disaccharides can be used as precursors in the synthesis of the trisaccharide unit of phenolic glycolipid-I and of neoglycoconjugates suitable for the serodiagnosis of leprosy.—Authors' Abstract

Hunter, S. W., Stewart, C. L. and Brennan, P. J. Antigenic carbohydrates of the leprosy bacillus. Fed. Proc. **44** (1985) 1407.

The major immunogens of *Mycobacterium leprae* are carbohydrate-based, either phenolic glycolipids or ill-defined polysaccharides. To better elucidate the immunochemistry of the latter, *M. leprae,* isolated from infected armadillo tissue was extracted with 70% ethanol and extracts fractionated on Bio-Gel P-6 to reveal excluded and included carbohydrate-containing peaks. The latter represented about 1% of the bacterial mass, and NMR, fast atom bombardment mass spectrometry and sugar analysis indicated a close similarity to the 6-*O*-meth-

ylglucose-containing lipopolysaccharide described by Ballou, *et al.* The Bio-Gel P-6 excluded material was anionic and was further fractionated on DEAE-Sephacel to yield three subfractions (A, B, and C). Fraction B with a MW >500 kD, according to Sephacryl gel filtration, contained 83% carbohydrate (all Ara, Man), 2.25% amino compounds (mostly Gly, Glu, Ala), and 2.28% PO_4^- in a molar ratio of 27:1:1.4. This unique anionic glycoconjugate is one of the dominant immunogens of the leprosy bacillus.—Authors' Abstract

Kato, L. A culture medium for cultivation of mycobacteria, probably *Mycobacterium leprae* from *Mycobacterium leprae* infected tissues. Indian J. Lepr. **57** (1985) 728–738.

Mycobacterium leprae suspensions were prepared from infected armadillos. The *M. leprae* cells were inoculated into culture media containing KH_2PO_4 4.7 g, Na_2HPO_4 2 g, sodium thioglycolate 1 g, $(NH_4)_2SO_4$ 2 g, $MgSO_4$ 0.1 g, ferric ammonium citrate 0.05 g, and lipoic acid (thioctic acid) 0.1 g in one liter distilled water. The solution was enriched with heat-killed, sonicated leprosy derived *Mycobacterium X* or crude mycobactin extract from *M. phlei* to contain + 0.2 μg mycobactin per 1 ml in the final medium. Twenty ml media was distributed into each of 25 ml screw cap tubes and autoclaved for 30 min. Positive growth was obtained from 7 out of 10 specimens when incubated at 34°C. The cultures developed as a sediment in the liquid media, suggesting preference for microaerophilic conditions. No growth was seen on the surface of the semi-solid agar media containing the same ingredients. Latency period of growth was estimated as 10–16 days and time of division as 6 days. Subcultures were obtained. Cells were long, acid-fast, arranged side by side or end to end, with a tendency to form long spiral cords or clumps when sedimented on siliconized slides. Pyridine extraction eliminated acid-fastness, but not gram positivity. Cultures did not grow on Dubos, Lowenstein or 7H10 media. They produce the disease in the foot pads of mice characteristic of *M. leprae.* Subcultures remain dependent on the heat-killed sonicated mycobacteria, or crude mycobactin extract, and reduced oxygen tension in the media. Results suggest that cultures might be identical to *M. leprae.*—Author's Abstract

Kovalenko, I. V. and Dorozhkova, I. R. [Substantiation and development of immunofluorescent techniques for the detection and identification of the L-form of mycobacteria.] Zh. Mikrobiol. Epidemiol. Immunobiol. **6** (1986) 35–38. (in Russian)

The complement fixation test and the immunofluorescence test have demonstrated that the L-forms of mycobacteria retain their species-specific and genus-specific determinants and possess serological activity. The L-variants obtained by different methods differ in size, depending on the degree of the destruction of their cell wall. Specific antisera to the L-forms of mycobacteria, suitable for use in the indirect immunofluorescence test, have been obtained. These antisera are highly specific and permit not only the rapid detection, but also identification of the L-forms.—Authors' English Summary

Lu, F., *et al.* [Multiplication of *Mycobacterium lepraemurium* in mouse peritoneal macrophages *in vitro.*] Chin. J. Dermatol. **19** (1986) 63–66. (in Chinese)

Mouse peritoneal macrophages survive a long period *in vitro* in a medium composed of TC199 supplemented with 40% pooled swine serum. A lag phase of multiplication of *Mycobacterium lepraemurium* in cell culture was observed during the first 2–4 weeks after inoculation, then followed with a logarithmic phase. The 95% confidence limit of doubling time of the organism in the latter phase is 4.9–5.5 days. The retardation and the rapidity of the growth of the organism during the two different phases are neither related to cellular acid phosphatase activity nor to the longevity of cells in culture. The growth of organisms is suppressed by the addition of rifampin or streptomycin in culture medium.—Authors' English Abstract

Prabhakaran, K. Biochemical studies on *Mycobacterium leprae.* J. Basic Microbiol. **26** (1986) 117–126.

Very little information is available on the basic biology of *Mycobacterium leprae.* It is not known why the organism fails to grow in bacteriological media or in cell cultures and why it has an unusual predilection for certain tissues in the human host where cells derived from the neural crest occur (e.g., skin, peripheral nerves, adrenal medulla). Biochemical studies have revealed that *M. leprae* contains an unusual form of the enzyme diphenoloxidase which has not been detected in other mycobacteria. The presence of a specific glutamic acid decarboxylase in the organism has been demonstrated. Although a few enzymes of glycolysis and tricarboxylic acid cycle have been investigated, nothing characteristic of the bacterium has been discovered, and how *M. leprae* derives energy for its survival and proliferation still remains obscure.—Author's Abstract

Singh, N. B., Srivastava, K., Gupta, H. P., Srivastava, A. and Mathur, I. S. Draining lymph node enlargement produced by immunogenic strains of cultivable mycobacteria. Indian J. Lepr. **58** (1986) 38–42.

Lymph node enlargement produced by strains of mycobacteria has a direct bearing on the immunogenicity characteristics. Two strains of mycobacteria namely *Mycobacterium habana* TMC 5135 and *M. marinum* (SATO) have been studied for their property to produce enlargement of draining lymph nodes besides other cell-mediated immune responses. Both strains are capable of producing the enlargements of inguinal and popliteal lymph nodes which is very significant. The enlargements of lymph nodes have been produced by these strains both in the live as well as killed state. Possibility of developing these strains as vaccine against leprosy has been discussed.—Authors' Abstract

Experimental Infections

Dhople, A. M. Armadillo as a model for studying chemotherapy of leprosy: preliminary studies. Indian J. Lepr. **58** (1986) 19–28.

In order to determine the suitability of the armadillo as a model of human leprosy for chemotherapeutic studies, especially in evaluating newer antileprosy drugs, uninfected armadillos were used to study the metabolic disposition of DDS. Serum DDS levels ranged from 500 ng/ml at 3 hr to 13 ng/ml at 96 hr after intravenous administration of DDS (1 mg/kg). In an *ad libitum* feeding trial of DDS it was found that the level of serum DDS varied according to the dose of DDS, and even at a dose of 0.0001%, the animals maintained MIC of DDS against *Mycobacterium leprae.* Finally, it was demonstrated that armadillos acetylate DDS to MADDS and 7–9% of DDS is acetylated by armadillos.—Author's Abstract

Dhople, A. M., Kazda, J., Green, K. J. and Storrs, E. E. Presence of "difficult to isolate" mycobacteria in armadillos. Indian J. Lepr. **58** (1986) 29–37.

Contrary to the findings with armadillos from Louisiana and Texas, armadillos from Florida are free of natural leprosy-like infection. Examination of ear clip, nasal, blood buffy coat, liver and spleen of inoculated armadillos from Florida did not reveal the presence of any acid-fast bacteria. However, using massive inocula, 6 out of 77 armadillo tissues were found to contain very negligible proportions of cultivable mycobacteria. The significance of these isolates in relation to *Mycobacterium leprae* and also to leprosy research is discussed.—Authors' Abstract

Ha, D. K. K., Lawton, J. W. M. and Gardner, I. D. Evaluation of phagocytic function in *Mycobacterium lepraemurium* in-

fection. J. Comp. Pathol. **96** (1986) 415–424.

Infection of mice with *Mycobacterium lepraemurium* (MLM) caused significant functional alterations of the mononuclear phagocyte system. Accelerated clearance of sheep red blood cells was consistently demonstrated throughout the infection and the infected mice showed progressive anemia. Infected mice showed an enhanced ability to limit growth of phagocytosed *Listeria monocytogenes* in spleens during the early stages of infection; whereas moribund leprous mice lost this ability. Autoradiography showed that uninfected Kupffer cells and splenic macrophages of moribund mice could still phagocytose *Listeria,* suggesting that MLM infection did not affect the capacity of *Listeria* to localize to macrophages but interfered in some way with subsequent killing of such bacteria. The possible mechanisms underlying these observations are discussed.—Authors' Summary

Job, C. K., Sanchez, R. M. and Hastings, R. C. Effect of repeated lepromin testing on experimental nine-banded armadillo leprosy. Indian J. Lepr. **57** (1985) 716–727.

Twenty-eight armadillos were lepromin tested and infected with *Mycobacterium leprae*; 18 intravenously and 10 intradermally. The lepromin test was repeated after 3 months and at intervals of 6 months thereafter until their death or sacrifice up to 30 months. The one animal with tuberculoid lepromin was resistant and 14 of the 16 with lepromatous lepromin developed generalized disease. Of the 11 with borderline lepromin, 6 developed disseminated disease and 5 were resistant. There is a definite relationship between resistance and tuberculoid lepromin in the armadillo. Repeated lepromin testing had no effect in the rate of infection and the course of the disease in animals infected intravenously. In the intradermally infected animals the results were inconclusive. Whereas all the 20 animals with disseminated disease showed lesions in the liver, spleen and lymph nodes, only four animals had sciatic nerve involvement. Peripheral nerve trunk is not necessarily the preferred site in the armadillo. Lung lesions were an important cause of death in lepromatous armadillos.—Authors' Abstract

Modlin, R. L., Ormerod, L. D., Walsh, G. P., Rea, T. H., Meyers, W. M., Binford, C. H., Martin, L. N., Wolf, R. H. and Gormus, B. J. In situ characterization of T lymphocyte subpopulations in leprosy in the mangabey monkey. Clin. Exp. Immunol. **65** (1986) 260–264.

Leprosy in the mangabey monkey is an experimental model which is similar both clinically and histologically to human lepromatous leprosy. The immunopathology of these diseases was compared using monoclonal antibodies against T lymphocyte subpopulations in frozen tissue sections with an immunoperoxidase technique. In both mangabey and human lepromatous granulomas OKT4 (or Leu3a) and Leu2a cells were scattered among macrophages with greater numbers of Leu2a as compared with OKT4 (or Leu3a) cells. The results suggest that from an immunopathological standpoint experimental leprosy in mangabeys will provide a suitable model for the investigation of the pathogenesis of human lepromatous leprosy and for the evaluation of new antileprosy vaccines.—Authors' Summary

Saito, H., Tomioka, H. and Kitagawa, T. The lack of therapeutic effects in mice of the combined gamma-irradiated *Mycobacteria leprae* and viable BCG against *Mycobacterium leprae* infection. Jpn. J. Lepr. **54** (1985) 57–61.

A combined vaccine of heat-killed *Mycobacterium leprae* and BCG protects mice against a challenge infection of *M. leprae* given 4 weeks later. However, the present study shows that a similar combined vaccine, consisting of γ-irradiated *M. leprae* and live BCG given subcutaneously as an immunotherapeutic agent "once biweekly" starting 2 weeks after infection of mice in the foot pad with *M. leprae* and continuing for up to 187 days later, had no significant inhibitory effect on growth of the organisms at the inoculum site.—C. A. Brown (Trop. Dis. Bull.)

Vidyasagar, P. B., Lokhandwalla, M. N. and Damle, P. S. Study of amplitude frequency spectra of compound action potentials recorded from normal and *M. leprae* infected mice using Fourier Series Analysis. Indian J. Lepr. **58** (1986) 58–68.

Compound action potentials recorded from normal and *Mycobacterium leprae*-infected mice sciatic nerves were analyzed in frequency domain using Fourier series analysis. Changes in myelinated fiber potentials were detected as early as 2nd post-inoculation month. This technique could be further developed to aid in early diagnosis of leprosy.—Authors' Abstract

Ye, S., *et al.* [Study on cell culture of *Mycobacterium leprae*: (1) Multiplication of *M. lepraemurium* in mouse peritoneal macrophages *in vitro*.] China Lepr. J. **1** (1985) 21–25. (in Chinese)

The study showed that marked multiplication of *Mycobacterium lepraemurium* could occur in mouse peritoneal macrophages that were cultured *in vitro*. The average number of bacilli per macrophage increased from a few to as much as occupying a whole cell. The growth requirements of *M. lepraemurium*, such as the cell type, medium, and incubation temperature, are discussed. The experiments might serve as a reference for cell culture of *M. leprae in vitro*.—Authors' English Abstract

Epidemiology and Prevention

Barth, V. J. and Dagnow, M. B. [Problems with leprosy care in an Ethiopian highland region.] Z. Klin. Med. **40** (1985) 47–49. (in German)

The following conclusions are drawn from an analysis of the registered leprosy cases of the years 1974 to 1983 in the Ethiopian highland region Gondar: 1. Less than a quarter of the suspected patients are registered by the health authorities. 2. In some years the defaulter rate was higher than that of new detected cases. 3. Detection of new cases and regular treatment of registered patients are of equal importance for the improvement of present situation in leprosy care. 4. These tasks can only be fulfilled by complex realization of different measurements; most of them are depending on a high engagement of qualified health workers.—Authors' English Summary

Blavy, G., Thiam, D., Ndoye, B., Diakhate, L. and Millan, J. [HLA and leprosy in Dakar: distribution of histocompatibility antigens in lepromatous leprosy and relationship with ENL reactions.] Acta Leprol. **4** (1986) 93–99. (in French)

Fifty lepromatous patients, among whom 34 shared repeating ENL reactions, and a reference group of 150 blood donors were typed for HLA antigens. In the comparison of the lepromatous group to the reference group, HLA-B 8 was the only antigen which turned out to be significantly increased within the lepromatous patients. Some changes reported by other authors have also been pointed out (decrease in HLA-A2 and HLA-A3, increase in HLA-AW 23 within the lepromatous patients) but those are not significant in this study. In the lepromatous group itself, not any significant change has been pointed out between the patients sharing ENL and those who did not show any. Nevertheless a nonsignificant increase in HLA-BW 35 in the patients with ENL is pointed out.—Authors' English Summary

Bona, S. H., Fonseca, A. De P., Silva, A. C. L. and Costa, R. L. [Acid-fast bacilli in *Culex quinquefasciatus*.] An. Bras. Dermatol. **60** (1985) 163–170. (in Portuguese)

Writing from the Biomedical and Dermatological Departments of the Federal University of Piauí in Brazil, these authors describe a study concerning the possibility that *Culex quinquefasciatus* (a notorious mosquito vector of filariasis) may be in-

criminated in the transmission of leprosy. They examined 194 mosquitoes from 100 homes of treated leprosy patients (L and B forms) and a further 42 mosquitoes from 19 homes of healthy (nonleprosy) individuals. Standard Ziehl-Neelsen preparations were made from smears of material from mosquito salivary glands, gut, feces and ovaries. In both the leprosy and the healthy (nonleprosy) groups, ". . . numerous bacilli were found in about 90% of the examined slides." Several tables record the bacillary findings in the various organs, classifying them as isolated, grouped or in globi and there are also black and white photomicrographs.

[The authors could not grow these "organisms" on Lowenstein-Jensen medium but they make absolutely no claim that the acid-fast "bacilli" are leprosy bacilli and emphasize that further studies of identification are in hand. These findings must certainly be interpreted with caution; for instance, keratin and chitin in preparations from arthropods may stain red with carbol fuchsin and look like "rods." Nevertheless, the possibility that a vector of filariasis may be concerned in the transmission of leprosy is of considerable interest, not only for South America, but for vast areas of Africa, and these studies should be pursued.]—A. C. McDougall (Trop. Dis. Bull.)

Demenais, F. and Feingold, N. [HLA and leprosy.] Pathol. Biol. (Paris) **34** (1986) 735–737. (in French)

Although there is now accumulating evidence that the host response to *Mycobacterium leprae* is genetically controlled, the nature of the genetic component is still unprecise. Case-control studies as well as family studies, in various populations, have shown that HLA-linked factors confer susceptibility to tuberculoid leprosy and lepromatous leprosy, respectively. Recently, associations between Gm allotypes and the disease have also been reported. Further studies of the familial cosegregation of the different forms of leprosy together with the HLA and Gm markers may permit a better understanding of the underlying genetic mechanisms.—Authors' Summary

Deng, Y., *et al.* [A study of prophylactic effects of DDS against leprosy during 16 years.] China Lepr. J. **1** (1985) 15–17. (in Chinese)

Wenchuan and Mengying districts of Chenggu County in Shanxi Province had a high prevalence of leprosy. Patients from these two districts were treated in the sanitorium, and the family members of Wenchuan patients who had close contacts with leprosy received DDS for 1 year, while those from Mengying served as the control group, not taking DDS.

In the course of 16 years, no new case of leprosy was discovered among the 178 contacts of the group given drugs for prevention. In the control group, there were 147 contacts, and six cases of leprosy were seen. Hence, the difference in incidence between these two groups was statistically significant ($0.05 > p > 0.01$).

The control observation showed clearly that DDS obviously has a long-term prophylactic effect against leprosy for the intrafamily contacts. In particular, oral DDS can control the incidence of leprosy among the family members of the multibacillary patients. The paper further discusses the questions of dosage of DDS and its duration as well as the aim of prevention. It is suggested that the period of observation should be at least as long as 10 years before the prophylactic effects of DDS can be evaluated.—Authors' English Abstract

Fine, P. E. M. The role of BCG in the control of leprosy (the Kellersberger Memorial Lecture, 1985). Ethiop. Med. J. **23** (1985) 179–191.

History has handed us a situation in which a vaccine developed for and widely used against tuberculosis may in some areas be of only marginal effectiveness against that disease. But, at the same time, we discover that this vaccine may be equally or even more effective against leprosy. How should we respond? Despite the published evidence, very few leprosy control programs incorporate BCG in their strategy. The reasons for this ommission are several: they include the traditional bias of leprosy control projects toward treatment of cases; a confusion over how to interpret the results

of the different BCG trials; an ambivalence towards tuberculosis programs for their contribution to prevention of leprosy; and maybe even a reluctance to discuss BCG's value in some circles, for fear it might detract from current efforts to develop an even better vaccine against leprosy. None of these reasons strikes me as sufficient for BCG to be totally neglected by leprosy control programs. I would thus recommend the following response to the current situation. Let us, first, take some delight that nature still holds such surprises for us. Second, let those of us in the field of leprosy thank our colleagues in the tuberculosis field for the gift of BCG—for not only proving that primary prevention against leprosy is a possibility, but for providing and delivering the vaccine. We should recognize that BCG not only has a role in leprosy control but that it is actually playing that role in many countries today.

Lastly, let me encourage researchers to look ever more carefully at this bizarre situation, in particular by defining more clearly and attempting to explain the geographic distribution of BCG's effectiveness. This would be of immense value for both the present and the future of leprosy control. It will help to identify those areas of the world where effective primary prevention against leprosy is now possible, and where BCG should be encouraged by leprosy control services. And it will help to identify those vaccine- or environment-related factors which affect vaccine-derived immunity against leprosy, and which can thereby help to guide current research towards vaccine preparations which can improve upon our old friend BCG.—(*From* the Lecture)

Fine, P. E. M., Ponnighaus, J. M., Maine, N., Clarkson, J. A. and Bliss, L. Protective efficacy of BCG against leprosy in northern Malawi. Lancet **2** (1986) 499–502.

The effectiveness of a BCG vaccination program in protecting against leprosy was assessed by case-control and cohort analyses of data from the Lepra Evaluation Project in Karonga District, northern Malawi. Results indicate that BCG provides at least 50% protection against leprosy in this population and that protection is independent of age, sex, schooling status, or location within the project area. Agreement between these findings and those from a controlled trial in Uganda indicates that BCG is sufficiently effective against leprosy in east and central Africa to be considered an important element of leprosy control in that region.—Authors' Summary

Lwin, K., Sundaresan, T., Gyi, M. M., Bechelli, L. M., Tamondong, C., Gallego Garbajosa, P., Sansarricq, H. and Noordeen, S. K. BCG vaccination of children against leprosy: fourteen-year findings of the trial in Burma. Bull. WHO **63** (1985) 1069–1078.

The value of BCG vaccination in preventing leprosy among children was studied in an area of high leprosy endemicity in Burma through a controlled trial; one group of 13,066 children received BCG and another group of 13,176 served as controls. The overall protective effect of BCG, which was only about 20% over the 14-year period, was found to vary with the batch of vaccine, as well as age, sex, and contact status of the children. BCG protection was found to be independent of the initial tuberculin status of the children. The protective effect of BCG against the lepromatous type of leprosy could not be measured because of the low incidence. Protection was observed throughout the 14 years of the study except for the first year. The results are compared with those of three other major BCG trials in leprosy. The trial has shown that BCG provides only a very modest level of protection and that BCG vaccination is not likely to be an important solution for leprosy control.—Authors' Abstract

Millan, J., Moulin, J. P. and Le Corroller, Y. [Hemotypological study of a leprosy population in Guadeloupe (F.W.I.).] Acta Leprol. **4** (1986) 101–113. (in French)

The target of this survey carried out in Guadeloupe (F.W.I.) is to search for eventual relationship between leprosy forms and ethnic features—made in people subjected to same environmental factors, such a study avoids usual bias of investigations on the epidemiological aspect of "racial" factors.

The 1522 investigated patients have been

divided into two categories: allergic paucibacillaries (Mitsuda +), and anergic multibacillaries (Mitsuda −). Three parameters were studied: morphological type empirically determined according to cutaneous pigmentation; ABO blood groups; and rhesus phenotype.

The results bring to the fore: a) Significant linkage between clinical forms and morphotype: the dominant Caucasian morphological typed subjects, with integument poor in melanin, are more numerous among the multibacillaries. This might confirm high sensitiveness of Caucasians to leprosy. b) No significant linkage between clinical forms and ABO blood groups. Nevertheless, variations are already reported in more homogeneous populations: predominance of A group in multibacillaries, of B and O groups in paucibacillaries. c) Significant linkage between clinical forms and rhesus phenotype. But this link does not seem to be imputable to ethnic factors because clinical forms distribution is the same in $\overline{cc}$Dee subpopulation (the most frequent in western Africa), and in ccddee subpopulation (quite frequent phenotype in western Europe). In fact, only the $\overline{cc}$DEe phenotype subpopulation is significantly different from all the others, because multibacillary forms are particularly frequent (49.3%) and strike evenly women and men in this subpopulation.—Authors' English Summary

Millan, J., Sanokho, A., Camara, M. and Pangou, D. [A school survey in Senegal: considerations of the method and importance of endemic disease in child population of leprosy villages.] Acta Leprol. **4** (1986) 37–49. (in French)

A mass case-finding survey has been carried out among the pupils as a test measure: in an ordinary rural village (2204 examined children; prevalence rate of leprosy: 0.90 per 1000) and in two leprosy villages (333 examined children; prevalence rate of leprosy: 125 per 1000).

The authors have emphasized: a) the difficulty of school survey and the necessity to entrust a skilled staff with this job. b) The general low prevalence of leprosy cases with children in Senegal (0.96 per 1000) inferior to the threshold of 4 per 1000 above which school survey is advised to be carried out. c) The high prevalence rate of leprosy with the children of the leprosy villages (140 times as much as general prevalence rate). This situation could be the result of the inefficiency of the chemoprophylaxis by DDS, and the existence of primary resistance cases to DDS (some of them clinically proved), a consequence of the numerous secondary resistance cases which have already been witnessed in these villages.—Authors' English Summary

Ramu, G., Malaviya, G. N., Bharadwaj, V. P., Sengupta, U., Sinha, S., Ramanathan, V. D., Pal, C. and Desikan, K. V. Studies on healthy contacts of leprosy patients—a preliminary report. Indian J. Lepr. **57** (1985) 796–803.

Ninety-one healthy contacts of leprosy patients were studied for subclinical infection and possibly the preclinical stage of the disease using a battery of tests. It was observed that the test based on competitive inhibition of monoclonal antibody binding to the MY2, a determinant of *Mycobacterium leprae,* identifies a preclinical stage of the disease.—Authors' Abstract

Rao, C. K. Monitoring and evaluation of National Leprosy Eradication Programme. J. Commun. Dis. **17** (1985) 126–130.

Leprosy continues to be a major public health problem in India. It is estimated that there are around 4 million leprosy cases in India of which 20% are infectious. The National Leprosy Control Programme which was launched in 1956 was converted to The National Leprosy Eradication Programme in 1982. The results achieved under the program and the strategies for future are being presented.—Author's Abstract

Sithambaram, M., Pandian, T. D. and Ramu, G. Survey of the unexamined population in the villages included in a sample survey of the ELEP Dharmapuri leprosy project. Indian J. Lepr. **57** (1985) 820–825.

In a sample survey of the ELEP Dharmapuri Leprosy Control Project out of a population of 62,984, 51,205 were exam-

ined (81.3%). Subsequently out of the enumerated unexamined population of 11,779, 5,761 were examined and 67 cases were detected, giving a prevalence of 11.62 which was less than the prevalence in the sample survey. With an examination of 90.45% of the population, there was not much of an alteration in the gross and child prevalence rates as also the lepromatous rate. A sample survey with examination of 80% of the population gives a representative view of the leprosy situation in an area.—Authors' Abstract

Truman, R. W., Shannon, E. J., Hagstad, H. V., Hugh-Jones, M. E., Wolff, A. and Hastings, R. C. Evaluation of the origin of *Mycobacterium leprae* infections in the wild armadillo, *Dasypus novemcinctus*. Am. J. Trop. Med. Hyg. **35** (1986) 588–593.

An enzyme-linked immunosorbent assay (ELISA) using the phenolic glycolipid-1 (PGL-1) antigen of *Mycobacterium leprae* and crossreactive antisera specific for human IgM was developed to detect IgM antibodies to *M. leprae* in the nine-banded armadillo (*Dasypus novemcinctus*). Statistical definitions for positive and negative interpretations in the ELISA were developed by screening animals recently captured and experimentally inoculated with *M. leprae*. The ELISA was shown to have high sensitivity and specificity. Modern-day armadillos of central Louisiana (U.S.A.) were observed to have a PGL-1 antibody prevalence rate as high as 20%, and a clinical disease rate as high as 5%. A retrospective serological survey of 182 armadillos taken in the years 1960–1964 and predating the use of armadillos in leprosy research was used to evaluate the 1968 environmental contamination hypothesis for the origin of *M. leprae* infections in the wild armadillo. Antibodies to the apparently species-specific PGL-1 antigen were detected in 17 of the samples taken in 1960–1964. Absorption with whole *M. leprae, M. intracellulare, M. terrae, M. rhodesiae, M. scrofulaceum, M. diernhoferi, M. kansasii, M. phlei, M. avium,* BCG, and two new armadillo-derived mycobacterial species showed these antibody reactions to be specific for PGL-1. Apparently, *M. leprae* was enzootic in armadillos as early as 1961, and original infection of these animals could not have occurred in 1968.—Authors' Abstract

Rehabilitation

Boucher, P., van Droogenbroeck, J. B. and Hirzel, C. [Correction of the claw hands of leprosy by the straight "Zancolli lasso" procedure and by two of its variations.] Acta Leprol. **4** (1986) 73–78. (in French)

The procedure of the Zancolli "lasso" or V direct Zancolli uses a flexor superficialis tendon which, after a distal section, is turned inside out and is fixed on itself after forming a loop around the proximal pulley of the sheath of the flexor. The mode of distal fixation being the same, the authors also study two different methods which resort either to one tendon for two, three or four fingers, or only to one strip of the flexor tendon for one finger. Forty-five cases of this kind of operation are reported. In the most important series in which the princeps procedure has been used, the results are good in 80% of the mobile claws and average in 70% of the stiffened claws. The cases operated according to the two different methods, less numerous, give approximately the same results. The suggested indications are in favor of the changes in the procedure.—Authors' English Summary

Caruana, A., Rodriguez, J., Reig, A., Garcia, J. A. and Ribera, D. [Comparative analysis of the psychological characteristics of hospitalized leprosy patients and cancer patients.] Rev. Fontilles **15** (1986) 403–407. (in Spanish)

This work shows the results of the application of personality, anxiety and depression questionnaires to two groups of pa-

tients: 27 leprosy patients from the Sanatorio de Fontilles (Alicante), and 65 oncologic patients hospitalized in Sevilla Institute of Oncology, receiving chemotherapy, cobalt therapy, and/or surgical treatment. We have compared the results of the two groups and have made an assessment of the similarities and differences so that the special characteristics of two illnesses become elicited. This is interesting because both of them are chronic illnesses, with a very different prognosis and treatment, and also with different expectations and quality of life for the patients.—Authors' English Summary

D'Almeida, L., Seck, A. M., Picard, P., Sylla, O. and Stephany, J. [The psychological distress of leprosy.] Acta Leprol. **4** (1986) 59–72. (in French)

This article is about the incidence of the Hansen's disease in the personality of 29 patients of Institut de Leprologie appliquée de Dakar, Fondation de l'Ordre de Malte. This approach of the distress of these patients was done by an inquiry based on sociocultural and clinical variables and compared to a study composed of tubercular and psychiatric patients. This study reports four distress levels (loss of identity, loss of objectivity, forlornness, culpability) which are distinguished by sex and age. The actual experience's analysis of the distress shows the important support of the traditional representations of these leprous patients psychology.—Authors' English Summary

Hirzel, C., Millan, J., Boucher, P., Naudin, J. C. and Diouf, B. [Prevention of painful perforating plantar ulcers; a trial conducted by a mobile unit.] Acta Leprol. **4** (1986) 79–92. (in French)

Aims: to prevent the appearance of plantar ulcerations, and then mutilations, by going in the field in order to: make suitable footwear, educate the patients, train the paramedical staff.

Means: 1 fitted lorry, 1 physiotherapist, 1 shoemaker, and 1 educator.

Results: In 1 year, 206 patients have been provided with shoes and followed up. Advice has been taken exactly in the leprosy villages in which the assiduity rate is of 98%; this rate varies between 47 to 70% in the all-purpose dispensaries. Paramedical workers of all-purpose health centers did not take great interest in this action. After 6–12 months under observation: 84% of good results for the feet without deformity or slightly deformed; 51% for the deformed feet. The results are quite satisfactory for the feet without plantar ulcer at the beginning, and that whatever the foot deformity stage. But for the feet wounded by plantar ulcer at the beginning, 33% recovery has been reported after wearing these shoes.—Authors' English Summary

Ndiaye-Niang, M., Diagne, M., Ndiaye, I. P., Boucher, P. and Millan, J. [Electromyographic examination in leprosy.] Acta Leprol. **4** (1986) 51–58. (in French)

In Dakar, during a definite period of time, all the new leprosy cases have been subjected to an electromyographic examination before treatment: a total of 37 patients and 518 examined nerves including all clinical forms: a) NCV: 33% of the examined nerves are found to be affected. The sensory nerves are frequently and early involved. In frequency order: sural (54%), posterior tibial (50%), sensory ulnar (35%), sensory median (29%), motor ulnar (28%), lateral popliteal (17%) and motor median (12%). b) The study of the SCV seems relatively more reliable than the sensory testing in the case of the ulnar and the median (75 comparisons): concordance in 69% of the cases; SCV only abnormal in 19%; sensory testing only abnormal in 12%. c) The EMG detection is superior to the motor testing and to the motor nerve conduction for the lateral popliteal (32 comparisons): 41% of concordant examination; 59% of differences among which 44% of anomalies revealed only by detection.—Authors' English Summary

Reddy, B. N., Sekar, B. and Neelan, P. N. Use of disability index to assess the extent & severity of disabilities in leprosy. Indian J. Med. Res. **83** (1986) 355–359.

In a prevalence survey on disabilities in leprosy carried out in a rural population in Chingleput District of Tamil Nadu (India) the paramedical personnel were able to detect and record disabilities accurately in 98.8% of patients. There was no difference

in the severity of disabilities among male and female patients when the disability index (DI) proposed by Bechelli was used for assessment. Disabilities in lepromatous (L) and intermediate group (N?L) of patients were more severe than in non-lepromatous (N) patients. All the three methods for calculating disability index were equally useful. Though DI(2) and DI(3) methods were more sensitive, the variability of the values of DI in patients was the least when DI(1) method was used; its calculation was also simple.—Authors' Abstract

Shah, A. Post decompression ulnar claw and its recovery. Indian J. Lepr. **58** (1986) 54–57.

There are no reports on the ulnar claw hand developing immediately after the nerve decompression although the possibility exists. A case report is presented in which the decompression for ulnar neuritis was complicated by the ulnar claw developing on the next day. Such complication can prove embarrassing to the surgeon and worrisome for the patient. However, it improved in 6 months along with recovery of other modalities of sensation and voluntary motor power.—Author's Abstract

Sharangpani, R. C., Kulkarni, V. N. and Mehta, J. M. A new approach in muscle training to rehabilitate the hand in leprosy. Indian J. Lepr. **57** (1985) 750–755.

Rehabilitation of the hand in leprosy with its deformities and anesthesia no doubt poses a formidable challenge as far as rehabilitation is concerned. Here we have applied a combination of latest concepts in sports physiology and the exercise followed by the students of ancient Indian martial art known as Krishni Vidya. This exercise consists of crumpling a newspaper sheet with a single hand without any external support. We are unable to explain the type of exercise done by the people before existence of newspaper. They might be using naturally occurring materials for the same, like wood bark. With this exercise we have been able to improve the function of the hand remarkably well and the rehabilitation time following surgery is drastically reduced, with function returning close to normalcy. The full function is achieved within 4 weeks from the date of removal of plaster as compared to 8 to 10 weeks or more with conventional physical therapy. This full function is not only in mobility but also in coordination, static and dynamic strength, speed of movement and flexibility required of a normal hand. Sixteen patients operated for lumbrical replacement (using sublimis as a motor from the long finger) at the Dr. Bandorawalla Leprosy Hospital were put under the paper crumpling exercise. It was observed that the average time for the achievement of fully closed fist was 2 weeks. (All of them had thumb function intact, i.e., either normal or operated—out of 16, four patients were operated for opponens prior to lumbrical replacement.)—Authors' Abstract

Other Mycobacterial Diseases and Related Entities

Emmerson, A. M. and Cremer, A. W. F. Rifampicin for non-tuberculous infections? Chemotherapy **31** (1985) 324–328.

Large populations of rifampin-sensitive strains of *Mycobacterium tuberculosis* have been exposed *in vitro* to changing concentrations of rifampin (RMP) in line with changes in the blood level of the drug observed during treatment, and to much lower concentrations. Experiments in which the organism was exposed to either 7 or 14 days of cyclically-changing rifampin concentrations have resulted in the elimination of the *M. tuberculosis* test strains without the emergence of resistance. The significance of these laboratory findings is discussed in relation to the debate as to whether rifampin should be used in short courses for the treatment of nontuberculous infections or whether it should be withheld for fear of inadvertently generating rifampin-resistant

strains of tubercle bacilli. It is argued that the evidence for withholding rifampin from use in short courses against nontuberculous infections is slight.—(*From* Excerpta Medica)

Gandhi, B. M., Bhargava, D. K., Irshad, M., Chawla, T. C., Dube, A. and Tandon, B. N. Enzyme linked protein-A: an ELISA for detection of IgG antibodies against *Mycobacterium tuberculosis* in intestinal tuberculosis. Tubercle **67** (1986) 219–224.

Enzyme-linked protein-A has been used to develop an enzyme-linked immunosorbant assay (ELISA) to detect circulating IgG antibodies to *Mycobacterium tuberculosis.* The specific binding of protein-A to IgG fractions through Fc receptors, makes the test more specific for detection of total IgG antibodies. The ELISA system has been used for detection of circulating antibodies to *M. tuberculosis* H37Ra in 22 patients with histologically proven intestinal tuberculosis and 88 healthy controls, in addition to 7 diseased controls. The ELISA has been found to be a sensitive test since it was positive in all 22 patients with intestinal tuberculosis. Its specificity was 85% in Indian controls and 97% in Norwegian controls. The test is easy to perform and may be recommended for the serological diagnosis of intestinal tuberculosis.—Authors' Summary

Grange, J. M., Beck, J. S., Harper, E. I., Kardjito, T. and Stanford, J. L. The effect of exposure of hospital employees to patients with tuberculosis on dermal reactivity to four new tuberculins. Tubercle **67** (1986) 109–118.

An early (6–8 hr) erythematous response to purified protein derivative (PPD) and to sonicate antigens (new tuberculins) prepared from *Mycobacterium tuberculosis, M. vaccae, M. scrofulaceum,* and *M. leprae* occurred much more frequently among hospital employees exposed to patients with tuberculosis than among factory workers. Biopsies taken from the skin test sites at 48 hr revealed a more intense inflammatory cell infiltrate in response to PPD and the sonicate of *M. tuberculosis* but not to the antigens of the other mycobacteria among the hospital employees thus indicating a degree of specificity. The early response appears to be directed towards species-specific antigens but not, apparently, to the same as those that elicit the 48-hr reactions. The hospital employees also had higher peripheral blood B-cell counts and total IgG levels, suggestive of an adjuvant effect. It is postulated that the early reaction results from repeated exposure to tubercle bacilli, and the possible nature of the reaction is discussed.—Authors' Summary

Hayman, J. and McQueen, A. The pathology of *Mycobacterium ulcerans* infection. Pathology **17** (1985) 594–600.

The pathology of cutaneous ulcers resulting from *Mycobacterium ulcerans* infection is reviewed. Initial infection causes ulceration with necrosis of the dermis and a septate panniculitis in subcutaneous fat. There is little cellular reaction despite the presence of large numbers of organisms. Recurrent or persistent infection produces a granulomatous reaction with epithelioid macrophages, variable numbers of giant cells of the Langhans type, and relatively few organisms. This type of reaction is associated with more successful treatment of the disease and appears analogous to the tuberculoid form of leprosy.

[The histological findings are not new, but they are well illustrated and valuable in that they are related to duration of the primary lesion and to recurrence.]—AS/D.S. Ridley (Trop. Dis. Bull.)

Hendrick, S. J., Jorizzo, J. L. and Newton, R. C. Giant *Mycobacterium fortuitum* abscess associated with systemic lupus erythematosus. Arch. Dermatol. **122** (1986) 695–697.

A 36-year-old woman with a 1½-year history of systemic lupus erythematosus was first seen in October 1984 with a 6-month history of several ulcerated and scarred lesions on the lower extremities. A biopsy specimen showed a granulomatous infiltrate of deep dermis and subcutaneous tissue. Over the next 3 weeks, the patient developed a violaceous, warm, indurated, tender, fluctuant lesion involving most of the left buttock. A culture showed a rapidly growing atypical acid-fast bacteria, which was later

identified as *Mycobacterium fortuitum*. The patient was treated with surgical drainage of the left hip abscess, followed by a 3-week treatment with doxycycline hyclate and amikacin sulfate. She was discharged while receiving oral doxycycline and ethambutol hydrochloride.—Authors' Abstract

Huminer, D., Pitlik, S. D., Block, C., Kaufman, L., Amit, S. and Rosenfeld, J. B. Aquarium-borne *Mycobacterium marinum* skin infection. Arch. Dermatol. **122** (1986) 698–703.

A 33-year-old fish fancier developed a protracted skin infection that ultimately was found to be caused by *Mycobacterium marinum*. The organism was isolated from the lesion as well as from infected fish taken from his home aquarium. The lesion resolved after a 6-week course of oral sulfamethoxazole and trimethoprim. Forty-four additional cases of culture-proved *M. marinum* skin infections acquired from aquariums and reported in the English-language literature are reviewed. Almost universally, the lesions remained circumscribed and were either single nodular (14 patients) or multiple sporotrichoid (31 patients). Diagnosis was supported by acid-fast smears (15 patients) and isolation of the organism from skin lesions (43 patients) or from fish (2 cases). *In vitro* studies, as well as clinical outcomes, suggest sulfamethoxazole-trimethoprim or ethambutol hydrochloride plus rifampin to be the drugs of choice.—Authors' Abstract

Jorizzo, J. L., Hudson, R. D., Schmalstieg, F. C., Daniels, J. C., Apisarnthanarax, P., Henry, J. C., Gonzalez, E. B., Ichikawa, Y. and Cavallo, T. Behçet's syndrome: immune regulation, circulating immune complexes, neutrophil migration, and colchicine therapy. J. Am. Acad. Dermatol. **10** (1984) 205–214.

Immune regulatory dysfunction, circulating immune complexes (CIC), and polymorphonuclear (PMN) cell migration were investigated in patients with Behçet's syndrome. Six patients meeting rigorous clinical criteria were evaluated. Only one patient showed evidence of immune regulatory dysfunction (increased T4/T8 ratio). Although Clq binding and Raji cell assays for CIC yielded positive results in only 1 of 5 patients, all five patients had *in vivo* "histamine trap test" evidence of CIC (all controls had normal results). Sera from all Behçet's syndrome patients increased migration of neutrophils to zymosan-activated serum. Colchicine therapy abolished the enhancing effect of the patient's sera on movement of PMN cells from patients and controls. An immune complex-mediated injury that is followed by an excessive accumulation of PMN cells may lead to the cutaneous lesions and other lesions in Behçet's syndrome. Further evaluation of cochicine therapy is warranted on the basis of these studies.—Authors' Abstract

Jorizzo, J. L., Solomon, A. R. and Cavallo, T. Behçet's syndrome; immunopathologic and histopathologic assessment of pathergy lesions is useful in diagnosis and follow-up. Arch. Pathol. Lab. Med. **109** (1985) 747–751.

Behçet's syndrome is a complex multisystem disease that, due to the absence of a pathognomonic laboratory test, must be diagnosed using clinical criteria. Clinical pathergy testing, the induction of a sterile pustule 24 hr after cutaneous trauma, has been proposed as a useful adjunct to diagnosis. We have expanded this concept by showing the usefulness of examining pathergy lesions by routine and immunofluorescence microscopy in the diagnosis of nine patients with Behçet's syndrome. Furthermore, histopathologic pathergy assessments correlated with clinical disease activity and/or response to experimental oral thalidomide therapy in 5 of 6 patients with Behçet's syndrome who were retested.—Authors' Abstract

Kirkpatrick, C. H., Rozzo, S. J. and Mascali, J. J. Murine transfer factor. III. Specific interactions between transfer factor and antigen. J. Immunol. **135** (1985) 4027–4033.

The interactions between dialyzable transfer factor and antigens have been studied. Incubation of transfer factor-containing dialysates from ferritin-sensitized mice or ferritin-coated plastic surfaces removed the

antigen-sensitizing activity; incubation of the same preparations on cytochrome c-coated surfaces did not. Similar results were obtained when cytochrome c-transfer factor was studied. Incubation on cytochrome c-coated surfaces removed the activity, but incubation on ferritin-coated surfaces did not. Specific transfer factor activities could be recovered by elution with 8 M urea or acetonitrile. The finding of interactions between transfer factor and antigens provides evidence for a molecular basis of the specificity of the immunologic effects of transfer factor. This technique may also enable us to obtain amounts of specific material that are adequate for chemical analysis.—Authors' Abstract

Lau, J. H. K. Hand infection with *Mycobacterium chelonei.* Br. Med. J. **292** (1986) 444–445.

Four women in Hong Kong developed *Mycobacterium chelonei* infections of the hand (and also the knee in one case) following multiple steroid injections for synovitis or arthritis. Treatment of the infections was by various chemotherapeutic regimens with synovectomy in two cases and, owing to delays in diagnosis, amputation of fingers in the two other cases. It was considered that the organism was introduced by use of contaminated needles and that the infections were exacerbated by the local immunosuppressive effects of the steroids. [This is a good example of the diagnostic and therapeutic difficulties posed by the relatively uncommon but serious infections due to "atypical" mycobacteria.]—J. M. Grange (Trop. Dis. Bull.)

Marinis, E. and Legakis, N. J. *In-vitro* activity of ciprofloxacin against clinical isolates of mycobacteria resistant to antimycobacterial drugs. J. Antimicrob. Chemother. **16** (1985) 527–530.

The activity of ciprofloxacin against 42 clinical isolates of mycobacteria was studied *in vitro* by the 1% standard proportion method on Lowenstein-Jensen medium. Ciprofloxacin was found active against all strains of *Mycobacterium tuberculosis* sensitive to streptomycin, isoniazid, ethambutol and rifampin. The MIC of ciprofloxacin was 3.2 mg/l. This concentration of ciprofloxacin was sufficient to inhibit almost all strains showing intermediate sensitivity or resistance to one or more of the above agents. The same phenomenon was also observed with the atypical isolates.—(*From* Excerpta Medica)

Orenstein, W. A., Bernier, R. G., Dondero, T. J., Hinman, A. R., Marks, J. S., Bart, K. J. and Sirotkin, B. Field evaluation of vaccine efficacy. Bull. WHO **63** (1985) 1055–1068.

This paper describes the epidemiological techniques available for measuring vaccine efficacy and recommends a practical approach to their use. Many of the examples relate to measles vaccine, the efficacy of which was tested by the techniques described, although the methods are applicable to other vaccines as well. The main advantages and disadvantages of the techniques are indicated.—Authors' Abstract

Orme, I. M. and Collins, F. M. Aerogenic vaccination of mice with *Mycobacterium bovis* BCG. Tubercule **67** (1986) 133–140.

The course of infection with *Mycobacterium bovis* BCG Pasteur was followed against time in groups of mice vaccinated by either the aerogenic or subcutaneous route. The generation of acquired protective immunity and immunological memory was determined in each group by adoptive immunization procedures. In addition, subcutaneously vaccinated mice were tested for their ability to resist an aerogenic challenge with a lethal dose of *M. tuberculosis.* No overall qualitative differences in the magnitude or longevity of antituberculosis immunity in mice vaccinated by the two procedures were observed. It is concluded that aerogenic vaccination offers no immunological advantage over vaccination by the subcutaneous route.—Authors' Summary

Orme, I. M., Roberts, A. R. and Collins, F. M. Lack of evidence for a reduction in the efficacy of subcutaneous BCG vaccination in mice infected with nontuberculous mycobacteria. Tubercle **67** (1986) 41–46.

Subcutaneous BCG vaccination of mice several weeks after intravenous or subcutaneous infection with either *Mycobacterium avium* or *M. kansasii* had no effect on the subsequent course of these nontuberculous mycobacterial infections. In some animals the growth of the BCG infection in the draining popliteal lymph nodes was reduced compared with the growth in controls, although these mice were as resistant as BCG-vaccinated controls to a subsequent airborne challenge infection with *M. tuberculosis.* Nonvaccinated, previously infected mice also showed some degree of resistance to the airborne challenge infection; this resistance was more pronounced in mice infected with nontuberculous mycobacteria intravenously than in those infected subcutaneously.—Authors' Summary

Orozco, L. C., Quintana, F. O., Beltran, R. M., de Moreno, I., Wasserman, M. and Rodriguez, G. The use of rifampicin and isoniazid entrapped in liposomes for the treatment of murine tuberculosis. Tubercle **67** (1986) 91–97.

Liposomes loaded with rifampin and isoniazid were used experimentally to treat mice with severe tuberculosis. The animals were distributed in four groups. The control group and the group treated with unloaded liposomes showed the severest disease. Both groups showed the lowest accumulated survival, about 50% after 30 days. The numbers of colony-forming-units (CFU) and root specific lung weight (RSLW) were the highest, and the histopathology of the lung showed marked diffuse lesions. However, the group treated with unloaded liposomes showed significantly higher growth of *Mycobacterium tuberculosis* compared with the control. The group treated with drug and drug-loaded liposomes showed a higher survival, about 85% after 30 days, and the lowest values of CFU and RSLW. The lung histology revealed considerably less inflammation which was focal. The parameters evaluated indicated a significantly better response in the group of animals treated with rifampin and isoniazid entrapped in liposomes.—Authors' Summary

Ridell, M. and Portaels, F. Immunodiffusion analyses of environmental mycobacteria isolated in Zaire. Zentralbl. Bakteriol. Mikrobiol. Hyg. [A] **260** (1985) 286–292.

Unclassified, acid-fast strains isolated from the environment in Zaïre were analyzed by comparative immunodiffusion for taxonomical purposes. These strains have previously been shown to differ physiologically and/or biochemically from all other known mycobacteria. The analyses confirmed that these strains belong to genus *Mycobacterium* and showed, furthermore, that they were more closely related to the slowly growing mycobacteria, including *Mycobacterium tuberculosis,* than to the rapidly growing ones. The result of the serological analyses also confirmed a previous grouping of these unclassified strains. An antigen designated β which, in all probability, is a ribonucleoprotein was shown in all but two of the test strains.—AS/J. K. Schonfeld (Trop. Dis. Bull.)

Sunderam, G., McDonald, R. J., Maniatis, T., Oleske, J., Kapila, R. and Reichman, L. B. Tuberculosis as a manifestation of the acquired immunodeficiency syndrome (AIDS). JAMA **256** (1986) 362–366.

Tuberculosis has not been well documented as a complication of the acquired immunodeficiency syndrome (AIDS). We studied 48 cases of mycobacterial diseases among a group of 136 adult patients with AIDS over a 43-month period. Twenty-nine of them had severe and unusual manifestations of disease due to *Mycobacterium tuberculosis,* predominantly extrapulmonary and disseminated. Tuberculosis was more common among Haitians (4/8) and intravenous drug abusers (24/102) than among homosexuals who did not abuse drugs (0/22). Twelve of 21 patients with tuberculosis who were treated responded well; whereas three developed progressive disease indicative of treatment failure. Severe and unusual presentation of overwhelming tuberculosis in appropriate clinical circumstances may be considered an infection predictive of the presence of AIDS.—Authors' Abstract

Wasserman, M., Beltran, R. M., Quintana, F. O., Mendosa, P. M., Orozco, L. C. and

Rodriguez, G. A simple technique for entrapping rifampicin and isoniazid into liposomes. Tubercle **67** (1986) 83–90.

A method for the preparation of liposomes loaded with rifampin and isoniazid is described. Optimal conditions were established; the lipid suspension was mixed with the aqueous solution of the drugs and was sonicated in a bath for 30 min at 50°C. The optimum composition tested was phosphatidyl choline, cholesterol and cardiolipin in a molar ratio of 7:2:1. The separation of unloaded drug was performed by centrifugation through three successive Sephadex G-25 columns. The liposomes were multilamellar vesicles with a size ranging from 100–300 nm. The drugs were trapped in concentrations from 6.5–9.5 mg/ml. This method is suitable for preparation of liposomes in small laboratories.—Authors' Summary

Youdim, M. B. H. and Ashkenazi, R. Serotonergic involvement in pharmacological action of the anxiolytic-sedatives thalidomide and supidimide. Eur. J. Pharmacol. **119** (1985) 39–46.

The anxiolytic-sedative drugs thalidomide and supidimide inhibited spontaneous motor activity in rats. Both compounds inhibited the serotonin (5-HT) behavioral syndrome induced by tranylcypromine (TCP) plus L-tryptophan (TRP) or clorgyline plus the selective 5-HT uptake blocker, LM 5008 (4-[2-(3-indoyl)ethyl]-piperidine) and delayed the behavioral effects of p-chloro-amphetamine, a releaser of 5-HT. The behavioral syndrome induced by the 5-HT agonist, 5-methoxy-N,N'-dimethyltryptamine (5-MeODMT) was unaffected by supidimide pretreatment. Thus supidimide does not possess 5-HT receptor antagonistic properties. This was further substantiated by the unaltered 5-HT-induced platelet aggregation in the presence of supidimide (10^{-7}–10^{-4} M). A decrease of 5-HT release into the synaptic cleft will lead to a diminished behavioral response to drugs that act presynaptically. Supidimide induced a greater increase in accumulation of brain 5-HT in TCP (5 mg/kg) plus TRP (100 mg/kg)-treated animals as compared to that in the corresponding controls. These data indicate that the behavioral and pharmacological actions of supidimide may be related to its inhibition of 5-HT release.—Authors' Abstract