CURRENT LITERATURE

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

General and Historical

Pfau, R. and Haq, G. Leprosy in Pakistan. Lepr. Rev. **57** (1986) 355–359.

Refugee movements, including the variable influx of Afghans and Biharis (the former with a considerable percentage of infectious cases), create logistic and administrative difficulties, calling for new approaches to ensure regularity of attendance, compliance to the ingestion of prescribed medication, and the adequate supervision of both staff and patients. However, progress has certainly been made; deformity rates are stabilizing and in at least one part of the country (Azad Kashmir), with a static population and good work performance, incidence rates have dropped. If we can extend and maintain the implementation of multiple drug therapy, there is a realistic hope that over 80% of our cases can be treated and discharged within the next 8 years.—Authors' Summary

Shu, H., Zhuo, D. and Bian, J. [Economic benefits of leprosy control.] China Lepr. J. 2 (1986) 62–65. (in Chinese)

The article reports the economic benefit of leprosy control. It performed the investigation and analysis of costs and their benefits for 25 years in Baoying County of Jiangsu Province for leprosy control. The result showed that leprosy control is worth investing in because of both the economic and social benefits that could be obtained from it. The former was 266 times the cost of the investment. The cost of treatment in hospital for each patient is 13.69 times higher than that of an outpatient. If counting in the living subsidies and loss of social labor values, the ratio would be much higher than mentioned above. The authors propose that the outpatient treatment for leprosy patients should be gradually popularized.—Authors' English Abstract

Soviero, D. J. The nationalization of a disease: a paradigm? Public Health Rep. **101** (1986) 399–404.

The early history of the federal involvement in Hansen's disease reflects the history of the Public Health Service itself. As a young and aggressive institution, the Public Health Service sought out contagious, infectious diseases that threatened the public health. National resources and national coordination were needed to fight the likes of malaria, hookworm, or smallpox. The customary attack would consist of a field study, determination of the etiology, the method of transmission, and then, perhaps, preventive measures. An eradication campaign would follow. Leprosy fit perfectly into the model—a disease of unknown etiology, an unknown method of transmission, thought to be highly contagious, and no known cure. The United States launched a major investigation in Hawaii, where the disease was prevalent and its victims conveniently segregated. The investigation failed. The Public Health Service then turned toward segregation and isolation as a way to fulfill its public health role. A bureaucracy was established around the idea that victims of leprosy must be incarcerated for the good of the public. The institutionalization of the Public Health Service and the philosophy upon which its treatment of leprosy was based proved difficult to change when researchers in the field made major scientific breakthroughs in the 1940s. The realization that the disease was only feebly contagious, activities of patient organizations, and pressure from the media and the Congress did not achieve as dramatic results as the sulfone drugs did. The Public Health Service moved, but slowly. What are the lessons in all of this?—Author's Synopsis

Chemotherapy

Chen, D. [Treatment of 519 cases of leprosy with combined regimens.] China Lepr. J. **2** (1986) 28–29. (in Chinese)

Five hundred nineteen cases of leprosy including multibacillary dapsone (DDS)-resistant (29.09%) and recurrent (10.79%) cases were treated with multidrug regimen. Combined chemotherapy was better than single drug dapsone. The combined drug therapy might retard or prevent the emergence of drug-resistant cases and be effective to some clinically DDS-resistant ones. There was no significant difference in effects between two-drug and three-drug regimens but the former was better for the DDS-resistant cases. Multidrug therapy had contributed to convert the patients with BI lower than 2.0 to negative ones.—Author's English Abstract

Davy, C., Riveau, E., Bousquet, J. C., Curet, P., Vayre, P., Cortez, A. and Grellet, J. [Small intestine transit anomalies in a patient with chronic abdominal pain and treated for leprosy.] J. Radiol. **67** (1986) 213–218. (in French)

This new case of enteropathy due to clofazimine provided demonstration of the diagnostic value of small bowel follow-through examination in this complication. Various small intestine anomalies have been reported: ileal or partial jejunal lesions, variations in caliber, loss of physiologic folds, irregularly outlined surface and border lacunae and persistence of suppleness of pathologic loops. Knowledge of these anomalies should avoid exploratory laparotomy. Clofazimine-induced enteropathy regresses after discontinuation of treatment. Repeat small bowel follow-up examinations can be performed to review the course of this regression.—Authors' English Summary

George, J. and Balakrishnan, S. Blood dapsone levels in leprosy patients treated with acedapsone. Indian J. Lepr. **58** (1986) 401–406.

The metabolism of the repository drug acedapsone (DADDS,4,4′-diacetyldiaminodiphenyl sulfone) was studied in 15 individuals receiving 225 mg of DADDS intramuscularly for a period of 75 days. Plasma levels of DDS were determined on the 2nd, 7th, 15th, 30th, 60th and 75th day after administration of the drug by the spectrophoto-fluorometric technique. The mean peak levels of DDS (85.36 ng/ml) were noticed on the 7th day followed by a gradual decrease in DDS concentration. The mean half-life levels (44.53 ng/ml) of DDS were observed around the 15th day. The mean DDS level for the entire period of observation after one dose was 41.95 ng/ml. On the 75th day, the DDS level reached the minimum value of 14.76 ng/ml which was still about five times more than the minimal inhibitory concentration level of DDS against *Mycobacterium leprae* (3 ng/ml). The results are discussed.—Authors' Abstract

Gonzalez, A. B., Hernandez, O., Suarez, O., Gonzalez-Abreu, E. and Rodriguez, J. E. Survey for primary dapsone resistance in Cuba. Lepr. Rev. **57** (1986) 341–346.

Only partial resistance at 0.0001% dapsone concentration in the mouse food was found exhibited by the bacilli recovered from three patients, representing 6.9% of the total tested at the same concentration. The role played by treatment in relation to such a low grade of dapsone resistance is discussed.—Authors' Summary

Gopalakrishnan, S. Dropouts during treatment for leprosy. (A study in the ELEP Leprosy Control Project, Dharmapuri District, Tamil Nadu, during 1975–1977). Indian J. Lepr. **58** (1986) 431–440.

Certain social and related factors responsible for 231 dropout leprosy patients from treatment are discussed. The dropout rate was lowest among lepromatous patients (1.2% vs 10.9% among nonlepromatous patients); patients with stigma/deformity were significantly less ($p < 0.001$); among dropouts, proportion of wage-earners was high in them ($p < 0.001$); student dropouts were few ($Z = 2.78$, $p < 0.05$, $\chi^2 = 10.32$, d.f. = 1, $p < 0.005$); there was little association between socioeconomic status and dropout

rate ($p > 0.5$); dropouts among patients who self-registered for treatment were much less than in those who were enlisted for treatment during survey ($p < 0.05$); 38% had dropped out within the first 6 months of registration for treatment; lepromatous patients attended clinics for more than 25 months before becoming dropouts; fear of loss of wages, belief that it was not leprosy, social stigma attached to the disease, disinterest for treatment when lesions were small and few, dissatisfaction with treatment, and belief that patches self-healed were the main causes for discontinuance of treatment; all those who dropped out due to shyness were women of 15–44 age-group.—Author's Abstract

Jacobson, R. R. Antibiotic therapy for leprosy. Antimicrob. Agents Ann. **2** (1987) 36–46.

There have been no major advances in the antimicrobial therapy of leprosy in the period under review. The degree to which the WHO-recommended regimens for the therapy of leprosy are successful will, to a considerable extent, influence further efforts and developments, and large-scale application of these regimens is only now being realized. Promising new drugs for this disease, however, are under study, particularly the newer rifamycins and at least one of the quinolines. Nonetheless, more research effort at the moment is directed toward serodiagnosis and immunotherapy in the form of vaccines and immunoactive agents such as IL-2 or γ-interferon.—Author's Summary

Krishna, D. R., Appa Rao, A. V. N., Ramankar, T. V. and Prabhakar, M. C. Pharmacokinetic interaction between dapsone and rifampicin in leprosy patients. Drug Devel. Indus. Pharm. **12** (1986) 443–459.

Different pharmacokinetic parameters of dapsone and rifampin following P.O. administration of dapsone 100 mg alone, rifampin 600 mg alone, and dapsone 100 mg plus rifampin 600 mg in 7 cases of untreated patients of leprosy were investigated. The blood levels, half-life, and $AUC_{0-8\ hr}$ of dapsone were significantly reduced with simultaneous increase in plasma clearance when it was administered along with rifampin. The pharmacokinetic behavior of rifampin was, however, not significantly affected in the presence of dapsone.—Authors' Abstract

Li, W., *et al.* [Therapeutic effects of rifampicin, clofazimine and dapsone in multibacillary leprosy in the fieldwork—results of a year's treatment.] Chin. J. Clin. Dermatol. **15** (1986) 175–177. (in Chinese)

In 1983–1984, 286 cases of active multibacillary leprosy in Yangzhou District and Dongtai County were treated with rifampin (RFP), clofazimine (B663), and dapsone for 1 year. Most of the patients showed improvement clinically. No deterioration of the disease was found in any patient. The bacterial index of the patients reduced about one unit in the period of 1 year. The average reduction of biopsy index was 37.7%. The severity and frequency of ENL and neuritis during the period of 6–12 months were markedly decreased in comparison with those before treatment. The main toxic side effect was skin pigmentation. The results indicate that the therapeutic effects of the combined regimen were satisfactory for multibacillary leprosy and can be recommended for mass treatment in other areas of our country.—Authors' English Abstract

Li, W., Zhang, Y., *et al.* [Seven years' follow-up of multibacillary patients treated with RFP or B663 for a short time.] China Lepr. J. **2** (1986) 24–27. (in Chinese)

Nine cases of multibacillary leprosy were treated with rifampin (RFP) 450 mg daily and 10 cases with clofazimine (B663) 100 or 200 mg daily for half a year and then both groups followed by dapsone monotherapy of 100 mg daily for 6.5 years. The results showed that clinical improvement and the decrease of average MI in the RFP group were more marked in comparison with the B663 group in the first 6 months. Within 5 years the clinical improvement and the decrease of average BI in the skin smears were similar in two groups. Within 7 years the average decreases in BI in two groups were 0.6 and 0.65 per year, respectively. No

deterioration of the disease was found in the patients. Negative skin smears in the two groups were found in 3 and 5 cases, respectively. There was 1 case who was hypersensitive to dapsone and 6 cases who were resistant to dapsone and they continued to improve without any treatment after stopping RFP or B663. It indicated that the multibacillary patients might be cured by an effective bacteriocidal drug for limited duration. However, in order to prevent drug resistance and decrease the relapse of leprosy, the present authors recommend introducing the combined therapy for multibacillary leprosy.—Authors' English Abstract

Pattyn, S. R. Rifabutin and rifapentine compared with rifampin against *Mycobacterium leprae* in mice. (Letter) Antimicrob. Agents Chemother. **31** (1987) 134.

Mice were inoculated in the left hindfoot pad with 5×10^3 *Mycobacterium leprae*. The drugs were administered once at the doses indicated on day 21 postinfection in a 0.5 ml volume administered by stomach gavage. In experiment 1, the minimal effective dose (MED) of rifampin was 20 mg/kg (body weight), and in experiment 2 it was equal to or lower than 10 mg/kg; in most experiments, the MED of rifampin is 20 mg/kg. The MED of rifabutin in both experiments was 2.5 mg/kg, and the MED of rifapentine was 5 mg/kg or less. In a previous experiment, the MED of rifapentine was 2.5 mg/kg. It may therefore be concluded that in single doses rifabutin and rifapentine are eight times more active against *M. leprae* than rifampin.—(*From* the Letter)

See, A., Hervio, P. and Bouvry, M. [Hepatotoxicity of ethionamide—a current problem.] Ann. Gastroenterol. Hepatol. **22** (1986) 129–130. (in French)

The authors discuss the case of a 22-year-old patient treated for lepromatous leprosy who developed acute hepatitis 2 years after beginning multidrug therapy with thalidomide, rifampin, ethionamide, and clofazimine. Besides the ethionamide, there was no hepatotoxic factor and the hepatic anomalies quickly disappeared upon termination of treatment with this product. This again draws attention to the hepatotoxicity of ethionamide.—Authors' English Summary

Venkatesan, K., Mathur, A., Girdhar, B. K. and Bharadwaj, V. P. The effect of clofazimine on the pharmacokinetics of rifampicin and dapsone in leprosy. J. Antimicrob. Chemother. **18** (1986) 715–718.

Fifteen untreated leprosy patients were given rifampin and dapsone for 7 days, and then rifampin, dapsone, and clofazimine for 7 days. Concentrations of rifampin and dapsone were estimated in timed plasma specimens and in 24 hr urine specimens on days 7 and 14. No significant differences in the pharmacokinetics of rifampin and dapsone were observed between the two occasions of sampling.—Authors' Abstract

Wang, Q., Chen, J., *et al.* [Three cases of multibacillary leprosy treated with B663 in four-drug regimen for one year.] China Lepr. J. **2** (1986) 33–35. (in Chinese)

Three cases of multibacillary leprosy were treated with 4 antileprosy drugs, i.e. clofazimine, rifampin, prothionamide, and dapsone for 1 year. The result showed that the four-drug regimen was better than the three-drug regimen. Clofazimine, with the dose of 50 mg daily plus 300 mg monthly, could also control the leprosy reactions, but the drug should be given for a prolonged period of time (about more than 6 months). The pigmentation from clofazimine in the skin lesions was obvious and the more serious the skin lesions, the heavier the pigmentation. Ichthyosis-like skin lesions appeared in 3 cases after about 2 months of clofazimine treatment, but no other side effect was found.—Authors' English Abstract

Zeng, J., Zhong, H., Liu, Z., *et al.* [Survey on regular drug taking in leprosy patients in Guangdong (China).] China Lepr. J. **2** (1986) 68–70.

The modified Bratton-Marshall's technique of examining dapsone (DDS) in the urine has been proved to be simple and exact and may be used as a routine method for detecting urine DDS in leprosy patients. The authors examined 149 and 105 leprosy

patients with this technique in 1982 and 1983, respectively, and found that the rates of regular drug taking increased from 57.7% to 83.8% after the technique had been used routinely after 1982.—Authors' English Abstract

Zheng, C., *et al.* [Treatment of 24 cases of multibacillary leprosy with DDS, RFP, and PTH.] China Lepr. J. **2** (1986) 35–36. (in Chinese)

Twenty-four multibacillary patients were treated by combined regimen of prothionamide (PTH), rifampin (RFP), and dapsone (DDS). After 6–24 months' treatment, their improvements, clinically and bacteriologically, were better than those treated with DDS only. Besides, the combined regimen was more efficient in turning the bacterial index into negativity, shortening the period of treatment and reducing apparent leprosy reaction. If given daily a dose of 200 mg PTH has no toxicity to the liver.—Authors' English Abstract

Zhou, S., Zhu, S., *et al.* [Sixty-eight cases of multibacillary leprosy treated with RFP or RFP plus DDS.] China Lepr. J. **2** (1986) 30–33. (in Chinese)

The result of treating 68 cases of multibacillary (LL or BL or BB type) leprosy patients with two different therapies was reported. Group I consisted of 39 cases treated with rifampin (RFP) and dapsone (DDS). Rifampin was given 600 mg daily in the first 2 weeks and then 600 mg once a month. In Group II there were 29 cases treated with rifampin and DDS. Rifampin was given 300 mg daily on the first 2 days and then 300 mg once a month. The dosage of DDS was 100 mg daily for the same period in both groups. After 1 year of treating, the authors found that the speeds of clinical resolution of skin lesions in both groups were similar, the average rates of falling of morphologic index were 95.1% and 78.3% in Group I and II, respectively, and those of bacterial index 46.0% and 43.3%. Evaluated from the clinical and histopathological observations, both therapy regimens were effective. The rate of efficacy in Group I was 97.4% and 93.1% in Group II; no statistically significant difference in the efficiency between the two groups. The two regimens caused no serious side effects. The authors inferred that if B663 were available, the combination use of the three drugs would be able to prevent dapsone resistance and relapse of leprosy.—Authors' English Abstract

Zuidema, J., Hilbers-Modderman, E. S. M. and Merkus, F. W. H. M. Clinical pharmacokinetics of dapsone. Clin. Pharmacokinet. **11** (1986) 299–315.

Dapsone (DDS) has for about four decades been the most important antileprosy drug. Concentrations of dapsone and its monoacetyl metabolite, MADDS, can be determined in biological media by high-performance liquid chromatography. After oral administration, the drug is slowly absorbed, the maximum concentration in plasma being reached at about 4 hr, with an absorption half-life of about 1.1 hr. However, the extent of absorption has not been adequately determined. The elimination half-life of dapsone is about 30 hr. The drug shows linear pharmacokinetics within the therapeutic range and the time-course after oral administration fits a 2-compartment model.

The concentration-time profile of dapsone after parenteral administration is reviewed. Of clinical importance is the development of a new long-acting injection, which permits monthly supervised administration as recommended by the World Health Organization. Following dapsone injection in gluteal subcutaneous adipose tissue, a sufficiently sustained absorption for this purpose has been reported.

Dapsone is about 70% to 90% protein bound and its monoacetylated metabolite (MADDS) is almost completely protein bound. The volume of distribution of dapsone is estimated to be 1.5 l/kg. It is distributed in most tissues, but *Mycobacterium leprae* living in the Schwann cells of the nerves might be unaffected. Dapsone crosses the placenta and is excreted in breast milk and saliva. Dapsone is extensively metabolized. Dapsone, some MADDS and their hydroxylated metabolites are found in urine, partly conjugated as N-glucuronides and N-sulfates. The acetylation ratio (MADDS : dapsone) shows a genetically determined bimodal distribution and allows the definition of "slow" and "rapid" acetylators. As en-

terohepatic circulation occurs, the elimination half-life of dapsone is markedly decreased after oral administration of activated charcoal. This permits successful treatment in cases of intoxication.

The daily dose of dapsone in leprosy is 50 to 100 mg, but varies from 50 to 400 mg in the treatment of other dermatological disorders. In malaria prophylaxis, a weekly dose of 100 mg is used in combination with pyrimethamine. Side effects are mostly not serious below a daily dose of 100 mg and are mainly hematological effects. The dapsone therapeutic serum concentration range can be defined as 0.5 to 5 mg/l. Alcoholic liver disease decreases the protein binding of dapsone; celiac disease and dermatitis herpetiformis may delay its oral absorption and severe leprosy has been reported to affect the extent of absorption. Rifampin increases the rate of elimination of dapsone; pyrimethamine increases the volume of distribution and probenecid decreases the renal clearance of dapsone.—Authors' Summary

Clinical Sciences

Akimov, V. G. [Differential diagnosis of leprous lesions in Africans.] Vestn. Dermatol. Venereol. **9** (1985) 58–60. (in Russian)

Specific features of differential diagnosis of leprous lesions in persons of the negroid race are described. The paper deals with clinical aspects of the course of various dermatoses more or less imitating leprous lesions in Africans.—Author's English Summary

Anandaraj, H. Psychosocial dimensions of drug default in leprosy. Indian J. Lepr. **58** (1986) 424–430.

The study focuses on the causes and factors related to drug default among leprosy patients; 52 cases were selected using a systematic random sampling technique on the basis of clinic records showing drug default. Awareness about the disease, motivation to be cured, age, caste, education, income, and knowledge of the significant others in the family regarding the patient's condition were taken as variables. Statistical analysis of association and relation reveal that motivation to be cured is very significantly different for high and low groups of awareness about the disease. In addition, high and low levels of motivation differed significantly when treated individually with other variables as age, education, and rural/urban background. These results demonstrate that improved health education rendered by the medical team can yield far better results in eliminating the problem of drug default.—Author's Abstract

Bazurov, G. I. [A case of delayed diagnosis of leprosy.] Vestn. Dermatol. Venereol. **4** (1986) 59–60. (in Russian)

A case of delayed diagnosis of leprosy is described. The diagnosis was verified by laboratory and histological examinations. This case is the evidence of insufficient knowledge of practicing physicians of the clinical picture and diagnosis of leprosy.—Author's English Summary

Char, G. and Cross, J. N. Ulnar nerve abscess in Hansen's disease. West Indian Med. J. **35** (1986) 66–68.

A case of abscess formation in a large peripheral nerve in a patient with leprosy is presented. The pathogenesis of such lesions is discussed, and their rarity in the local community is emphasized.—Authors' Abstract

Chatterjee, B. D., Chakraborti, C. K. and Chaudhuri, S. Microflora in the trophic ulcers of the foot in leprosy. J. Trop. Med. Hyg. **88** (1985) 333–336.

Out of 25 cases of trophic ulcers of the foot, 10 (40%) were both aerobic and anaerobic, 14 (56%) only aerobic, and 1 (4%) showed no growth of bacteria. With the ex-

ception of 2 cases (8%) in the aerobic group, all others showed mixed infections. A wide range of bacteria is reported. Topical application of gentamicin and chloramphenicol is recommended, based on the results of *in vitro* sensitivity.—Authors' Summary

Chattopadhyay, S. P., Bhate, R. D. and Gupta, C. M. Clinico-histopathological evaluation of modified pilocarpine test in early diagnosis of leprosy. Indian J. Lepr. **58** (1986) 415–419.

A modified pilocarpine test was done in 112 patients of which 89 cases were under investigation (group I) and 23 cases were confirmed tuberculoid leprosy cases (group II). In group I, 70 cases (78.6%) showed deficient sweating of varying degree and 36 cases (40.4%) showed definite histopathological changes of paucibacillary leprosy in skin; 22 cases (95.6%) in group II showed deficient sweating. Twenty-four cases under investigation who had deficient sweating but who did not show definite histopathological changes of leprosy initially were followed up for 1 year. At the end of 1 year 10 cases (41.6%) showed confirmatory changes of leprosy on histopathological examination. The modified pilocarpine test has been found to be a simple and very useful test in the early diagnosis of leprosy.—Authors' Abstract

Daluz, W. [Clinical manifestations and biologic perturbations in the course of erythema nodosum leprosum.] Doctor of Medicine thesis, Dakar, 1986. (in French)

After providing an outline on leprosy, the author focuses attention in Part II on the etiopathogenesis of erythema nodosum leprosum (ENL) and on the modern tendency of the approaches to this area. In Part III, the author provides the findings of a retrospective survey concerning 127 cases of ENL. Various etiological factors are analyzed: age, sex, clinical aspect, bacterial index, and antibacillary treatment. Polychemotherapy accelerates the occurrence of ENL. The frequency and association of general signs, the clinical and biological signs are then determined. A brief outline of the treatments applied and of the short and medium terms of the tendency of the disease with regard to recurrence and attacks of neuritis are provided. Two observations show various degrees of severity between early and late ENL.—(*From* Author's English Summary)

Husser, J. A., Daumerie, D., Grossetête, G. and Nebout, M. [Erythema nodosum leprosum with necrotic development.] Acta Leprol. **4** (1986) 239–250. (in French)

For 2 years, 25 lepromatous patients were hospitalized in the Hansen complications room of Institut Marchoux. Among these patients, 9 developed a necrotic erythema nodosum leprosum. A review of the observed clinical effects is established and three types of signs are isolated and discussed: necrotic extension after big nodes on chest and arms, a punch crater complicating small nodes, and a localized scleroderma on arms and legs. The course of this complication is estimated at about 6 months average, with pauses and relapses with general and subjective symptoms. The final course shows side effects: anemia, denutrition, functional disabilities of joint movements and cutaneous straps. In the group of 9 patients, 3 died. We do not find relationships between the necrotic phenomenon and therapy or concurrent diseases.

The best drug to stop the necrotic process is thalidomide 400 mg daily decreased to 100 mg when the signs fall near normal. One or 2 mg/kg each day corticosteroids were tested: the effect is inconsistent; the duration of action is shorter. Side effects occur rapidly and the patient will become corticosteroid dependent. The importance of bathing with disinfectants is high. We did not observe superinfection.—Authors' English Summary

Levy, M. L., Rosen, T., Tschen, J. A., McGavran, M. H. and Kalter, D. C. Hansen's disease following lymphoma. J. Am. Acad. Dermatol. **15** (1986) 204–208.

We report two instances of Hansen's disease as a complication of lymphoma. Although patients with leprosy may be at risk for the development of neoplasia, the converse has only rarely been reported. Nonetheless, granulomatous lesions in patients with lymphoreticular malignancy should

suggest appropriate studies to rule out Hansen's disease, as illustrated by the cases detailed herein.—Authors' Abstract

Li, S., Fu, Q., *et al.* [Survey of eye diseases in 527 leprosy patients.] China Lepr. J. **2** (1986) 42–43. (in Chinese)

Five hundred twenty-seven leprosy patients were examined for eye diseases in 8 leprosy settlements in Han District, Hainan, of which 81 cases were suitable for surgical operations; 87 blind eyes (8.25%) were found in 65 patients (12.33%), of which 10 cases (12 eyes) might be operated on for sight restoration with a possibility of success.

Corneal sensation loss was found in 589 cases (55.88%), loss of eyebrows and eyelashes in 382 eyes (36.24%), and lagophthalmos in 174 eyes (16.51%). The authors found that the longer the duration of leprosy, the more serious the eye diseases in the patients.—Authors' English Abstract

Okhandiar, R. P., Sinha, R. K. and Sinha, R. K. Study of hydration of stratum corneum in leprosy. Indian J. Lepr. **58** (1986) 395–400.

The study of the hydration power of the stratum corneum of lesions shows highly significant poor water uptake at low temperatures ($p < 0.001$), a defect not recorded after removal of water-soluble fractions. Secondly, the lesions show significant poor water-diffusive power ($p < 0.001$). The findings suggest a qualitative alteration in the stratum corneum of leprosy patients, probably in its water-soluble protein fraction.—Authors' Abstract

Rao, K. N., Lakshmi, V. and Saha, K. Undernutrition in lepromatous leprosy, Part I. Is it associated with poverty or with disease? Lepr. Rev. **57** (1986) 299–309.

Body dimensions (weight, height, and skinfold thickness) were measured in 339 normal subjects and 239 BL and LL patients of both sexes, belonging to semiurban and rural areas of a mining district of an eastern state of India. Of these patients, 56 belonged to higher per capita income and the remaining 183 to lower per capita income. Their daily intake of food was estimated by questionnaire and weighing food items. It was observed that both the patients (52%) as well as normal subjects (39%) with low per capita income suffered from grade I and II undernutrition. In contrast (13%) patients and (14%) normal subjects with higher per capita income showed only signs of grade I undernutrition. Importantly no patient suffered from severe undernutrition. Furthermore, the intake of protein, fat, calories, and vitamin A was significantly less in the normal as well as patients of low per capita income than that of higher per capita income. It was concluded that moderate undernutrition observed in lepromatous patients was associated with poverty and deprivation of food and not with the disease.—Authors' Summary

Rao, K. N. and Saha, K. Undernutrition in lepromatous leprosy, Part II. Altered levels of serum elements; their association with the disease and not with food deprivation. Lepr. Rev. **57** (1986) 311–316.

The study found that the diet of lepromatous leprosy patients was not deficient in dietary zinc, copper, calcium and magnesium, and this was comparable to that of healthy individuals. However, the serum of these patients showed significantly low levels of zinc, calcium and magnesium but increased copper in comparison to that in healthy control subjects.—Authors' Summary

Singh, R. G., Usha, Kumar, N. S., Singh, G., Kaur, P. and Singh, K. G. Bedside urinalysis in untreated leprosy patients. Indian J. Lepr. **58** (1986) 407–414.

The study included 53 patients with untreated leprosy attending University Hospital, Banaras Hindu University during a study period of 1½ years. The various types of leprosy included 9, 14, 16, and 14 cases of tuberculoid, borderline, lepromatous, and leprosy with type II reaction, respectively. The majority of the patients were below the age of 49 years with male preponderance; 66.04% of the patients came from the rural area. Painful micturation (dysuria) (13.20%) was the commonest urinary complaint re-

corded on enquiry. Specific gravity of urine did not show any change. Abnormal proteinuria was noted in 16.98%, 11.32%, 7.54%, and 3.77% of patients of leprosy with reaction, lepromatous, borderline, and tuberculoid group, respectively. Significant hematuria, pyuria, and epithelial cells were noted in all the groups. Hematuria was recorded in focal segmental glomerulonephritis (GN), mesangioproliferative, and diffuse endocapillary glomerulonephritis incidences of which were 7.89%, 7.89%, and 5.26%, respectively, in the biopsy tissues. Significant pyuria was noticed in all the groups except minimal change GN.—Authors' Abstract

Travers, C., Le Hoang, P., Badelon, I., Dhermy, P., Cabane, J. and Fontaine, M. [An etiology of anterior segment diseases not to be ignored: leprosy.] Bull. Soc. Ophthalmol. Fr. **85** (1985) 859–860.

Lepromatous leprosy is responsible for major ocular complications and blindness. We report a case of an 77-year-old Vietnamese male with typical anterior segment involvement.—Authors' English Summary

Ye, S.-H., Tang, M.-Y., Lu, W.-Q., Fan, H.-X., Yu, L.-C. and Zhou, W.-Q. [Incidence of bacteremia in leprosy and a comparison of various detecting methods.] Chung Kuo I Hsueh Ko Hsueh Yuan Hsueh Pao **7** (1985) 323–325. (in Chinese)

In this article, the authors observed an incidence of bacteremia in 63 patients with leprosy of various types under different detecting methods (leukocyte adherence, thick smear, hemolysis and trypsin digestion), the total positive rate being 53.9%. In 53 cases of multibacillary leprosy, bacteremia was confirmed in 33 (55.9%). The concentration of acid-fast bacilli in blood was 2.68–9.96 × 10^4/ml. In comparison of sensitivity of four methods used, it was shown that the positive rates of hemolysis and trypsin digestion methods were higher than those of the others. The clinical and epidemiological significance of bacteremia was discussed. The authors suggest that bacteremia be a reference criterion for efficacy in leprosy chemotherapy.—Authors' English Abstract

Zhang, J., Lu, S., *et al.* [The differentiation of hereditary sensory radicular neuropathy from pure neuritic leprosy.] China Lepr. J. **2** (1986) 44–47. (in Chinese)

Eight cases of hereditary sensory radicular neuropathy were reported. The pedigrees of two families were analyzed. In one of them, in which consanguinous marriages were seen in two generations, six patients were found. The histopathology, pathogenesis, mode of transmission, and clinical manifestations of the concerned condition were analyzed. Misdiagnosis could be made due to the similarity of clinical symptoms between this disease and pure neuritic leprosy. A differentiation might be achieved on scrutinizing the types of sensory disturbance, the hypertrophic peripheral nerve, the presence of muscular atrophy and tendon reflex, the family history and the age at onset and, if necessary, a histopathologic examination would help.—Authors' English Abstract

Immuno-Pathology

Arruda, W. O., Hacbarth, E., Doi, E., Santa-Maria, J. R., Barbosa, J. and Kajdacsy-Balla, A. A. [Effect of thalidomide on serum levels of immunoglobulins IgM and IgA, rheumatoid factor and isohemagglutinins anti-A and anti-B in patients with lepromatous leprosy: a double-blind study.] Rev. Inst. Med. Trop. São Paulo **28** (1986) 12–14. (in Portuguese and English)

A double-blind study was performed in a group of patients with lepromatous leprosy [45 in total] to evaluate the response of IgM and IgA serum levels and of serum titers of rheumatoid factor and isohemagglutinins anti-A and anti-B to administration of thalidomide 100 mg each day for 18 days. No significant effect was detected at the end of the study.—(*From* Trop. Dis. Bull.)

Barnass, S., Mace, J., Steele, J., Torres, P., Gervasoni, B., Ravioli, R., Terencio de las Aguas, J., Rook, G. A. W. and Waters, M. F. R. Prevalence and specificity of the enhancing effect of three types of interleukin 2 on T-cell responsiveness in 97 lepromatous leprosy patients of mixed ethnic origin. Clin. Exp. Immunol. **64** (1986) 41–49.

Peripheral blood mononuclear cells from 97 predominantly lepromatous leprosy patients and 11 control subjects were tested in a lymphoproliferative assay for response to *Mycobacterium leprae* (whole and sonicated), and sonicated *M. vaccae, M. tuberculosis,* and *M. scrofulaceum,* in the presence and absence of three types of interleukin 2 (IL-2) (crude, purified, and recombinant). IL-2 enhanced the response to sonicated *M. tuberculosis,* and *M. leprae* organisms more often in patients than in control subjects, but not significantly so and only in a minority of patients. This effect was significantly more common (though still only found in a minority of 46%) using *M. leprae* organisms as antigen, than when using sonicates of *M. leprae* (19%) or *M. vaccae* (19%). However it was nearly as frequent using sonicated *M. tuberculosis,* or *M. scrofulaceum.* Thus in only nine patients was the effect specific to *M. leprae.*

Enhancement by IL-2 could not be related to the type of IL-2 used, the dose of antigen, or the amount of endogenous IL-2 released by the cells tested. Similarly it was not related to the extent to which IL-2 caused increased background proliferation in control wells, which occurred to an equal extent using cells from control subjects, nor was it related to the extent of antigen-driven proliferation.

The data have also been analyzed in relation to duration of disease (50 years to a few weeks) and ethnic origin. No correlations have been revealed.

Thus enhancement by IL-2 of the lymphoproliferative response to mycobacterial antigens does occur using cells from lepromatous leprosy patients, but it is found in a minority of patients, it is not specific to *M. leprae,* and can occur with cells from normal donors.—Authors' Summary

Britton, W. J., Hellqvist, L., Garsia, R. J. and Basten, A. Dominant cell wall proteins of *Mycobacterium leprae* recognized by monoclonal antibodies. Clin. Exp. Immunol. **67** (1987) 31–42.

A cell wall fraction of *Mycobacterium leprae* has enhanced potency in activating immune T cells. By using a panel of monoclonal antibodies (MoAb), the dominant immunogen in this preparation was shown to be a complex of proteins of apparent molecular weight (M_r) 65 to 50 kD with a major antigen of 65 kD. Antigen capture assays supported the results of immunoblots and ELISA that this protein was concentrated in the cell wall. By varying the MoAb used as capture or tracer antibody, 1 of the 3 MoAb-defined epitopes on the 65 kD protein proved to be unique to *M. leprae,* while the other 2 were shared by *M. bovis* (BCG) and *M. tuberculosis.* The crossreactive epitope defined by MoAb L22 was present on a protein of M_r 12 kD as well as the 65 kD protein. The 12 kD protein was strongly radiolabeled with ^{125}I, and was immunoprecipitated by L22 but not by 2 other MoAb, L12 or L14. By contrast the higher molecular weight forms were only weakly precipitated by the 3 MoAb. Competitive inhibition assays with lepromatous leprosy sera demonstrated that the MoAb-defined epitopes were recognized by human B cells. The proteins bearing 1 of the crossreactive determinants were purified from *M. bovis* (BCG) sonicate by affinity chromatography with MoAb L22 coupled to Sepharose 4B. This antigen fraction stimulated proliferation in peripheral blood mononuclear cells from BCG-vaccinated, Mantoux positive individuals, indicating that the cell wall protein has cellular as well as humoral reactivity. The 3 MoAb defined epitopes are encoded by the DNA clone Y3178 recently isolated from *M. leprae.*—Authors' Summary

Brown, A. E., Vithayasai, V., Scollard, D. M., Nelson, K. E., Moses, V., Schauf, V. and Makonkawkeyoon, S. Lymphocyte transformation in lepromatous leprosy: a study of the influence of disease activity and symptom duration. Southeast Asian

J. Trop. Med. Public Health **17** (1986) 104–110.

The lymphocyte hyporesponsiveness to *Mycobacterium leprae* of patients with active lepromatous leprosy has been well described. This immune defect is less well understood in terms of its time of origin, possible reversibility, and specificity. To further examine the persistence and specificity of this abnormality, lymphocyte transformation tests of 93 leprosy patients to lepromin, BCG, and PHA were studied. Among lepromatous patients, a decreased response to *M. leprae* was seen, whether the disease was active or inactive. Decreased responses to BCG were found in lepromatous patients with active disease, but not in those with inactive disease. The duration of patient symptoms was not associated with differences in LTT responses among the active lepromatous patients.—Authors' Summary

Chatterjee, D., Cho, S.-N., Brennan, P. J. and Aspinall, G. O. Chemical synthesis and seroreactivity of *O*-(3,6-di-*O*-methyl-β-D-glucopyranosyl)-(1 → 4)-*O*-(2,3-di-*O*-methyl-α-L-rhamnopyranosyl)-(1 → 9)-oxynonanoyl-bovine serum albumin—the leprosy-specific, natural disaccharide-octyl-neoglycoprotein. Carbohydr. Res. **156** (1986) 39–56.

The outer disaccharide segment, namely, *O*-(3,6-di-*O*-methyl-β-D-glucopyranosyl)-(1 → 4)-2,3,-di-*O*-methyl-α-L-rhamnopyranose, of the trisaccharide-containing, leprosy-specific, phenolic glycolipid-I has been synthesized as the 8-(methoxycarbonyl)octyl glycoside in high yield and absolute stereospecificity by a series of modified Koenigs-Knorr and Helferich reactions. A particular feature of the synthetic pathway involves methylation of the 2-hydroxyl group of the rhamnose moiety under neutral conditions, after first preparing the 8-(methoxy carbonyl)octyl glycoside as the α anomer via the 1,2-orthoacetate, and thus precluding the possible formation of an anomeric mixture. The 8-(methoxy carbonyl)octyl *O*-(3,6-di-*O*-methyl-β-D-glucopyranosyl)-(1 → 4)-2,3-di-*O*-methyl-α-L-rhamnopyranoside was converted into the crystalline hydrazide, and this was coupled to bovine serum albumin (BSA), via intermediate acyl-azide formation, to produce the corresponding neoglycoprotein, *O*-(3,6-di-*O*-methyl-β-D-glucopyranosyl)-(1 → 4)-*O*-(2,3-di-*O*-methyl-α-L-rhamnopyranosyl)-(1 → 9)-oxynonanoyl-BSA, the so-called natural disaccharide-octyl-BSA. Extensive serological testing of this product against sera from leprosy patients and control populations, and comparison with the native glycolipid and previously synthesized neoglycoproteins, have shown that it is unparalleled in terms of sensitivity and specificity, and highly suited to replace the native glycolipid for the serodiagnosis of worldwide lepromatous leprosy.—Authors' Abstract

Chiplunkar, S., De Libero, G. and Kaufmann, S. H. E. *Mycobacterium leprae*-specific Lyt-2+ T lymphocytes with cytolytic activity. Infect. Immun. **54** (1986) 793–797.

Mice were immunized intradermally with 10^7 irradiated *Mycobacterium leprae* organisms, and draining lymph nodes were collected after 4 weeks. Lymph node cells were restimulated *in vitro* with soluble *M. leprae* antigen and accessory cells. The resulting T-cell line was propagated *in vitro* in the presence of *M. leprae* antigen, accessory cells, and interleukin-2-containing supernatants from concanavalin A-stimulated rat spleen cells. Long-term cultured T cells were Thy-1+ L3T4− Lyt-2+ as revealed by analysis with the fluorescence-activated cell sorter. From this line, T-cell clones with the same phenotype were established. The T-cell clone A4 failed to secret interleukin-2 after stimulation with antigen and accessory cells, and its growth depended on exogeneous interleukin-2. A4 T cells produced gamma-interferon in an antigen-specific, *H*-2-restricted, and interleukin-2-dependent way. Importantly, this T-cell clone was capable of lysing bone marrow macrophages presenting *M. leprae* antigen. Other T-cell clones as well as native Lyt-2+ T cells from *M. leprae*-immunized mice were also capable of lysing bone marrow macrophages expressing *M. leprae* antigens. These findings suggest that specific Lyt-2+ T cells participate in the immune response to *M. leprae*. It is postulated that cytolysis of *M. leprae*-infected macrophages or Schwann cells contributes to protection against and pathogenesis of leprosy.—Authors' Abstract

Cree, I. A. and Beck, J. S. The influence of killed *Mycobacterium leprae* and other mycobacteria on opsonized yeast phagocytosis. Clin. Exp. Immunol. **64** (1986) 35–40.

The influence of killed mycobacteria on the metabolic burst associated with phagocytosis of opsonized zymosan by normal human polymorphonuclear leukocytes (PMNL) or monocytes was studied by chemiluminescence (CL) measurements. *Mycobacterium leprae* reproducibly reduced the peak and total CL of both types of phagocyte to a small, but highly significant extent. Electron microscopy showed that *M. leprae* were phagocytosed: cells with ingested or adherent *M. leprae* phagocytosed fewer zymosan particles. *M. leprae* did not cause aggregation of the phagocytes or quenching of CL. *M. lepraemurium* did not influence the CL response to zymosan. Addition of *M. tuberculosis* caused an increased response with PMNL but not with monocytes.—Authors' Summary

Hsu, P.-S., Izaki, S., Hibino, T. and Izaki, M. Elastase activity in granulomatous inflammation in experimental murine leprosy. Exp. Mol. Pathol. **45** (1986) 84–92.

Proteolytic activity for [^{3}H]elastin, pyro-Glu-Pro-Val-pNA(S-2484), and Suc-$(Ala)_3$-pNA(AAApNA) was demonstrated in the bound fraction extracted with 2 M KSCN + 0.1% Triton X-100 from hypersensitivity-type murine lepromas in C57BL/6N mice, while elastase-inhibitor activity was separately observed in the soluble fraction extracted with a Tris–saline buffer. Sepharcyl S-200 gel chromatography showed a peak of elastolytic activity with approximately 20,000 in molecular weight. The following DEAE–Sepharose chromatography demonstrated three fractions of elastolytic activity (E-I, II, III). The inhibitory profile showed that E-I is a thiol proteinase, while E-II and E-III belong to serine proteinase-type elastases. Both E-II and E-III showed different properties with neutrophil elastase or elastase secreted from cultured macrophages, but identical characteristics to membrane bound-type elastase of monocytes. A lower level of elastolytic activity was detected in the bound fraction of non-hypersensitivity-type murine lepromas in CBA/N mice, suggesting more involvement of membrane bound-type elastase from monocytes/macrophages during the tissue remodelings of hypersensitivity-type granulomas.—Authors' Abstract

Itty, B. M., Mukherjee, R. and Antia, N. H. Adherence of *Mycobacterium leprae* to Schwann cells *in vitro*. J. Med. Microbiol. **22** (1986) 277–282.

Adherence of *Mycobacterium leprae* was studied *in vitro* in monolayer cultures of purified mouse Schwann cells. The optimum temperature and time for adherence were determined. Pretreatment of Schwann cells with lipase reduced adherence, but pretreatment with trypsin enhanced it and with four monosaccharides—L-arabinose, L-galactose, L-rhamnose and D-glucose—there was no significant effect, indicating that the receptors involved in adherence may be lipid.—Authors' Summary

Levis, W. R., Meeker, H. C., Schuller-Levis, G. B., Gillis, T. P., Marino, L. J., Jr. and Zabriskie, J. Serodiagnosis of leprosy: relationships between antibodies to *Mycobacterium leprae* phenolic glycolipid-I and protein antigens. J. Clin. Microbiol. **24** (1986) 917–921.

Sera from leprosy patients and controls were assayed for immunoglobulin M (IgM) and IgG antibodies to the *Mycobacterium leprae*-specific phenolic glycolipid-I (PGL-I) by enzyme-linked immunosorbent assay, for IgG antibodies to *M. leprae* protein antigens by Western immunoblot, and for antibodies to a 65-kilodalton (kD) protein antigen of *M. leprae* by a competition antibody binding assay. Elevated levels of anti-PGL-I IgM were seen in lepromatous and borderline lepromatous patients, and elevated levels of anti-PGL-I IgG were seen in borderline lepromatous patients. There was a significant correlation between the bacillary index (BI) and anti-PGL-I IgM whether all leprosy patients or only multibacillary patients were analyzed. A significant correlation was seen between anti-PGL-I IgG and BI when all leprosy patients were used for analysis, but not when only multibacillary patients were used. IgG antibodies to protein antigens of *M. leprae,* as detected by Western immu-

noblot, were more prevalent in lepromatous and borderline lepromatous patients than in borderline tuberculoid patients, while 1 of 8 controls showed 1 weak band. There were significant correlations between the number of *M. leprae* protein antigens detected by the sera of patients and both BI and the level of anti-PGL-I IgM. The 65-kD competition antibody binding assay detected active multibacillary leprosy. Patients positive for antibody to the 65-kD antigen had a significantly higher BI and levels of anti-PGL-I IgM and anti-PGL-I IgG than did patients who were negative. In addition, the level of antibody to the 65-kD antigen correlated with both the BI and anti-PGL-I IgM. We conclude that testing for antibodies to protein antigens of *M. leprae* may provide a useful adjunct to testing for antibodies to PGL-I.—Authors' Abstract

Lindh, J., Anderson, U., Britton, S. and De Ley, M. A single cell assay for the study of γ-interferon formation in leprosy patients. Clin. Exp. Immunol. **67** (1987) 51–54.

The number of γ-interferon-producing cells in the peripheral blood of leprosy (LL and BT) patients and controls was studied by the reversed protein A plaque assay before and after exposure *in vitro* to *Mycobacterium leprae* bacilli and Epstein-Barr virus (EBV). The level of spontaneous γ-interferon production was significantly higher in BT patients compared to LL patients and controls. *M. leprae* induced a specific γ-interferon response in lymphocytes from BT patients and from healthy contacts, whereas in LL patients and nonexposed controls the response was low or nonexisting. There were no significant differences in the γ-interferon response to EBV between the above groups.—Authors' Summary

Liu, J., Xia, M., Zhu, Y., *et al.* [Ultrastructure of Langerhans' cell in the skin of borderline leprosy patients.] China Lepr. J. **2** (1986) 51–52. (in Chinese)

The ultrastructural changes of Langerhans' cells (LC) in the skin lesions of 6 cases of borderline leprosy were presented. The number of LC was reduced in various degrees. The appearance of some LC was still normal. Many Langerhans' granules were seen in their cytoplasm and processes. Due to their convoluted nuclei and no tonofilament in the cytoplasm as well, they were quite different from the surrounding keratinocytes. Some LC with minimal changes were smaller in size and their processes were reduced in number. In LC with severe changes their processes were almost diminished, so they became round or oval in shape; their Langerhans' granules were few and small. Mitochondria showed definite degeneration: disruption, vacuolation or loss of their cristae. Nuclear membrane was partly obscure. Some LC had only a small amount of cytoplasm surrounding the nuclei, which were still irregular in configuration.

The authors emphasized that results of this observation might confirm their previous findings on LC in leprosy and suggested that LC might play an important role in the pathogenesis of leprosy.—Authors' English Abstract

Mehra, V., Sweetser, D. and Young, R. A. Efficient mapping of protein antigenic determinants. Proc. Natl. Acad. Sci. U.S.A. **83** (1986) 7013–7017.

A recombinant DNA expression strategy has been used to deduce the amino-acid sequences of six different antigenic determinants in a single protein of *Mycobacterium leprae,* the etiologic agent of leprosy. The gene encoding the *M. leprae* 65-kD antigen was sequenced and a λgt11 gene sublibrary was constructed with fragments of the gene. Recombinant DNA clones producing specific antigenic determinants were isolated by screening with monoclonal antibodies, and the sequences of their insert DNAs were determined with a rapid primer-extension method. The amino-acid sequence of each determinant was deduced from the minimum overlap of insert DNAs from multiple antibody-positive DNA clones. Amino-acid sequences for six different epitopes were elucidated. A peptide containing sequences for one of these epitopes was synthesized and shown to bind the appropriate monoclonal antibody; this antigenic determinant is unique to *M. leprae.* The approach de-

scribed here can be used to rapidly elucidate protein epitopes that are recognized by antibodies or T cells.—Authors' Abstract

Millikan, L. E., Krotoski, W. A., Mroczkowski, T. F., Douglas, J. T. and Courrege, M. L. Preliminary study of a *Mycobacterium leprae* bacterin vaccine in a human volunteer population in a nonendemic area. Int. J. Dermatol. **25** (1986) 245–248.

Seventeen volunteers who had never resided in areas with significant transmission of leprosy (Hansen's disease) were inoculated intradermally with 1.5×10^8 killed, purified armadillo-derived *Mycobacterium leprae* in a standardized preparation being tested for possible vaccine use. The peak of local skin responses, consisting of induration with or without ulceration similar to the post-lepromin Mitsuda reaction, occurred between the 21st and 28th days after injection. The maximum mean induration diameter was 17.2 mm; the minimum, 6.1 mm. Sera tested with the ELISA technique revealed no humoral response to either the sonicated bacilli, *M. leprae*-specific phenolic glycolipid-I antigen, or three semisynthetic analogues reactive with lepromatous patients' sera. The dose of *M. leprae* inoculated appeared to be safe and without unacceptable reactions at the injection site. One volunteer developed a generalized skin rash parallel to the local reaction, but the relationship of the former to the inoculation was unclear.—Authors' Abstract

Mohagheghpour, N., Gelber, R. H. and Engleman, E. G. T cell defect in lepromatous leprosy is reversible *in vitro* in the absence of exogenous growth factors. J. Immunol. **138** (1987) 570–574.

T lymphocytes from patients with lepromatous leprosy (LL) characteristically fail to respond to *Mycobacterium leprae.* This specific immunologic defect is thought to contribute to the aggressive clinical course that typifies patients with LL. We report that although fresh CD4+ (helper) T cells from most LL patients are specifically unresponsive to *M. leprae,* after culture in medium alone for 48 hr the same cells respond to *M. leprae* antigens. The recovery of T-cell function is specific for *M. leprae,* occurs at the level of responder CD4+ T cells, and is not affected by monocytes or CD8+ (suppressor) T cells. Recovery of T-cell reactivity is blocked by the presence of *M. leprae* bacilli in the preculture medium. These findings indicate that despite the apparent specific anergy seen in patients with LL, the T cells of most LL patients can respond to *M. leprae.* Their failure to do so, *in vivo,* may be due to the persistence of antigen, which renders antigen-reactive T cells nonresponsive either directly or via activation of CD4+ suppressor cells.—Authors' Abstract

Montreewasuwat, N., Curtis, J. and Turk, J. L. Accessory cell function of cells isolated from *Mycobacterium leprae*-induced granulomas. Cell. Immunol. **102** (1986) 346–354.

The large cells from *Mycobacterium leprae*-induced granulomas in guinea pig lymph nodes were separated by Percoll discontinuous density gradient centrifugation and on a fluorescence-activated cell sorter (FACS) using crossreacting monoclonal antibody to human MHC Class II antigens. Large Percoll-separated cells (83% Class II antigen positive and 52% macrophage-specific antigen positive) and FACS-separated cells are able to act as antigen-presenting cells for T-cell proliferation to PPD. In previous studies, macrophage antigen-positive cells consistently failed to act as accessory cells. This indicates that there is a population of accessory cells which are macrophage antigen negative and MHC Class II antigen positive present in these *M. leprae*-induced granulomas.—Authors' Abstract

Muthukkaruppan, V. R. A possible role for E-receptor in immunosuppression in leprosy. Indian J. Lepr. **58** (1986) 389–394.

It is proposed that the direct product(s) of *Mycobacterium leprae* or the macrophage-processed material derived from *M. leprae* when available in sufficient quantity in the micro-environment of immunocompetent cells would interact with the E-receptor (sheep erythrocyte binding site) of T cells in such a manner as to suppress the proliferative response of T cells stimulated

by antigens and mitogens. This results in the generalized or "specific" immunosuppression depending on the bacterial load of the system from which the lymphocytes are obtained.—(*From* the article)

Nelson, E. E., Wong, L., Uyemura, K., Rea, T. H. and Modlin, R. L. Lepromin-induced suppressor cells in lepromatous leprosy. Cell. Immunol. **104** (1987) 99–104.

The presence or absence of suppressor cells in leprosy patients was investigated by measuring peripheral blood lepromin-induced suppression of the ConA response. Significant suppressor activity was measured in 15 of 15 untreated or recently treated patients with lepromatous leprosy and 3 of 5 patients with borderline lepromatous leprosy. In addition, in patients with lepromatous leprosy, suppressor cell activity was found in 10 of 14 patients who had been under treatment for more than 1 year but in only 2 of 27 patients who had active or thalidomide-controlled erythema nodosum leprosum. Suppression was observed in only 5 of 29 tuberculoid leprosy patients, 1 of 6 patient contacts, and 0 of 11 normal controls. The differences between the lepromatous or borderline lepromatous group as compared with the tuberculoid group were statistically significant ($p < 0.001$). Our findings confirm the presence of lepromin-triggered suppressor cells in the peripheral blood of patients with lepromatous leprosy. These suppressor cells may contribute to the selective unresponsiveness of lepromatous patients to the antigens of *Mycobacterium leprae*.—Authors' Abstract

Ohkawa, S., Martin, L. N., Fukunishi, Y. and Gormus, B. J. Regulatory role of FcR+ and FcR− monocyte subsets in *Mycobacterium leprae*-induced lymphoproliferative response *in vitro*. Clin. Exp. Immunol. **67** (1987) 43–50.

We investigated 9 rhesus monkeys (*Macaca mulatta*) inoculated with *Mycobacterium leprae* and 3 normal human contacts. Peripheral blood monocytes were separated into Fc receptor positive (FcR+) and Fc receptor negative (FcR−) fractions, and their regulatory role in the lymphoproliferative response *in vitro* to *M. leprae* was studied. FcR− monocytes had strong antigen presentation activity and produced no suppressor effect while FcR+ monocytes had weak antigen presentation activity and produced a nonspecific suppressor factor spontaneously. With this assay system we determined that *M. leprae*-inoculated rhesus monkeys could be divided into three groups: good responders, very weak responders, and nonresponders.—Authors' Summary

Olcén, P., Harboe, M. and Warndorff van Diepen, T. Antigens of *Mycobacterium leprae* in urine during treatment of patients with lepromatous leprosy. Lepr. Rev. **57** (1986) 329–340.

Eighteen lepromatous leprosy patients were studied for urine *Mycobacterium leprae* antigen excretion during effective treatment. The amounts of antigen excreted varied during treatment and were in most cases decreasing during effective treatment.—Authors' Summary

Ottenhoff, T. H. M., Neuteboom, S., Elferink, D. G. and de Vries, R. R. P. Molecular localization and polymorphism of HLA class II restriction determinants defined by *Mycobacterium leprae*-reactive helper T cell clones from leprosy patients. J. Exp. Med. **164** (1986) 1923–1939.

MHC class II molecules carry the restriction determinants (RDs) for antigen presentation to antigen-specific Th lymphocytes. This restriction of T-cell activation endows those molecules with a key role in the induction and regulation of antigen-specific immune responses. Moreover, class II molecules are the products of class II immune response (Ir) genes. The polymorphism of these Ir genes leads to genetically controlled differences in immune responsiveness between different individuals. An important human example is leprosy, in which HLA class II-linked Ir genes determine the immune response against *Mycobacterium leprae*, the causative organism of the disease. Since the immune response against *M. leprae* is entirely dependent on Th cells, the HLA class II-linked Ir gene products may well regulate the immune response by con-

trolling the presentation of *M. leprae* antigens to Th cells. We therefore have investigated the HLA class II RD repertoire of *M. leprae*-reactive Th cell clones (TLC) by means of extensive panel and inhibition studies with fully class II-typed allogeneic APCs and well-defined HLA class II-specific mAbs. The TLC studied (N = 36) proliferated specifically towards *M. leprae,* produced IFN-γ upon activation, and had the CD3+CD4+CD8− phenotype.

The results show in the first place that the majority of the RDs for *M. leprae* reside on DR and not on DP or DQ molecules. This indicates a major role for DR molecules in the immune response to *M. leprae* and suggests that these molecules are the main products of *M. leprae*-specific Ir genes. Furthermore, since the expression of DR molecules is much stronger than that of DP and DQ molecules, these findings suggest that the localization of RDs for *M. leprae* on class II molecules correlates with the quantitative expression of these molecules. The observation that the RDs on DR molecules coded by a DR4 haplotype were situated only on those DR molecules that are known to be highest in expression can be explained in the same way.

Second, four distinct RDs related with but not identical to the Dw13 allodeterminant were carried by the DR+DRw53− ($\alpha\beta_1$) molecules of a DR4Dw13 haplotype. Since the known amino acid residue differences between the allelic DR4 related Dwβ_1 chains cannot explain the observed RD-polymorphism, this observation suggests that multiple distinct RDs unique for the DR4Dw13 haplotype are expressed by these molecules.

Only 2 of 36 TLC were not restricted by DR. One of these TLC recognized a new DP determinant; whereas the other TLC defined a remarkably polymorphic RD on a DQ molecule, which was distinct from the known DQ-related allospecificities. These TLC therefore define novel and functionally relevant polymorphisms on class II molecules. Finally, 3 of the 36 TLC reacted also with a restricted number of allogeneic APC in the absence of *M. leprae* antigen, indicating crossreactivity between self class II RD in combination with *M. leprae* antigens and allodeterminants.—Authors' Summary

Prasad, H. K., Mishra, R. S. and Nath, I. Phenolic glycolipid-I of *Mycobacterium leprae* induces general suppression of *in vitro* concanavalin A responses unrelated to leprosy type. J. Exp. Med. **165** (1987) 239–244.

Using a costimulant assay, *in vitro* ConA responses of patients across the leprosy spectrum were found to be markedly suppressed by phenolic glycolipid-I (PGL-I), a unique antigen of *Mycobacterium leprae.* The degree of inducible suppression as well as the number of leprosy patients showing suppression of mitogenic responses was higher with PGL-I as compared with integral *M. leprae* ($p < 0.05$ to <0.01). Both untreated lepromatous (60%) as well as tuberculoid leprosy (67%) patients showed significant suppression ranging from 13% to 64% and 12% to 79%, respectively. Thus, PGL-I appears to have a universal suppressive effect on ConA responses and is unlikely to play a central role in determining the leprosy spectrum.—Authors' Summary

Samuel, N. M. and Stanford, J. L. Phytohemagglutinin as a skin test for the evaluation of immune competence in patients with leprosy and tuberculosis and in controls. Asian Med. J. **28** (1985) 507–523.

Phytohemagglutinin (PHA), a mitogen derived from *Phaseolus vulgaris,* was used as a skin test in patients with leprosy and tuberculosis, and in normal controls. The time course of the cutaneous response was correlated with intradermal skin tests such as *Candida albicans,* tuberculin and streptokinase-streptodornase. Cellular morphology at the skin-test sites shows perivascular collections of mononuclear cells, absence of basophils and presence of eosinophils.—Authors' Abstract

Sasiain, M. del C., de la Barrera, S., Ruibal-Area, B., Cardama, J. E., Gatti, J. C. and de Bracco, M. M. de E. Suppressor response in lepromatous leprosy patients: role of Leu2a cells. Immunology **60** (1987) 13–18.

The contribution of nonspecific suppressor mechanisms to the overall immunoregulatory defect observed in lepromatous

leprosy was evaluated. ConA-induced suppression was assayed using the standard two-stage test in 27 lepromatous leprosy patients, 19 of them during the quiescent stage (LL) and 8 during erythema nodosum leprosum (ENL). Lymphocytes from normal individuals react in this assay, yielding higher suppression as the numbers of ConA-induced suppressor cells (Leu2a+ cells) increase. In contrast, two patterns of response were observed in both LL and ENL patients, those giving lower suppression as the number of suppressor cells increased (LL-A and ENL-A) and those responding with the normal pattern (LL-B and ENL-B). The abnormal dose-response profile was not related to the disease stage, as both ENL and LL patients were included in groups with normal or atypical response. Reaction of the potential suppressor cells with anti-Leu2a antibody abolished suppression in LL-B and normals, whereas ConA-induced suppression was unchanged or higher in ENL-A, ENL-B, and LL-A, indicating that in these patients Leu2a+ cells interfered with the generation of ConA-induced suppression. The contribution of spontaneous suppression was examined and it was shown that suppressor activity in the absence of ConA stimulus was higher in ENL (both ENL-A and ENL-B) and LL-A. Thus, it appears that the occurrence of high spontaneous suppressor activity, probably related to *in vivo* activation, is associated with a relative inability to generate *de novo* suppression after ConA stimulation in these patients.—Authors' Summary

Sehgal, V. N., Gautam, R. K. and Sharma, V. K. Immunoprofile of reactions in leprosy. Int. J. Dermatol. **25** (1986) 240–244.

The immunologic profile during erythema nodosum leprosum (ENL) revealed increased percentage and absolute count of B lymphocytes, in addition to considerably lowered levels of complement component C3. Serum immunoglobulins—IgG, IgA, and IgM—were significantly raised after subsidence of ENL; whereas upgrading reaction showed an increase of absolute count of total T lymphocytes and percentage and count of B lymphocytes. In addition, a raised serum IgM level was noted after regression of ENL. Downgrading reaction demonstrated a decreased percentage of early T lymphocytes and raised the absolute count of B lymphocytes. Serum IgA levels were found to be increased after amelioration of ENL.—Authors' Abstract

Sibley, L. D. and Krahenbuhl, J. L. *Mycobacterium leprae*-burdened macrophages are refractory to activation by gamma interferon. Infect. Immun. **55** (1987) 446–450.

Mycobacterium leprae grows to enormous numbers in the *nu/nu* mouse foot pad, producing granulomas resembling those of lepromatous leprosy in humans. Foot pad granuloma cells gorged with *M. leprae* were established in primary cell culture to examine their functional capabilities. These cells were classified as macrophages by the following criteria: positive staining for nonspecific esterase, reduction of nitro blue tetrazolium during phagocytosis of *Candida albicans,* possession of Fc receptors, and possession of Mac-1 antigen. Foot pad macrophages also phagocytized and supported the intracellular growth of *Toxoplasma gondii.* However, unlike peritoneal macrophages, foot pad macrophages could not be activated to kill or inhibit *T. gondii* by macrophage-activating factor produced by mitogen-stimulated spleen cells or by recombinant gamma interferon. Thus, although the lepromatous macrophages appeared to be normal in many of their functions, they were defective in response to macrophage-activating signals.—Authors' Abstract

Uyemura, K., Dixon, J. F. P., Wong, L., Rea, T. H. and Modlin, R. L. Effect of cyclosporine A in erythema nodosum leprosum. J. Immunol. **137** (1986) 3620–3623.

Erythema nodosum leprosum (ENL) is a reactional state of lepromatous leprosy in which the loss of suppressor cell function, decrease in suppressor cell numbers, and increase of interleukin 2 production are observed. We reasoned that cyclosporine A (CsA), by opposing these immune responses, could suppress the ENL reaction and restore patients to the quiescent lep-

romatous state. We tested this hypothesis *in vitro* by measuring the effect of CsA on *Mycobacterium leprae*-triggered suppressor cells. In 24 of 25 patients with ENL, suppressor cell activity was restored by CsA. The target of CsA appeared to be macrophages. These findings are significant in that they provide the first evidence for the potential efficacy of CsA in the treatment of ENL. Preliminary clinical trials indicate a beneficial therapeutic effect associated with increased T-suppressor cells in lesions.—Authors' Abstract

Microbiology

Baquillon, G., Testa, J. and Saint-André, P. [Staining of *Mycobacterium leprae:* comparison between Lapeyssonnie and Causse's technique and THELEP's technique to evaluate the bacteriological index.] Med. Trop. **46** (1986) 161–168. (in French)

In the present review, two staining techniques have been compared to evaluate bacteriological index: the Lapeyssonnie and Causse's technique, used in French-speaking Africa, and the one recommended by the WHO scientific panel on the chemotherapy of leprosy, THELEP.

It appears that the former facilitates the finding of a greater number of bacilli. More efficient, it is also easier and faster than the latter one and, consequently, more adapted to logistic constraints attached to the fight against leprotic endemia in Africa.—Authors' English Summary

Dhariwal, K. R., Yang, Y.-M., Fales, H. M. and Goren, M. B. Detection of trehalose monomycolate in *Mycobacterium leprae* grown in armadillo tissues. J. Gen. Microbiol. **133** (1987) 201–209.

Trehalose-6-monomycolate (TMM) was isolated from the lipids of armadillo-derived *Mycobacterium leprae.* Only meager amounts of this glycolipid were recovered, but its structure was unequivocally established. Only α-mycolates were detected in the TMM by ^{252}Cf plasma desorption mass spectrometry. Electron impact mass spectrometry showed the alpha branch to be principally C_{20}. Trehalose dimycolate (cord factor) was not detectable. Since we have also found TMM in *M. lepraemurium* and in every *Mycobacterium* species so far examined, we suggest that this glycolipid is truly ubiquitous among mycobacteria.—Authors' Abstract

Hall, R. M. and Ratledge, C. Exochelin-mediated iron acquisition by the leprosy bacillus *Mycobacterium leprae.* J. Gen. Microbiol. **133** (1987) 193–199.

Exochelins, water-soluble siderophores of mycobacteria, were isolated and partially purified from culture filtrates of iron-deficiently grown cultures of *Mycobacterium neoaurum* NCTC 10439 and an armadillo-derived mycobacterium (ADM 8563). Two biologically active fractions mediating iron uptake were isolated from each bacterium which not only were able to transport iron into the producing organism but also into suspensions of *M. leprae* isolated from armadillo liver. The rate of exochelin-mediated iron uptake into *M. leprae* was about 1.5% of the rate observed into the producing organisms. The process of iron uptake appears to be by facilitated diffusion as it was not inhibited by $HgCl_2$, NaN_3, KCN, dinitrophenol or carbonyl cyanide *m*-chlorophenylhydrazone. Since no uptake of iron occurred into iron-sufficient ADM cells, this may indicate that *M. leprae,* as recovered from an animal tissue, had been growing iron-deficiently in order for iron uptake to have been demonstrated *in vitro.*—Authors' Abstract

Kusaka, T. and Mori, T. Pyrolysis gas chromatography—mass spectrometry of mycobacterial mycolic acid methyl esters and its application to the identification of *Mycobacterium leprae.* J. Gen. Microbiol. **132** (1986) 3403–3406.

Pyrolysis gas chromatography-mass spectrometry of methyl mycolates from 32 species of mycobacteria, including *Mycobacterium leprae,* was carried out. The mycobacteria could be classified into four groups in respect to the fatty acid ester patterns detected within the range C_{20} to C_{26}. The applicability of this pyrolysis-gas chromatographic method for identifying *M. leprae* is discussed.—Authors' Abstract

Li, F. [Modified method of counting acid-fast bacilli with agarose gel.] China Lepr. J. **2** (1986) 48–50. (in Chinese)

A method of counting the number of acid-fast bacilli was reported. The bacilli suspension was diluted with warm liquefied 1% agarose solution, then a small amount of it was dipped into a hemacytometer. After cooling and drying, the acid-fast bacilli on the chamber were stained and counted. With this method, using *Mycobacterium lepraemurium* as the test bacilli, the author proved statistically that this bacilli counting method is quite an accurate one.—Author's English Abstract

Lygren, S. T., Closs, O., Bercouvier, H. and Wayne, L. G. Catalases, peroxidases, and superoxide dismutases in *Mycobacterium leprae* and other mycobacteria studied by crossed immunoelectrophoresis and polyacrylamide gel electrophoresis. Infect. Immun. **54** (1986) 666–672.

The five mycobacteria *Mycobacterium lepraemurium, M. leprae, M. bovis* BCG, *M. smegmatis,* and *M. intracellulare* were studied. Catalase and peroxidase activities were demonstrated in polyacrylamide and crossed immunoelectrophoresis gels for *M. lepraemurium, M. intracellulare,* and BCG, but not for *M. leprae.* Peroxidase and catalase activities were associated with the same precipitate line in crossed immunoelectrophoresis for *M. lepraemurium, M. intracellulare,* and BCG, showing that in these mycobacteria the two enzyme activities resided in the same molecule. *M. smegmatis* peroxidase and catalase activities were closely associated on polyacrylamide gel electrophoresis, but on the crossed immunoelectrophoresis catalase and peroxidase activities were associated with two different precipitate lines. Catalases without peroxidase activity were demonstrated in crossed immunoelectrophoresis and polyacrylamide gel electrophoresis in *M. intracellulare* and *M. smegmatis.* The catalase without peroxidase activity in *M. intracellulare* was heat resistant and therefore classified as an m-catalase. In *M. smegmatis* the catalase without peroxidase activity was only partially heat resistant. All of the catalases with peroxidase activity were heat-sensitive t-catalases. Superoxide dismutase activity in the crossed immunoelectrophoresis was associated with the *M. leprae* antigen no. 4 and with crossreacting antigens in the other mycobacteria studied. Several superoxide dismutases were demonstrated in *M. duvalii.* They were antigenically different from the other superoxide dismutases in this study, as shown by lack of reactivity with a monospecific antibody to *M. lepraemurium* superoxide dismutase. Molecular weights were estimated for all the enzymes in this study by sodium dodecyl sulfate-polyacrylamide gels.—Authors' Abstract

Portaels, F., Asselineau, C., Baess, I., Daffé, M., Dobson, G., Draper, P., Gregory, D., Hall, R. M., Imaeda, T., Jenkins, P. A., Lanéelle, M. A., Larsson, L., Magnusson, M., Minnikin, D. E., Pattyn, S. R., Wieten, G. and Wheeler, P. R. A cooperative taxonomic study of mycobacteria isolated from armadillos infected with *Mycobacterium leprae.* J. Gen. Microbiol. **132** (1986) 2693–2707.

Seventeen strains of mycobacteria, recovered from 6 armadillos experimentally infected with *Mycobacterium leprae,* were examined in 10 different laboratories. This collaborative study included use of conventional bacteriological tests, lipid analyses, determination of mycobactins and peptidoglycans, characterization by Py-MS, and immunological, metabolic, pathological and DNA studies. These armadillo-derived mycobacteria (ADM) formed 5 homogeneous groups (numbered ADM 1 to 5) on the basis of phenetic analyses. However, DNA studies revealed only 4 homogeneous groups since group ADM 1 and 1 of the 2 strains in group ADM 3 showed a high level of DNA relatedness. The phenetic and DNA studies confirmed that the ADM strains dif-

fered from all other known mycobacteria. Cultural, biochemical, metabolic and pathogenic properties as well as DNA-DNA hybridizations clearly differentiated these ADM from *M. leprae.*—Authors' Abstract

Prabhakaran, K. Biochemical studies on *Mycobacterium leprae.* Indian J. Lepr. **58** (1986) 461–474.

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* contain 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

Talati, S. and Mahadevan, P. R. Lipase activity in *Mycobacterium leprae*—an indicator of metabolic function. Indian J. Lepr. **58** (1986) 367–372.

The presence of lipase in *Mycobacterium leprae* obtained from human nodules and infected armadillo tissues has been detected by demonstrating the ability of the bacteria to hydrolyze tributyrin. This capacity is expressed during incubation of the bacteria with the substrate and needs a source of carbon and other energy metabolites. The activity is blocked by the anti-*M. leprae* drug rifampin. It is concluded that expression of lipase activity is a metabolic event of *M. leprae* while they are maintained in an energy providing medium.—Authors' Abstract

Vasanthakumari, R., Jagannath, K. and Rajasekaran, S. A cold staining method for acid-fast bacilli. Bull. WHO **64** (1986) 741–743.

The Ziehl-Neelsen method is probably the best known and most frequently used procedure for staining tubercle bacilli. The method requires controlled heating for its success. However, in developing countries, such as India, where most laboratories rely mainly on spirit lamps as a source of heat, the Ziehl-Neelsen method often cannot be carried out because rectified spirit is difficult to obtain. The study describes a cold staining technique that uses the same staining solutions as the conventional Ziehl-Neelsen method. For direct smears, the correlation of results of the cold staining procedure with those of the Ziehl-Neelsen method was 97% and for concentrated smears was 99%. The method described is suitable for use in basically equipped laboratories.—Authors' Abstract

Experimental Infections

Brett, S. J. and Butler, R. Resistance to *Mycobacterium lepraemurium* is correlated with the capacity to generate macrophage activating factor(s) in response to mycobacterial antigens *in vitro.* Immunology **59** (1986) 339–345.

The kinetics of cell-mediated immunity developed during the course of *Mycobacterium lepraemurium* infection were determined in resistant (C57BL) and susceptible (BALB/c) mice. Control of *M. lepraemurium* growth following foot pad infection was T-cell dependent in C57BL mice as shown by the finding that T-cell deprived mice had enhanced bacterial counts in the foot pad. In contrast, T-cell deprivation did not significantly alter the course of infection in BALB/c mice. However a T-cell dependent inflammatory response, resulting in an increase in size of the infected foot pad, occurred in both strains, although it developed

slightly later in BALB/c mice. Cells isolated from the lymph nodes, draining the infected foot pads, were assayed for their proliferative responses to heat-killed *M. lepraemurium* (HK-MLM) antigens. Although lymph-node cells from both mouse strains proliferated to HK-MLM early in the infection (1–2 weeks) both C57BL and BALB/c mice developed diminished *in vitro* proliferative reactivity within 4–6 weeks post-infection. Supernatants derived from cultures of lymph-node cells that had been stimulated with concanavalin A (ConA) or HK-MLM antigens were assayed for the presence of macrophage-activating factor (MAF) activity using a tumor cytostasis assay and interferon (IFN) activity using a viral growth inhibition assay. Significantly higher levels of MAF and IFN were found in culture supernatants derived from HK-MLM-stimulated lymph-node cells from infected C57BL mice than from BALB/c mice during the first 8 weeks of infection. However, cells from infected mice of both strains produced similar amounts of both MAF and IFN in response to ConA.—Authors' Summary

Ganguly, N. K., Vaishnavi, C., Kumar, B. and Kaur, S. ADCC function in *Mycobacterium leprae* inoculated normal and immunosuppressed mice. Indian J. Lepr. **58** (1986) 377–381.

Normal and immunosuppressed mice were inoculated with *Mycobacterium leprae* obtained from untreated lepromatous patients. Besides monitoring the acid-fast bacilli counts in the foot pads at 3, 6 and 9 months post-inoculation, antibody dependent cellular cytotoxicity (ADCC) function was studied. The ADCC function was seen to be largely unaltered in the *M. leprae* infected animals, comparable to the observation made in human leprosy.—Authors' Abstract

Gelber, R. H. The killing of *Mycobacterium leprae* in mice by various dietary concentrations of dapsone and rifampin. Lepr. Rev. **57** (1986) 347–353.

The killing of *Mycobacterium leprae* by various dietary concentrations of dapsone and rifampin was assessed by the proportional bactericidal test. Dapsone 0.00001% and 0.0001% in mouse food were not bactericidal, while dapsone 0.001% and 0.01% were both found 87% (±22%) bactericidal. Concentrations of dapsone required for killing the strain of *M. leprae* were higher than had previously been found necessary for inhibition of bacterial multiplication (0.0001%). Rifampin 0.01% and 0.005% in mouse food were found to be, respectively, 99.9% (±0.1%) and 90% (±6%) bactericidal. Rifampin 0.003%, 0.001%, and 0.0003% did not result in significant killing. The strain studied was found to be killed by high dietary concentrations of rifampin similar to that of previous studies but was far more resistant to killing by lower dietary concentrations of rifampin than had been reported previously for other strains. The implications of these findings are discussed.—Author's Summary

Hoffenbach, A. and Bach, M.-A. Bacillary growth, interleukin-2 production defect, and specific antibody secretion governed by different genetical factors in mice infected subcutaneously with *Mycobacterium lepraemurium*. Cell. Immunol. **102** (1986) 273–286.

Different mouse strains were infected subcutaneously in the foot pad with 10^7 *Mycobacterium lepraemurium* (MLM). At various stages of the infection, the number of acid-fast bacilli (AFB) in different organs, spleen cell interleukin-2 (IL-2) production, and specific IgM and IgG serum antibodies to MLM sonicate were assessed. Strains were separable into two distinct groups depending on the number of AFB recovered from the different organs, without any obvious influence of the *Bcg* gene. Thus C57BL/6, DBA/2, (C57BL/6 × DBA/2)F_1 and C3H/Pas mice belonged to the high-resistance group and DBA/1, BALB/c, and CBA strains to the low-resistance group. IL-2 production was depressed only in C57BL/6 and C3H/Pas mice. Anti-MLM antibody response also markedly varied according to strains, in terms of antibody titers, Ig class distribution, and species specificity, but with a different genetic pattern from that observed for MLM growth control.—Authors' Abstract

Job, C. K., Sanchez, R. M. and Hastings, R. C. Lepromatous placentitis and intrauterine fetal infection in lepromatous nine-banded armadillos (*Dasypus novemcinctus*). Lab. Invest. **56** (1987) 44–48.

Three pregnant lepromatous armadillos along with the three sets of four fetuses and their placentae were studied histopathologically. *Mycobacterium leprae* were present in the decidual tissue, trophoblastic cells which line the chorionic villi, and in the cells that form the internal structure of the villi. Acid-fast organisms were also seen in the spleens of three fetuses. Congenital infection is clearly possible in leprosy in the armadillo and may also occur in humans.—Authors' Abstract

Rojas-Espinosa, O., Mendez, P., Oltra, A. and Arce, P. Antimycobacterial antibodies in *Dasypus novemcinctus* infected with *Mycobacterium leprae* and their correlation with the serum levels of lactate dehydrogenase. Lepr. Rev. **57** (1986) 317–327.

Discovery of armadillos (*Dasypus novemcinctus*) as animals susceptible to infection with *Mycobacterium leprae* has allowed the experimental study of leprosy to extend beyond the limits of the mouse foot pad. Armadillos, however, do not all become equally infected with a given dose of *M. leprae*. Therefore, it would be advantageous to establish a technique for the early identification of those animals bearing the disease.

Infection in armadillos originates systemic involvement which includes liver damage and the consequent release of LDH into circulation before the appearance of the clinical signs of the disease. In this study, where an enzyme-linked immunoassay for the detection of antimycobacterial antibodies was developed, those very same animals that showed an increase in their serum LDH activity showed the presence of anti-*M. leprae* antibodies to significant titers and eventually the presence of disease. From the results with some animals, it appears that the presence of antimycobacterial antibodies occurs before the elevation in the serum LDH activity.

Periodical measurement of both antimycobacterial antibodies and LDH activity in the sera of *M. leprae*-inoculated armadillos may help one to detect the early infection, decide whether or not an animal is indeed infected, and decide how to proceed with the animals under investigation. The results also reveal some of the immunological and biochemical consequences of the *M. leprae*-infection in the armadillo.—Authors' Summary

Vaishnavi, C., Ganguly, N. M., Kumar, B., Chakaravarti, R. N., Kaur, H. and Kaur, S. Sciatic nerve in experimental leprosy. Indian J. Lepr. **58** (1986) 373–376.

Swiss albino mice were inoculated with *Mycobacterium leprae* obtained from untreated lepromatous patients. Histopathological study of sciatic nerves showed no abnormality. However a few free acid-fast bacilli were detected in the sciatic nerves taken from the inoculated limbs during the early stages of infection, suggesting the nerve-fiber route of travel as seen in humans in experimental leprosy, too.—Authors' Abstract

Wang, H.-Y. [Preliminary observation on the effect of thymic peptide in experimental infection of mice with *Mycobacterium leprae*.] Chung Kuo I Hsueh Ko Hsueh Yuan Hsueh Pao **7** (1985) 227–228. (in Chinese)

CFW strain mice, infected with *Mycobacterium leprae* through the foot pad, were treated with thymic peptide (CTP) using the kinetic method. CTP was injected i.m. early in the infection and its effect on the bacterial growth curve was observed. The results indicate that CTP may increase the capacity against experimental infection in mice. However, it seems that the effect of long-term treatment is better than that of a short one.—Author's English Abstract

Epidemiology and Prevention

Cai, Z. and Hong, D. [Epidemic of leprosy and the effects of its control in the South Prefecture, Jiangxi Province (China).] China Lepr. J. **2** (1986) 8–10. (in Chinese)

This article reports the epidemic condition of leprosy in 19 counties and cities in the south area of Jiangxi Province and summarizes the results obtained in 24 years of control, which revealed that the spread of leprosy in the area showed a tendency to decline markedly.—Authors' English Abstract

Cartel, J. L., Gallais, J. J., Naudillon, Y., Remy, J. G. and Grosset, J. H. [The epidemiology of leprosy in Guadeloupe from 1970 to 1984.] Acta Leprol. **4** (1986) 161–173. (in French)

Analysis of computerized data compiled according to the OMSLEP system in the leprosy control service in Guadeloupe has shown that from 1970 to 1984, 80% of the patients were detected by passive case-finding (symptomatic patients), 10% by active case-finding among the school population and 10% by active case-finding among the household contacts of known patients. During the same period of time, global incidence of new cases of leprosy declined from 24 to 11 per 100,000 inhabitants. The decline was greater for paucibacillary cases ($y = -0.94$) than for multibacillary cases ($y = -0.45$), and much greater among persons under 15 years of age ($y = -3.22$) than among those older ($y = -0.67$). Simultaneously 118 relapses, an annual incidence of 1.3%, were observed among the multibacillary patients previously treated by dapsone monotherapy for 5 years or more. All cases the biopsies of whom were inoculated for drug sensitivity testing in the mouse foot pad yielded dapsone-resistant *Mycobacterium leprae*. The proportions of relapses among the annual sources of infection increased from 16% in 1970 to 47% in 1984. Chemoprophylaxis of relapses among multibacillary patients already treated for more than 5 years with dapsone monotherapy is one of the priorities for leprosy control in Guadeloupe.—Authors' English Summary

Lei, G. [Survey on leprosy in Henan Province (China).] China Lepr. J. **2** (1986) 10–13. (in Chinese)

The epidemiological status of leprosy in Henan Province was analyzed. Since 1957, 858 cases were found and admitted to hospitals, of which 729 cases were cured (84.96%). Now there are still 63 active patients under treatment. The patients were distributed in small clusters over the whole province. The incidence had decreased from 0.11/100,000 (1958) to 0.003/100,000 (1983), by 97.27%; the prevalence from 0.0042‰ to 0.0008‰ by 80.95%. The peak of the age at onset shifted backward and the type rate decreased. In Gushi county, where leprosy patients were most abundant among the counties of the province in the past, only one case was found during the period of 1980 to 1984. The incidence in that county was 0.0016/100,000, and there were only 6 cases in 1984, the prevalence rate being 0.0048‰. The incidence and prevalence rates in the province now are lower than the standard of basic eradication of leprosy issued by the Ministry of Public Health. The author considers that although the seriousness of the epidemic of leprosy in Henan Province has been decreasing, the leprosy control work should be strengthened in order to eliminate leprosy in Henan fully.—Author's English Abstract

Lu, J. [Effects of controlling leprosy in Wuhan City (China).] China Lepr. J. **2** (1986) 18–20. (in Chinese)

Leprosy control in the city of Wuhan has been launched since 1952. Comprehensive measures, including prevention, treatment and investigation, have been adopted. By the end of the year of 1984, a total of 2622 cases of leprosy was found, of which 2584 (98.6%) cases were treated and 2269 (87.8%) were clinically cured. There remains only 82 active patients now. The prevalence reduced from 0.04% (1956) to 0.025% (1984), and the incidence reduced from 10.62/100,000 (1952) to 0.20/100,000 (1981).

The prevalence and incidence have reached, respectively, the standards of

"controlled" and "basically eradicated" levels issued by the Ministry of Public Health. In the comprehensive control measures, the key points are to detect and treat leprosy patients, especially multibacillary patients. A joint effort of leprosy control units with the general health network is necessary.—Author's English Abstract

Oughanem, M., Ysmail-Dahlouk, M., Ait-Khaled, A., Cheikh, F. and Discamps, G. [Epidemiological profile of leprosy in Algeria.] Acta Leprol. **4** (1986) 175–178. (in French)

Hansen's disease does not create, now or before, a public health problem in Algeria. There are, now, 21 cases of leprosy; 18 indigenous and 3 imported cases. Northeast of the country and particularly the Kabyle region represent the origin of the majority of indigenous leprosy patients (13 cases) and Morocco for the foreign ones (2 cases). Lepromatous forms are the most numerous, both among indigenous (15 cases) and foreigners (2 cases).—Authors' English Summary

Paties, C., Schena, C., Piva, G., Bassi, F., Dei Cas, A. and Alberici, F. Hansen's disease: a new endemic focus in the Piacenza Province? A description of four diagnosed cases by cutaneous biopsy. Bol. Ist. Sieroter. Milan **65** (1986) 125–130.

Four cases of Hansen's disease (2 lepromatous leprosy, 1 tuberculoid leprosy and 1 indeterminate leprosy) diagnosed from 1982 to today in Piacenza with histological and ultrastructural data are described in this study. Two cases (1 lepromatous leprosy and 1 indeterminate leprosy) are probably imported, while the other 2 are apparently autochthonous. In all the cases the diagnosis or the suspicion of the disease are triggered after histological examination of the cutaneous biopsy, without any pre-existing clinical suspicion. In the discussion of the epidemiological significance of the number of cases the authors hypothesize the possible formation of an endemic area in Piacenza, and intend to call attention of medical officials to the alarming fact of the probable existence of Hansen's disease in Italy.—Authors' Summary

Rao, P. S. Retrieval of "left the area leprosy cases" by cross-notification. Indian J. Lepr. **58** (1986) 420–423.

It has been noticed that a large number of cases registered as leprosy under National Leprosy Control Programme are being deleted (approximately 20%–25% of total cases) as "left the area" every year. It is not known what is happening to these "left the area cases." It is resulting in loss of regularity of treatment to the patient, continuation of transmission of infection in the community and multiple registration of the same case as a new case at several places giving rise to false incidence rates. A system of cross-notification is suggested to overcome this problem.—Author's Abstract

Ren, X. and Xie, Z. [Review of leprosy control in Jiangsu Province (China).] China Lepr. J. **2** (1986) 66–68. (in Chinese)

This article reports 35-years' experience of leprosy control in Jiangsu Province. A total of 53,815 leprosy patients were found during 1949–1984. Of them, 41,493 were cured, 8,659 died or moved away to other places. The prevalence rate dropped from $0.63/10^3$ (1973) to $0.59/10^4$. The average incidence declined from $5.76/10^5$ (1956–1960) to $0.32/10^5$ (1980–1984). The index of controlling prevalence was reached in 45 out of 75 counties or cities in the province. It is expected to basically eliminate leprosy in Jiangsu in 1998.—Authors' English Abstract

Yang, X. [Epidemic of leprosy and its control in Guangdong (China).] China Lepr. J. **2** (1986) 14–17. (in Chinese)

The history of the prevalence of leprosy in Guangdong before the liberation was described and the major causes for the prevalence were discussed. After liberation, 93,426 leprosy patients were found by the end of 1980 in the whole province of Guangdong, with an incidence rate of 0.156‰, of whom 67,250 patients had been cured. According to the survey in 1970, 94.5% of the counties and cities were high or moderate epidemic areas, scattered mainly in Sahntou, Zhanjiang, Feshan and Guangzhou Prefectures. The leprosy pa-

tients were distributed in foci. In Zhanjiang Prefecture, where the number of patients was at the top of the list, the number of the villages where there were leprosy patients was only 3.95% of all the villages in the 11 counties comprising the prefecture.

In order to find the patients most thoroughly, several measures were taken. General and regular treatment of the patients was the most important measure in the control of the disease. The main sources of the infection were patients within the families and the villages. About 90.02% of the patients were infected from them. The incidence rate in the members of the lepromatous and borderline patient families was 12.52‰. Most of the patients found during the last 30 years have been cured and the prevalence and the incidence rates of the disease decreased significantly.—Author's English Abstract

Zhou, T. [Survey on leprosy in the Southwest Prefecture, Guizhou Province (China).] China Lepr. J. **2** (1986) 6–8. (in Chinese)

The Southwest Prefecture of Guizhou Province is a national autonomous region inhabited mainly by Buyi and Miao nationalities. A clue survey of leprosy was carried out there from 1982 to 1985, and 783 new patients were found. Now there are 1689 active patients, amounting to 0.75‰ of the population of the region, decreased by 72% from accumulated number of patients. Of the newly detected 783 patients, the range of their ages is 6–78 years; the proportion of male to female is 3.07 to 1; durations of their disease are 4 months to 41 years, with an average of 11.1 years; the type rate is 55.42% and the proportion of patients having a history of contact with leprosy patients accounts for 55.1%.—Author's English Abstract

Rèhabilitation

Bell-Krotoski, J. and Tomancik, E. The repeatability of testing with Semmes-Weinstein monofilaments. J. Hand Surg. **12A** (1987) 155–161.

Forty-one filament kits were measured for filament application force, single and multitester application force repeatability, and comparison of filament repeatability with that of other hand-held instruments. Results of this study show that if their lengths and diameters are correct, the filaments produce application forces that are repeatable within a predictable range. All hand-held instruments vary in application force. The Semmes-Weinstein monofilaments vary relatively little, and are a controlled reproducible force stimulus for use in clinical testing.—Authors' Abstract

Brandsma, J. W., de Jong, N. and Tjepkema, T. Disability grading in leprosy; suggested modifications to the WHO disability grading form. Lepr. Rev. **57** (1986) 361–369.

Disability prevention should be the primary objective of a leprosy control program. Although the initial purpose of the WHO recommended disability grading system is to provide an index of the presence of disabilities, regularly performed disability assessment will also be very useful to a leprosy control program to assist in planning measures to prevent disabilities and to evaluate the effectiveness of a disability prevention program. Modifications of the WHO disability grading form are proposed.—Authors' Summary

Lu, J. [Formation and origin of leprophobia.] China Lepr. J. **2** (1986) 57–61. (in Chinese)

The author describes the historic and social sources of leprophobia as follows: 1) Superstition and the believing of God's will: People believe that God makes one suffer from leprosy as punishment for one's offensive utterings and behavior. 2) Religious and feudal morality: According to the retribu-

tion theory in Buddhism, the disease is a retribution to the patient for his (or her) crime committed in his previous incarnations. 3) The influence of former cruel laws: Based on the laws of Qin Dynasty issued in 217 B.C., a criminal leprosy patient should be drowned. 4) Discrimination and persecution: For example, a Cantonese warlord killed a lot of leprosy patients by shooting or burning in 1935. 5) Poor plots of novels, dramas or films: They improperly exaggerated the leprophobia. 6) Burnt-out symptoms of leprosy: Such as clawhands, dropped feet and leontiasis, etc.

The author indicates that leprophobia is not only a problem in medical science, but also a social problem. It is necessary to mobilize the people of the press, the literary, the art and the educational circles to educate the public for reducing and clearing up the leprophobia.—Author's English Abstract

Patil, K. M., Babu, T. S., Oommen, P. K. and Srinivasan, H. Foot pressure measurement in leprosy and footwear designs. Indian J. Lepr. **58** (1986) 357–366.

Leprosy patients deprived of sensory feedback allow excessive pressures to be applied to feet, thereby causing foot ulcers. Quantitative knowledge of the pressure distribution under leprotic feet is helpful to prevent further damage to the foot by designing suitable footwear. This paper describes a barographic technique for the measurement of pressures under leprotic feet and the design of special footwear for prevention of foot ulcers.—Authors' Abstract

Rao, P. T. and Jena, S. K. Surgical treatment of plantar ulcers in leprosy. Int. Orthop. **10** (1986) 75–78.

Plantar ulcers present a serious problem in the management of leprosy. After studying the mechanism of ulceration and the causes of their indolence, it appears that the treatment of the disease by antileprotic drugs is not sufficient. The underlying causes, such as anesthesia, bony deformities and paralysis, should usually be treated by surgical means. Anesthesia can be reversed by decompression of the posterior tibial nerve if this is done early. Deformities should be corrected by procedures on the soft tissues or bones, and chronic infection eradicated to prevent recurrence of the ulceration. A combination of procedures may sometimes be needed.—Authors' Summary

Wintsch, K. [Reconstruction of the nose after leprosy.] Handchir. Mikrochir. Plast. Chir. **18** (1986) 231–235. (in German)

For the reconstruction of the nostril a nasolabial flap is recommended. According to the method of Pers (1967), the upper part of the flap is used for lining and the lower part for the outside coverage of the defect. In order to avoid lateral traction on the nostril, the author recommends that a small triangular flap with an inferior pedicle is left between the nasolabial flap and the nostril.

For total reconstruction of the nose, a frontal flap with a primary cantilever bone graft as described by Millard (1966) is suggested. We advise to take one half of forehead skin. This gives a less obvious donor site and enough length in the diagonal direction for the dorsum of the nose and the columella.

For the leprotic nose it is emphasized that no skin loss is present; there is only a loss of lining and support. In all advanced cases a large septal defect is encountered. The reliable postnasal inlay of Gillies is mentioned but the drawback to this method is that the care of the postnasal prosthesis may be difficult for leprosy patients with disabled hands. Secondary bone grafting after this procedure has a high failure rate because of infection. For these reasons the reconstruction of lining by two nasolabial flaps according to Farina (1957) is described. The author has regularly used this method with a primary cantilever graft. A modification is again suggested. A small triangular skin flap is raised with the ala, thus avoiding lateral traction on the nostrils after closure of the donor site.—Author's Summary

Other Mycobacterial Diseases and Related Entities

Masur, H., Tuazon, C., Gill, V., Grimes, G., Baird, B., Fauchi, A. S. and Lane, H. C. Effect of combined clofazimine and ansamycin therapy on *Mycobacterium avium-Mycobacterium intracellulare* bacteremia in patients with AIDS. J. Infect. Dis. **155** (1987) 127–129.

The purpose of this study was to examine the effect of drug combinations that include both clofazimine and ansamycin on one objective measurement of MAI infection—a positive culture of blood—to provide a preliminary insight into the use of such regimens for treating this infection.

The microbiological response generally did not correlate with drug regimen, duration of therapy, or *in vitro* susceptibility testing. All patients received 100 mg of clofazimine orally each day. All patients also received 150 mg of ansamycin orally each day, except for one patient who received 300 mg each day.

In this preliminary study, combination therapy with ansamycin and clofazimine, with or without other antimycobacterial agents, was not highly effective in eradicating MAI bacteremia among patients with AIDS. Of 13 patients followed up for at least 30 days, bacteremia persisted for 19–178 days (median, 92 days). Only 6 of the 13 patients with AIDS ultimately demonstrated two or more consecutive negative cultures of blood; 2 of these 6 later relapsed, with persistent bacteremia, despite continuing the original treatment regimen. A conversion to culture negativity correlated with clinical improvement in only one patient.—(*From* the article)

Nakanishi, M. Attenuated *Mycobacterium lepraemurium* vaccine non-protective against *Mycobacterium intracellulare* infection in mice. Hiroshima J. Med. Sci. **35** (1986) 67–69.

Since *Mycobacterium lepraemurium* (*Mlm*) is closely related to *M. intracellulare*, with respect to its antigenicity, attenuated *Mlm* obtained by passages on 1% Ogawa egg medium was examined for possible effects as a vaccine against *M. intracellulare* infection. Four weeks after subcutaneous injection of *Mlm* (1.4×10^7 bacilli), mice were infected intravenously with 2.4×10^7 organisms per mouse of *M. intracellulare*. During the first 12 weeks, no difference was noted in the rate of progression of *M. intracellulare* infection between mice given or not given *Mlm*-vaccine, when severity of the infection was measured on the basis of the number of viable *M. intracellulare* in the lungs and spleen. Therefore, *Mlm*-vaccine is probably not efficacious in protecting mice against *M. intracellulare* infection.—Author's Abstract

Rey, J. L., Villon, A., Saliou, P. and Gidel, R. [Studies on the tuberculosis infection in a cattle breeding area in sahelian Africa.] Ann. Soc. Belge Med. Trop. **66** (1986) 235–243. (in French)

After assessing the prevalence of bovine tuberculosis in a sahelian area of Burkina Faso, the authors examined the dynamics of tuberculous infection in man in villages located in the southwestern part of the country where cattle breeding is almost absent. In the 0 to 19 years age group, the tuberculin index is higher in the sahelian villages than in the villages of the savannah area. The annual risk of tuberculous infection is three times higher in a village with high prevalence of bovine tuberculosis than in a village with healthy cattle. As the prevalence of tuberculosis-disease is inversely related to tuberculosis-infection and bovine tuberculosis rates, the authors believe that contact with *Mycobacterium bovis* might protect people, especially children, against pulmonary tuberculosis. They argue that more elaborate investigations are necessary, which should involve a better coordination between medical and veterinary services.—Authors' English Summary