CURRENT LITERATURE

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

General and Historical

Le, K. Z., Ngyen, D. T., Smirnov, V. S., Ngyen, N. and Nguen, A. K. Clinical features and treatment of leprosy in Vietnam. Vesta. Dermatol. Venerol. **8** (1983) 66–68. (in Russian)

The incidence of occurrence of the disease, problems of detection of patients by examinations of the entire general population, current methods of diagnosis and therapy with new drugs are discussed. The late results of treatment and long-term observation of the patients are presented.—Authors' English Summary

Naafs, B., Matemera, B. O., Lyons, N. F. and Ellis, B. P. B. Diagnosis of leprosy. Cent. Afr. J. Med. **30** (1984) 289–293.

The paper gives a simple introduction in diagnosis and classification of leprosy.—Authors' Summary

Chemotherapy

Chandorkar, A. G., Burte, N. P., Gade, R. K. and Bulakh, P. M. Once monthly rifampicin (1200 mg) plus daily dapsone (100 mg) and clofazimine (100 mg) in the initial treatment of lepromatous leprosy. Indian J. Lepr. **56** (1984) 63–70.

The therapeutic effect of rifampin 1200 mg once monthly and 100 mg clofazimine daily for the first six months of treatment was evaluated in 30 bacteriologically positive lepromatous leprosy patients. Moderate to marked clinical improvement was seen in all the patients and a very rapid bacteriological regression was indicated by the decrease in bacteriological and morphological indices of the skin within one week. Seven patients became MI negative at one month and three months and 13 at the end of nine months. Two patients became MI and BI negative at the end of six months and six at the end of nine months. These observations clearly establish the high therapeutic efficacy and practicability of the three-drug regimen. Once monthly rifampin is highly effective and well tolerated, and has many advantages such as low cost, better patient compliance and reliability of the treatment. The addition of clofazimine to rifampin and dapsone prevents the emergence of ENL reactions which were seen during treatment with once monthly rifampin and daily dapsone. This regimen is thus ideal for initial, intensive treatment of lepromatous leprosy and may help in preventing the spread of the disease and development of dapsone resistance.—Authors' Abstract

Chandorkar, A. G., Burte, N. P., Jadhav, J. H., Gade, R. K., Bulakh, P. M., Tayshete, S. N. and Kale, V. M. Thalidomide in lepra reaction (ENL) in lepromatous leprosy patients. Indian J. Lepr. **56** (1984) 264–268.

Six male bacteriologically highly positive patients with lepromatous leprosy with ENL reaction not adequately controlled by conventional antireaction drugs were put on thalidomide 400 mg per day in four divided doses. The reaction was controlled between the 13th to 18th day of therapy. There was no change in the bacteriological status. Liver functions, renal functions and hemogram were normal before therapy and remained unaltered at the end of treatment. Apart from fatigue, drowsiness and occasional consti-

pation, thalidomide had no adverse effect. Control of ENL reaction by thalidomide in these patients is probably due to its immunosuppressive effect, more likely by its stabilizing action on lysosomes.—Authors' Abstract

Clemmensen, O. J., Olsen, P. Z. and Andersen, K. E. Thalidomide neurotoxicity. Arch. Dermatol. **120** (1984) 338–341.

Of six patients treated with thalidomide for either prurigo nodularis or discoid lupus erythematosus, four had paresthesias in the hands and feet and one also complained of muscular pain and stiffness. Clinical neurological findings in all four patients were normal. Subsequent electrophysiological examination disclosed a peripheral neuropathy in 5 of the 6 patients; 2 had electrophysiological signs of a polyneuropathy and 3 of a carpal tunnel syndrome. Symptoms and abnormal electrophysiological findings were still present in one patient one year after the discontinuation of thalidomide therapy. Since reports on thalidomide neurotoxicity have shown that the neurological symptoms are long standing and possibly irreversible, it is obviously important to inform patients of this possible side effect and to evaluate them closely for the symptoms and electrophysiological signs of evolving neurological changes.—Authors' Abstract

Jenner, P. J., Ellard, G. A. and Swai, O. B. A study of thiacetazone blood levels and urinary excretion in man, using high performance liquid chromatography. Lepr. Rev. **55** (1984) 121–128.

The pharmacokinetics of thiacetazone, a bacteriostatic drug with both antituberculosis and antileprosy activity, have been studied in healthy volunteers and tuberculosis patients using a high pressure liquid chromatographic method. Urinary excretion of thiacetazone was measured over a period of 7 days following the ingestion of a single oral dose of 150 mg of the drug. Peak plasma concentrations of thiacetazone during supervised daily treatment averaged 1.8 μg/ml. From the rate of decline of thiacetazone plasma concentrations and urinary excretion, it was calculated that thiacetazone concentrations capable of inhibiting the multiplication of *Mycobacterium leprae* would only be maintained for about three days in the event of patients discontinuing to take the drug. It was concluded that thiacetazone cannot be recommended for use in the multidrug treatment of lepromatous leprosy.—Authors' Summary

Kamala, A. N., Shetty, V. P. and Antia, N. H. Evaluation of the neurotoxicity of dapsone in the mouse model. Indian J. Lepr. **56** (1984) 251–256.

The effect of dapsone (DDS) was studied using the mouse model. It was observed that DDS did not have any neurotoxic effect. On the contrary, it showed a protective action towards the nerve when administered in the early stages following definite establishment of nerve lesions.—Authors' Abstract

Kaur, S., Sharma, V. K. and Kumar, B. Treatment of leprosy—newer concepts. Indian J. Lepr. **56** (1984) 307–312.

The latest time bound WHO regimens for the treatment of paucibacillary (I, TT, BT) and multibacillary leprosy are discussed. The rationale, indications of above regimens, and cautions necessary are highlighted.—Authors' Abstract

Krenzien, H. N. Chemotherapy of the mycobacterial diseases—leprosy and tuberculosis. Indian J. Chest Dis. Allied Sci. **24** (1982) 223–232.

Mycobacterioses are generalized infectious diseases caused by mycobacteria. Leprosy and tuberculosis are the most important in the human. Since the two mycobacterioses are similar in many ways, it was hoped that it would be possible to treat them with a common therapy. Clinical experience has confirmed this. The relevant principles of treatment of the mycobacterioses with reference to leprosy and tuberculosis are described. The traditional treatment of leprosy and tuberculosis has been critically reviewed. The urgency of using the experience gained from treatment of tuberculosis and its relevance to leprosy is stressed. Suggestions for the treatment of light-skinned patients suffering from leprosy and tuberculosis are presented. The most suitable combination is considered to

be rifampin and Isoprodian.—Author's Summary

Krishna, D. R., Appa Rao, A. V. N., Ramanakar, T. V., Reddy, K. S. C. and Prabhakar, M. C. Pharmacokinetics of rifampin in the presence of dipyrone in leprosy patients. Drug Dev. Indus. Pharmacy **10** (1984) 101–110.

Some pharmacokinetic parameters such as elimination rate, half-life, area under the curve (AUC), etc., of rifampin following p.o. administration of rifampin 600 mg alone and 600 mg rifampin in combination with 1000 mg dipyrone were determined in untreated leprosy patients. Statistical comparison of the mean values of the parameters suggests that the pharmacokinetic behavior as well as the bioavailability of rifampin are not statistically affected in the presence of dipyrone.—Authors' Summary

Kumar, A. Treatment compliance by leprosy out-patients and its monitoring under field condition. Indian J. Lepr. **56** (1984) 313–318.

The widely experienced poor treatment compliance by leprosy outpatients has interfered with effective leprosy control and contributed to the problem of drug (dapsone) resistance. This paper summarizes 1) the pattern of treatment compliance by rural and urban patients in a leprosy hyperendemic area, and 2) various methods to monitor the treatment compliance, especially under field conditions.

Two simple methods of monitoring the dapsone intake by patients, i.e. "physical verification of DDS tablets with patients" and "paper spot test," when applied together by a field worker in the field were found to be operationally very feasible, economical and acceptable and had good correlation with each other. Thus these methods are recommended to be used on a large scale in a leprosy control program. The paper spot test was found to be 98% reliable when compared with DDS/Cr. ratio estimation. In addition, communities and patients should be continuously educated about leprosy and its control; and for the optimal utilization of medical care services by patients, they should be organized in the background of the consumers.—Author's Abstract

Kundu, S. K., Hazra, S. K., Chaudhury, S. and Chatterjee, B. Evaluation of multidrug therapy with rifampicin, clofazimine and D.D.S. in multibacillary leprosy cases. Indian J. Lepr. **56** (1984) 78–85.

Rifampin, clofazimine and dapsone have been tried in 15 active untreated lepromatous cases for a period of two years. Compared to dapsone monotherapy remarkable clinical and bacteriological improvement was observed with this combined therapy with attainment of negative BI in ten cases. Use of this combination therapy is thus advocated to achieve noninfectivity in a shorter period and to prevent emergence of dapsone resistance thereby causing the path of leprosy control before it becomes unmanageable due to dapsone resistance.—Authors' Abstract

Niwa, Y. and Ozaki, M. Antileprotic agents (clofazimine). Jpn. J. Clin. Hematol. **24** (1983) 1039–1048. (in Japanese)

The capacity to generate oxygen intermediates (OI; O_2^-, H_2O_2, OH·) and chemiluminescence, and to release lysosomal enzyme (lysozyme, β-glucuronidase), and the superoxide dismutase (SOD) activity of polymorphonuclear leukocytes (PMNL) and monocytes from 14 leprosy patients manifesting a bacillary index above 2.2 was examined to determine the mechanism of action of clofazimine. Significantly enhanced SOD activity, and a decrease in O_2^-, and OH· production were observed in the patients with more than four years' history. The generation of OH· was significantly increased, in a dose-dependent manner, by clofazimine, with a subsequent decrease in H_2O_2 and chemilluminescence, while SOD activity of the PMNLs and monocytes was not affected. In the medium supplemented with $FeSO_4$ or EDTA containing Fe^{++}, OH· production was further markedly elevated by the drug. Phagocytic SOD in PMNLs and monocytes of the patients was both host- and bacillus-derived because the presence of potassium cyanide, to which human-derived cupric SOD is susceptible, did not completely abrogate SOD activity. The difficulty in treating leprosy may be partly ascribable to the decreased phagocytic OH· generation in this disease, which in leprosy patients is induced by increased Hansen ba-

cillus-derived SOD uptaken by the patients. Clofazimine may be effective in leprosy by potentiating the catalyzing activity of Fe^{++} which facilitates the Haber-Weiss reaction to increase OH· formation from H_2O_2 without affecting SOD activity which was enhanced by their uptake.—Authors' English Abstract

Pattyn, S. R. Ervaringen met therapieschema's voor lepra te velde. [Field experiences with therapy protocols in leprosy.] Verh. K. Acad. Geneeskd. Belg. **45** (1983) 303–314. (in Flemish)

A review on prospective clinical trials in the treatment of leprosy is presented, with the therapeutic regimens applied. Positive experiences and certain difficulties are also mentioned.—Author's English Summary

Pattyn, S. R. Incubation time of relapses after treatment of paucibacillary leprosy. Lepr. Rev. **55** (1984) 115–120.

Data are presented on the incubation time of 21 relapses after stopping dapsone monotherapy in paucibacillary leprosy in central Africa. The results are comparable with those of other studies: 50% of relapses occur during the first 2–3 years. This figure is most important to analyze the results of drug trials in paucibacillary leprosy. This figure should also be relevant for regimens including more bactericidal drugs than dapsone, since the kind of antibacterial treatment should influence the minimal necessary duration of treatment but not the incubation time of relapses. The same mechanisms prevailing in relapses of multibacillary leprosy, their incubation periods should be identical.—Author's Summary

Warndorff-van Diepen, T., Aredath, S. P. and Mengistu, G. Dapsone-resistant leprosy in Addis Ababa: A progress report. Lepr. Rev. **55** (1984) 149–157.

Two hundred twelve lepromatous patients, presenting with suspected dapsone-resistant leprosy in the five-year period 1973–1977, were taken into trial treatment with dapsone. Clinically, 55% have been proven to be dapsone resistant and the remainder are continuing to respond to full dosage dapsone after 4.5 to 9 years.

This clinical observation contrasts with results of the dapsone-sensitivity studies in mice which demonstrated in 86% of the 43 patients examined dapsone-resistant bacilli. The relevance of partial dapsone resistance, diagnosed in mouse foot pad tests, is challenged and a modified definition of dapsone resistance is suggested. The annual incidence of proven dapsone-resistant leprosy over the period 1973–1977 was 1.8% resulting in a prevalence in 1978 of 119 per 1000 lepromatous cases on register in Addis Ababa.—Authors' Summary

Clinical Sciences

Arruda, M. S. P., Arruda, O. S. de, Astolfi, C. S., Nogueira, M. E. S., Bastazini, I., Opromolla, D. V. A. and Ura, S. Reacão de Rubino. Criterio de branqueamento para pacientes virchowianos. [The Rubino reaction. A criterion for care for lepromatous patients.] Med. Cutan. Iber. Lat. Am. **11** (1983) 423–430. (in Portuguese)

Approximately 55% of active lepromatous patients respond positively to the Rubino reaction. With arrested cases this rate of positivity lowers considerably to about 15%. In an effort to associate this reaction with the presence of bacilli, a study of 796 cases was undertaken. The patients were divided into: a control group, active tuberculoid cases, arrested tuberculoid cases, active borderline cases, arrested borderline cases, active lepromatous cases, and arrested lepromatous cases.

The patients were submitted to the following tests: Rubino reaction, presence of cryoglobulins, and VDRL and PCR positivity. By the results obtained we may conclude that: a) A positive Rubino reaction may be present in all forms of leprosy studied, this reaction having an inverse relationship with the organism's resistance to *Mycobacterium leprae*. b) The Rubino reaction has specificity to leprosy. c) This reaction does not depend on the number of bacilli present in

the host. d) A positive Rubino reaction is not related to the presence of cryoglobulins in the serum, nor to VDRL or PCR positivity, nor to the length of time the patient's disease has been arrested.

The authors present these findings and suggest that this reaction be used as one of the criteria for determining cure.—Authors' English Summary

Brandt, F., Adiga, R. B. and Pradhan, H. Lagophthalmus und hintere Synechien der Iris bei der Behandlung der Lepra mit Diamino-diphenyl-sulfon. [The development of lagophthalmos and posterior synechiae of the iris during treatment of leprosy with diaminodiphenylsulfone.] Klin. Monatshl. Augenheilkd. **184** (1984) 28–31. (in German)

Four years after controlled and standardized chemotherapy with diaminodiphenylsulfone (DDS), 316 patients in the leprosarium at Khokana, Nepal, were re-examined for ophthalmological findings. Patients who, four years earlier, had not had lagophthalmos in either eye, nor posterior synechiae of the iris, had only developed these complications in the meantime if they were suffering from DDS-resistant leprosy. New posterior synechiae of the iris were only found in patients with inactive leprosy who had already had a posterior synechia in the fellow eye four years previously. In cases of inactive leprosy there was also a tendency for existing posterior synechiae to increase. It is emphasized that the development of lagophthalmos or posterior synechiae of the iris indicates that a previously inactive leprosy may have become reactivated in spite of treatment with DDS.—Authors' English Abstract

Brinton, L. A., Hoover, R., Jacobson, R. R. and Fraumeni, J. F., Jr. Cancer mortality among patients with Hansen's disease. J. Natl. Cancer Inst. **72** (1984) 109–114.

For the evaluation of cancer risks associated with immunodeficiencies experienced by patients with Hansen's disease (leprosy) and for the assessment of possible adverse effects of dapsone therapy, a follow-up study was conducted of 1678 patients admitted to the National Hansen's Disease Center in Carville, Louisiana, U.S.A., between 1939 and 1977. Overall, no substantial cancer mortality was observed (standardized mortality ratio = 1.3), nor was there any excess among patients exhibiting defects in cellular immunity by virtue of lepromatous forms of the disease. Notable was the absence of any significant excess of lymphoma (5 observed vs. 2.3 expected), despite the predominance of this tumor in certain other immunodeficiency states. Several cancer sites (oral, bladder, and kidney) occurred excessively, but reasons for the elevations were obscure. Although dapsone has been implicated as a carcinogen in laboratory animals, the use of sulfones, including dapsone, did not appear to affect significantly the risk of any cancers in this population.—Authors' Abstract

Dong Li-Wen, *et al.* Malignancy of trophic ulcer in leprosy: Report of two cases. Chin. J. Clin. Dermatol. **12** (1983) 310–311. (in Chinese)

Malignancy of trophic ulcer was observed in two cases of different types of leprosy. In one case the skin ulcer revealed grade I squamous cell carcinoma, and in the other case a tumor in the left inguinal region manifested as metastatic squamous cell carcinoma.

Malignancy should be seriously suspected and histopathologic examination performed if a leprosy ulcer develops rapidly in depth with cauliflower-like hypertrophy of granulation and extensive necrosis of tissue in spite of conservative treatment.—Authors' English Abstract

Duncan, M. E. and Pearson, J. M. H. The association of pregnancy and leprosy—III. Erythema nodosum leprosum in pregnancy and lactation. Lepr. Rev. **55** (1984) 129–142.

Seventy-six women with lepromatous leprosy were studied during 79 pregnancies and followed up during lactation for up to 24 months. Ten out of 45 BL patients (22%) and 20 out of 34 LL patients (59%) developed erythema nodosum leprosum (ENL) during the course of the study. Only 4 out of 30 patients were BI negative, although the duration of effective treatment for leprosy ranged from 1–14 years. Thirteen of the 30 ENL patients were suspected of de-

veloping dapsone resistance during the study period. The incidence of ENL was highest in the first trimester with a second peak in the third trimester, coinciding with the peak of relapse. Fifteen percent of the women suffered from ENL almost continuously from the third trimester to 15 months postpartum. In pregnancy, ENL was seen more frequently in skin than in nerve or other tissue; however, after delivery, particularly in the recurrent or persistent episodes, ENL was seen more commonly in nerve than in skin. Significant sensory and/or motor loss occurred in 30 out of 38 episodes of ENL nerve involvement. The significance of these findings is discussed.—Authors' Summary

Dutta, R. K. Diagnosis of early leprosy. Indian J. Dermatol. **28** (1983) 103–108.

Diagnosis of leprosy in the incipient or in the evolving phase of the disease is of paramount importance to prevent progression, future deformities, and eradication of the disease. Antileprosy treatment far below the normal requirement may prove to be an effective weapon and important hallmark for a successful leprosy control program.—Author's Abstract

Ellis, C. J. Leprosy in Birmingham—a review. Postgrad. Med. J. **59** (1983) 652–654.

Twenty-three men and seven women from the West Midlands conurbation (population 2.7 million) have been investigated and treated for leprosy since 1970. The clinical features of the patients at presentation are described with an account of treatment given and the outcome. The pattern of this disease in Britain is different from that seen in the U.S.A. and poses little threat to public health. The disease can be cured by chemotherapy but neuropathy is unlikely to recover if it is a presenting symptom. The diagnosis of leprosy should be considered in all patients who have lived in an endemic area who present with disorders of peripheral nerves or skin. Early diagnosis is essential to minimize nerve damage and resulting deformity.—Author's Summary

Ersek, R. A. and Lorio, J. The most indolent ulcers of the skin treated with porcine xenografts and silver ions. Surg. Gynecol. Obstet. **158** (1984) 431–436.

Cutaneous ulcers associated with Hansen's disease have long been recognized as among the most indolent of all ulcers. We have successfully treated such ulcers with porcine xenograft, achieving healing in ulcers which had been present for as much as three decades. These results suggest that this regimen may be applicable to other cutaneous ulcers wherever skin is missing. The newly available antibacterial effects of silver-impregnated porcine xenografts should have the result of increasing the effectiveness of the treatment still further.—Authors' Summary

Goldenring, J. M. and Castle, G. F. Leprosy in teenage immigrants. Case reports and clinical review. J. Adolesc. Health Care **5** (1984) 53–55.

Two cases of newly diagnosed leprosy (Hansen's disease) are presented to remind physicians of the nature of this disorder and its increasing prevalence due to migration to the United States from endemic areas. In both cases, leprosy was not initially considered by the American physicians. Important clinical clues to diagnosis are reviewed.—Authors' Abstract

Gourie-Devi, M. Greater auricular nerve conduction in leprosy. Indian J. Lepr. **56** (1984) 182–190.

Greater auricular sensory nerve conduction was performed in 18 control subjects (36 nerves) and normal values for various parameters were determined. In 10 (16 nerves) of the 12 (24 nerves) leprosy patients, in whom a similar study was performed, abnormal conduction was found. All of the eight thickened nerves and 8 of 16 clinically normal nerves in leprosy patients were found to have electrophysiological abnormalities. The usefulness of this procedure in the diagnosis of leprosy is emphasized.—Author's Abstract

Jacyk, W. K. and Lechner, W. Epidermodysplasia verruciformis in lepromatous leprosy. Dermatologica **168** (1984) 202–205.

Two African patients (sisters) suffering from lepromatous leprosy had epidermodysplasia verruciformis. Both patients had, in addition, recalcitrant superficial fungal infections and extensive relapsing scabies. The question is raised whether a generalized impairment of cell-mediated immunity, found in lepromatous leprosy, predisposes toward other particularly viral infections.—Authors' Abstract

Jacyk, W. and Lechner, W. Fokale epitheliale Hyperplasie bei lepromatöser Lepra. [Focal epithelial hyperplasia in a patient with lepromatous leprosy.] Z. Hautkr. **58** (1983) 1481–1492. (in German)

Focal epithelial hyperplasia Heck (FEH) is most likely caused by human papilloma virus. It mainly occurs in children and young people showing no associated diseases. For the first time, we describe a case of FEH in a patient with lepromatous leprosy who due to persistent erythema nodosum leprosum has been treated with a long-term glucocorticoid therapy. The question of the competence of lepromatous patients in resisting certain viral infections arises.—Authors' English Summary

Joffrion, V. C. and Brand, M. E. Leprosy of the eye—a general outline. Lepr. Rev. **55** (1984) 105–114.

Ocular complications from leprosy (Hansen's disease) seriously threaten a patient's quality of life. The eye (the anterior segment structures) may be infiltrated and damaged by the mycobacteria directly; may suffer damage from inflammation (Type II reaction), and be damaged as a result of changes in the extraocular structures. These are features of the disease at or near the lepromatous end of the spectrum.

In addition to direct damage, the eye in about 15–20% of patients irrespective of their disease type is subject to abnormal exposure due to nerve damage. This may be motor (C.7) causing lagophthalmos, or sensory (terminal branches of ophthalmic division of C.5) causing corneal hypesthesia. Secondary infection by other pathogens complicates the damage initiated by dryness and trauma.

The patient most at risk is the one with active, long-standing lepromatous disease. He/she will possibly have diminished pain sensitivity. Symptoms will be unreliable. Routine objective examination of such patients becomes mandatory. Fortunately, most of the significant pathology is visible with the help of relatively unsophisticated instruments. A useful examination may be done in two or three minutes once the routine has become established.

An outline of pathophysiology, diagnosis and management of the main features of ocular leprosy has been presented in this article. Its aim has been to help the physician or other health worker to assume responsibility for the primary eye care of their leprosy patients and thus reduce the possibility of blindness. Loss of sensation of the extremities is a serious handicap to any individual. Blindness superimposes an intolerable burden.—Authors' Summary

Kagame, G. K. Ocular leprosy in Africa. Soc. Sci. Med. **17** (1983) 1737–1742.

A clinical examination of 199 leprosy patients in Kenya showed that 62.5% had abnormal ocular findings, 51.2% of which were leprosy related. The potentially blinding lesions were uveitis, keratitis and lagophthalmos and these were found in 22.1% of the patients; 6 patients (3%) had a visual acuity of less than 3/60 in the better eye and were classified blind. In all, there were 31 blind eyes of which only 12 had leprosy-related causes; 10 of these (83%) belonged to lepromatous patients and 2 (17%) to tuberculoid patients. All of the ten eyes of the lepromatous patients were blind due to uveitis. It was shown that lepromatous leprosy patients are at a greater risk of leprosy-related blindness, especially from uveitis. The socio-psychological and economic implications of leprosy are discussed. Practical recommendations for the primary eye care of the leprosy patient are suggested.—Author's Abstract

Kannan, V. and Vijaya, G. Endocrine testicular functions of leprosy. Horm. Metabol. Res. **16** (1984) 146–150.

Pituitary testicular functions were evaluated in leprosy. Forty-three men with leprosy were studied by basal estimations of plasma LH, FSH, prolactin, testosterone; 17-β estradiol, metoclopramide stimulated

prolactin responses and hCG stimulated testosterone responses. Fifteen young healthy men with proven fertility were studied as control subjects. The hormone estimations were related to the histologic changes observed in the testicular biopsies of leprous hypogonadism.

In lepromatous leprosy (n = 18) the basal plasma gonadotropin levels were significantly increased (FSH 29.5 ± 2.3 mIU/ml; LH 21.5 ± 1.9 mIU/ml, mean ± SE). The plasma gonadotropins were in the normal range in tuberculoid leprosy. In borderline leprosy, the basal mean plasma FSH was normal, whereas LH levels were significantly increased (22.5 ± 1.2 mIU/ml). The basal plasma testosterone levels were significantly decreased in lepromatous leprosy (1.6 ± 0.12 ng/ml), tuberculoid leprosy (4.2 ± 1.7 ng/ml) and borderline leprosy (1.8 ± 0.18 ng/ml). The basal plasma 17-β estradiol levels were significantly elevated in all the three types of leprosy.

The basal plasma prolactin levels in plasma were significantly increased in lepromatous and tuberculoid leprosy. During hCG stimulation tests, the peak plasma testosterone responses were significantly reduced in both lepromatous leprosy and tuberculoid leprosy subjects.

The blunted testosterone responses during hCG stimulation tests in leprosy correlated with the high basal 17-β estradiol levels ($r = 0.58$; $p < 0.05$). These results strongly suggest that hypogonadism in leprosy results from primary testicular failure. The significant elevation of plasma 17-β estradiol levels in lepromatous, tuberculoid and borderline leprosy could play a role in hypogonadism of leprosy.—Authors' Summary

Kou Liang, *et al.* Hormonal changes in male patients with lepromatous leprosy. Chin. J. Dermatol. **17** (1984) 15–17. (in Chinese)

Testosterone (T), estradiol (E_2), cortisol (compound F) and luteinizing hormone concentrations were determined in 15 male patients with lepromatous type leprosy by using radioimmunoassay technique.

The age of patients ranged from 18 to 55 years (mean, 37 years). The duration of disease varied from 2 to 34 years (mean, 15.3 years); 8 of the patients were married; 4 patients were infertile. Control group consisted of 43 normal healthy men whose age ranged from 21 to 50 years.

Hormone assays showed that mean plasma T concentration in patients was significantly lower than that of the reference value. Mean plasma E_2 concentration and E_2/T ratio in patients were markedly higher than that of the reference values. And mean serum LH level in patients increased significantly, but mean plasma F concentration and serum T4 level were within normal ranges.

The present study suggested that patients with lepromatous leprosy had testicular lesions.—Authors' English Abstract

Kumar, B., Kaur, S., Gupta, S. K., Rajwanshi, A. and Darshan, H. Acid fast bacilli in lymph node aspirate and smears from ear lobules and fingers in long treated patients. Indian J. Lepr. **56** (1984) 71–77.

Skin slit smears from fingers and ear lobules and lymph node aspiration smears stained with Ziehl-Neelsen stain were studied in 43 patients with LL or BL disease. All the patients had taken dapsone monotherapy for 3–7 years. None of the patients had clinical evidence of dapsone resistance. Small numbers of bacilli were detected in 16 patients. Lymph node aspirate was positive in 5 cases; whereas ear lobule and fingers yielded bacilli in 12 and 13 cases, respectively. It is recommended that in addition to the traditional ear lobe it is imperative to study other sites as well. Study of fingers is recommended for the sake of simplicity. Where facilities are available, sampling of the lymph node may also be attempted to advantage.—Authors' Abstract

Lamba, P. A. and Santoshkumar, D. Repositioning of pupil for visual disability. Indian J. of Lepr. **56** (1984) 4–9.

The authors have successfully utilized the technique of photocoagulation of the iris in 35 cases for improving the visual acuity in cases suffering from ocular leprosy. The photocoagulation was considered to be very useful in cases with corneal scars and highly vascularized adherent leukomas, where keratoplasty stands a poor risk. It has also been

recommended for cases with pinpoint pupil not dilating with drugs for diagnostic and prognostic value.—Authors' Abstract

Morley, K. D., Vickers, H. R. and Hughes, G. R. V. An unusual cause of arthritis. Postgrad. Med. J. **59** (1983) 522–524.

We present a case of leprosy, an uncommon infection in the United Kingdom, which mimicked features of widely known rheumatic diseases and resulted in subsequent delay of diagnosis.—Authors' Summary

Nsibambi, J. K. Rheumatic manifestations in leprosy: A case report. East Afr. Med. J. **60** (1983) 805–808.

A case is reported of an adult male who presented to a hospital with joint pains and numbness in the extremities. The knee and elbow joints were involved; there was sensory impairment below the ankles and nodular lesions on the extremities. Rheumatoid factor was positive and skin biopsy showed chronic inflammation. A diagnosis of rheumatoid arthritis was made. In view of sensory changes leprosy was suspected. The patient was referred to the All Africa Leprosy and Rehabilitation Training Centre (ALERT) where the presence of leprosy was confirmed.

This patient was experiencing attacks of rheumatic manifestations of leprosy which are common, especially during the erythema nodosum leprosum (ENL) reaction.

In this paper rheumatic manifestations in leprosy are discussed and medical practitioners are alerted to the possibility of leprosy patients presenting with arthritis which may resemble rheumatoid arthritis clinically and by similar positive laboratory findings.—Author's Summary

Prasad, V. N., Narain, M., Mukhija, R. D., Bist, H. K. and Khan, M. M. A study of ocular complications in leprosy. Indian J. Lepr. **56** (1984) 241–250.

A total of 380 leprosy patients were studied in four different leprosy hospitals. Involvement of the eye was found in 18.95% of cases of which 10.97% were in lepromatous leprosy and 8.16% in nonlepromatous leprosy cases. In the total cases studied 52.63% were lepromatous leprosy and 47.37% were nonlepromatous leprosy. Among them 11.05% were males and 18.95% were females. In 72 cases of ocular involvement, males constituted 80.56% and females 19.44% of the cases. The maximum cases (52.78%) of ocular involvement were in leprosy patients with 5 to 10 years of disease duration. Blindness among the total leprosy patients studied was 1.84% which was mainly due to corneal opacity following exposure keratitis and ulceration, iridocyclitis and its complications.—Authors' Abstract

Prendiville, J. S., Cream, J. J., Rose, F. C., Scott, J. T., Woodrow, D. F. and Waters, M. F. R. Leprosy masked by steroids. Br. Med. J. **288** (1984) 770–771.

A 24-year-old Saudi Arabian man developed a rash and fever 18 months before admission to a hospital in London. He had been treated for eight months with corticosteroids for his symptoms but a definite diagnosis had not been made. Appropriate studies led to the diagnosis of early subpolar lepromatous leprosy (lepromatous leprosy that had evolved from borderline leprosy). The case illustrates the need to palpate peripheral nerves in patients complaining of persistent unexplained rash or of anesthesia with or without muscle wasting. Secondly, the injudicious use of systemic steroids in an undiagnosed illness may obscure the diagnosis of any infectious disease, including leprosy.—(*From* the article)

Rawal, R. C., Kar, P. K., Desai, R. N. and Shah, B. H. A clinical study of eye complications in leprosy. Indian J. Lepr. **56** (1984) 232–240.

A study was conducted to find out the incidence of ocular complications in leprosy. The ocular lesions were found in 6.6% of lepromatous leprosy and 1.6% in nonlepromatous leprosy. Out of 150 patients with eye lesions 74% were males and 80% belonged to lepromatous leprosy. The age group in all the patients varied from the 3rd to the 6th decade. Mean duration of leprosy in lepromatous leprosy was 6.2 years. The important eye complication observed were lagophthalmos (8.1%), corneal ulcers (10%) and iridocyclitis (24%). The loss of eye-

brows (76%) was found to be most frequent in this study, followed by corneal lesion (62%). It is concluded that examinations of eyes are essential in all types of leprosy.—Authors' Abstract

Samuel, S., Samuel, S. N., Thangaraj, R. H. and Shreshta, K. B. Ulnar nerve calcification and abscess formation in two cases of primary mononeuritic leprosy. Lepr. Rev. **55** (1984) 173–176.

Since 1980, four patients have presented at the Shantha Bhawan and Patan Hospitals in Nepal with nerve abscesses. This paper describes the clinical, radiological and surgical operation findings in two of these patients who had ulnar nerve calcification.—Authors' Summary

Singh, T. R., Agrawal, S. K., Bajaj, A. K., Singh, R. K. and Singh, M. M. Evaluation of audiovestibular status in leprosy. Indian J. Lepr. **56** (1984) 24–29.

One hundred twenty-five cases of lepromatous leprosy and 25 cases of tuberculoid leprosy were investigated for audiovestibular status. Impaired hearing was detected in 52% and vestibular hypofunction in 7.2% of lepromatous cases. Conductive deafness was due to eustachian tube catarrh secondary to atrophic rhinitis associated with the disease. The perceptive deafness and vestibular hypofunction were due to end organ lesion probably due to ENL reaction. The vestibulocochlear nerve involvement was considered to be unlikely. In tuberculoid leprosy derangement in hearing was not observed in any cases.—Authors' Abstract

Sritharan, V., Bharadwaj, V. P., Venkatesan, K., Girdhar, B. K. and Desikan, K. V. High density lipoprotein cholesterol (HDL-C) analysis in leprosy patients. Lepr. Rev. **55** (1984) 167–171.

A study was undertaken to find out the levels of circulating high-density lipoprotein (HDL) cholesterol and the ratio of this fraction to total blood cholesterol in lepromatous leprosy patients before and after drug therapy. The healthy contacts of these patients were considered as control subjects of the study. The subjects were distributed in three groups on the basis of their age. HDL-cholesterol to total cholesterol ratio was significantly raised in both treated and untreated patients in all three groups compared to the healthy controls. The data may explain the low risk of myocardial infarction due to atherosclerosis in leprosy patients.—Authors' Summary

Suzuki, T. [Pupillary reactions in leprosy.] Nippon Ganka Gakkai Zasshi **87** (1983) 581–586. (in Japanese)

Analysis on pupillary reactions of patients with leprosy in a national leprosarium, Zenshou-en (Higashimurayama-city, Tokyo, Japan) has been attempted and a total of 1432 patients were examined. As a result, extreme miosis smaller than 1.5 mm in darkness was noted in a considerable number of the patients; 10.8% among the patients of 40, 17.5% among the 50, 24.3% among the 60, and 27.0% among the 70 years of age.

One hundred eyes of 51 patients who presented extreme miosis or anisocoria without posterior synechia nor apparent signs of iridocyclitis were selected for the further investigations of pupillary reactions to light, near vision, and pharmaceutical stimulations. The drugs used were 5% phenylephrine, 0.125% pilocarpine, and 0.4% tropicamide. The pupillary reactions were recorded with the aid of infrared photo devices. The results were: The mydriasis by either sympathomimetic or antiparasympathomimetic agents were reduced in proportion to the initial miotic change. Denervation supersensitivity of the iris was not observed either to sympathomimetic or parasympathomimetic agents. Light-near vision dissociation was not observed. Marked correlation between the miotic change and mild iridocyclitis was recognized. Consequently, peripheral involvements of iris musculature by long-standing subclinical iridocyclitis was suggested to be the most possible etiologic factor in making the extreme miosis in leprosy patients.—Author's English Abstract

Thielen, T., Bahmer, F. and Mielke, U. Lepra aus neurologischer Sicht. [Leprosy from a neurologic point of view.] Nervenarzt **54** (1983) 504–512. (in German)

The neurologic aspects of leprosy, one of

the principal causes of peripheral neuropathy in the world, are described from the basic itiopathogenesis through the clinical manifestions. Additionally, three cases presenting during the years 1981–1982 are described. Two of the patients had dimorphous leprosy and one had tuberculoid disease.—(*From* the Authors' Summary)

Velikanova, L. P., *et al.* [Acute psychogenic disorders in leprosy patients.] Zh. Nevropatol. Psikhiatr. **84** (1984) 265–270. (in Russian)

The authors carried out clinical follow-up and psychological examinations of 40 patients suffering from leprosy and treated at the Astrakhan Institute for Leprosy Research. Under study there were acute psychogenic reactions arising in the patients on diagnosing the disease and putting them into the leprosarium. Clinical variants of adequate situational reactions (21 patients) and anomalous neurotic and psychopathic ones (19 patients) are described. These reactions were found to depend on the premorbid characteristics of the patient's personality and influence the subsequent course of the underlying disease.—Authors' English Summary

Immuno-Pathology

Birdi, T. J., Mistry, N. F., Mahadevan, P. R. and Antia, N. H. Antigen specific macrophage-lymphocyte interaction in lepromatous leprosy. J. Clin. Lab. Immunol. **13** (1984) 189–194.

Peripheral blood-derived macrophages from lepromatous leprosy patients were unable to interact with lymphocytes in the presence of *Mycobacterium leprae.* This lack of interaction is probably not associated with membrane HLA-DR antigens since trypsin and colchicine restored *M. leprae*-induced depression in the latter but were unable to bring about a positive interaction. Two possible defects exist therefore in the lepromatous macrophage. These are an innate inability to process and present *M. leprae* antigens to lymphocytes and an induced inability to express some membrane receptors, an event detrimental to the normal functioning of a macrophage.—Authors' Summary

Birdi, T. J., Mistry, N. F., Mahadevan, P. R. and Antia, N. H. *In vitro* studies on the effect of levamisole in lepromatous leprosy. J. Clin. Lab. Immunol. **13** (1984) 93–96.

Our previous studies have demonstrated a defective macrophage response to *Mycobacterium leprae* in lepromatous leprosy patients. In the present study we report the restoration of Fc receptor and HLA-DR antigen expression as well as antigen specific macrophage-lymphocyte interaction on treatment with levamisole *in vitro.* These results indicate that levamisole activates the macrophages which in turn results in an improved cell-mediated immune response in lepromatous leprosy. This may also be applicable in other disease situations.—Authors' Summary

Birdi, T. J., Salgame, P. R., Mahadevan, P. R. and Antia, N. H. An indomethacin sensitive suppressor factor released by macrophages of leprosy patients. J. Biosci. **6** (1984) 125–134.

Reduction in Fc receptor expression as assayed by "erythrocyte" rosetting of macrophage cultures from long-term treated lepromatous leprosy patients (bacteriologically negative) was seen in the presence of viable *Mycobacterium leprae.* Macrophages with and without intracellular bacilli demonstrated this reduction. On the basis of this observation, the conditioned medium of *M. leprae*-infected macrophage cultures of lepromatous patients were tested on macrophages from normal individuals for [^{3}H]-leucine incorporation and antigen-specific physical interaction with lymphocytes. Both these parameters showed decreased values as compared to the controls which were not exposed to this conditioned medium. Lymphocyte transformation to *M. leprae* in leukocyte cultures of normal individuals was also reduced in the presence of the condi-

tioned medium from lepromatous patients' macrophages. The indication that this factor may be a prostaglandin was suggested by the observation that its synthesis was inhibited by indomethacin. Its importance in the nonspecific depression in cell-mediated immunity seen in lepromatous patients is discussed.—Authors' Abstract

Chugh, K. S., Kaur, S., Kumar, B., Nath, I. V. S., Damle, P. B., Sharma, B. K., Sakhuja, V. and Datta, B. N. Renal lesions in leprosy amongst north Indian patients. Postgrad. Med. J. **59** (1983) 707–711.

Sixty consecutive patients with leprosy were investigated for renal involvement. Clinically overt renal disease was present in 4 patients; 3 presented with a nephrotic state and 1 patient with progressive renal failure. Urinalysis showed daily protein loss ranging from 0.4–8.9 g in eight patients and microscopic hematuria in four cases. Elevated levels of blood urea and creatinine were seen only in one patient with diffuse proliferative glomerulonephritis. Of the 36 patients in whom distal tubular functions were evaluated, concentration and/or acidification defects were detected in nine patients (25%). Renal histology revealed no abnormality in any of these patients. Serum C3 levels were decreased in five patients with lepromatous leprosy and three patients with borderline leprosy.

Histological evidence of renal involvement was detected in nine patients (15%). Amyloid deposits were seen in 3 (5%) patients of whom 2 had lepromatous leprosy and 1 had tuberculoid leprosy with chronic trophic ulcers. Mesangial proliferative lesions were seen in five (8.3%) and diffuse proliferative lesions (with crescents in more than 70% of glomeruli) in one patient. All of them had lepromatous leprosy. Three of the five patients with mesangial proliferative glomerulonephritis had erythema nodosum leprosum at the time of biopsy. Immunofluorescence studies revealed granular deposits of IgA, IgM and C3 in one patient with mesangial proliferation and IgA/IgM with or without C3 in three more patients in whom renal histology was normal. Glomerulonephritis associated with leprosy appears to be immune mediated but confirmation requires identification of lepra antigen in the glomerular immune complex deposits.—Authors' Summary

da Sylva, F. C., Biron, G. and Stach, J.-L. Etude du statut immunitaire des lepréux par utilisation d'un multitest cutané. [Study of the immune status of leprosy by the use of multiple skin tests.] Dakar Med. **28** (1983) 257–263. (in French)

Forty leprosy patients, hospitalized in the Malta Ward of the Institute of Leprosy, were studied from an immunologic point of view. From the results of our work it is evident that leprosy patients are not deprived from the point of view of cell-mediated immunity. Lepromatous patients without antecedent ENL do not demonstrate delayed hypersensitivity to a variety of skin test antigens; whereas lepromatous patients having had antecedent ENL and tuberculoid patients do show delayed hypersensitivity to these antigens. It seems, therefore, that the supervention of ENL in lepromatous leprosy patients contributes to the restoration of general cell-mediated immunity.—(*From* Authors' English Summary)

Furukawa, F., Ohshio, G., Ozaki, M. and Hamashima, Y. Anti-hapten antibodies and autoantibodies in Japanese patients with lepromatous leprosy. Arch. Dermatol. Res. **276** (1984) 195–198.

In the sera of patients with lepromatous leprosy anti-DNP antibodies were detected in order to determine the mode of polyclonal B-cell activation. Anti-DNP antibodies were found in 30% of the patients with active lepromatous leprosy and in 8% of those with inactive lepromatous leprosy. The level of anti-DNP antibodies in active patients was significantly higher than the level in inactive patients and controls. However, the presence of anti-DNP antibodies was unrelated to the production of circulating immune complexes and antinuclear antibodies. These results suggest that polyclonal B-cell activation might occur but that the B-cell clones stimulated by *Mycobacterium leprae* are different from patient to patient.—Authors' Summary

Gomez-Estrada, H., Morales-Ortiz, R., Gonzalez-Mendoza, A., Barba-Rubio, J. and Ceja-Mendoza, S. Deficiencia de per-

oxidasa en los histiocitos de pacientes con lepra lepromatosa nodular. [Peroxidase deficiency in histiocytes of patients with nodular lepromatous leprosy.] Arch. Invest. Med. (Mex.) **14** (1983) 127–137. (in Spanish)

The purpose of this study was to investigate the presence of peroxidase (PO) in the histiocytes which are found in the lepromatous lesions of patients with nodular lepromatous leprosy (NLL). We studied dermoepidermal biopsy specimens from lepromatous lesions and blood smears of 10 patients with NLL, 8 males and 2 females 28 to 63 years of age (average 45 ± 6.2), of which 9 had the stable form of the disease and 1 was in lepromatous reaction. Six had received treatment with diaminodiphenylsulfone for more than six months, and the other four, none. As controls we studied the blood smears of 10 healthy controls and 10 rat liver sections. PO was investigated in histiocytes, Kupffer cells, and polymorphonuclears by dichlorhydrate oxidation, according to the technique of Kaplow. By means of Fite-Faraco's stain, all 10 cases proved to have abundant phagocytized *Mycobacterium leprae.* PO was not found in histiocytes of lepromatous lesions in nine cases of stable NLL, while it was weakly positive in the patient with NLL in lepromatous reaction. PO was present in Kupffer cells, in polymorphonuclears of patients with NLL and in controls. No difference was found either in the PO or *M. leprae* contents between treated and untreated patients. The PO deficiency in histiocytes of patients with NLL may be related to an incapacity of these cells to destroy *M. leprae.*—Authors' English Abstract

Jayalakshmi. Histopathology of skin lesions in leprosy. Malays. J. Pathol. **3** (1980) 39–45.

A review of skin biopsies performed at the University Hospital, Kuala Lumpur, over a ten-year period (1968 to 1978) revealed 76 cases of leprosy. The lesions have been classified as tuberculoid, borderline tuberculoid, borderline, borderline lepromatous, and lepromatous leprosy. Their histological appearances and relationship to nerve involvement are discussed.—Author's Summary

Jayasingh, K. and Bhatia, V. N. DNCB contact sensitization in leprosy: Its comparison with other CMI tests. Indian J. Lepr. **56** (1984) 207–211.

Seventy-six lepromatous, 50 nonlepromatous cases of leprosy, and 20 apparently healthy individuals were tested for dinitrochlorobenzene contact sensitization. Only one lepromatous case and one apparently healthy individual showed a negative result. E-rosette counts and leukocyte migration inhibition tests were performed in 22 lepromatous, 10 nonlepromatous cases, and 10 apparently healthy individuals who were all DNCB positive. Of these, 2 lepromatous, 8 nonlepromatous cases, and all the 10 apparently healthy individuals showed lepromin positivity. Average E-rosette counts (percentage) and mean leukocyte migratory indexes were significantly lower in lepromatous as compared to nonlepromatous cases.—Authors' Abstract

Klatser, P. R., van Rens, M. M. and Eggelte, T. A. Immunochemical characterization of *Mycobacterium leprae* antigens by the SDS-polyacrylamide gel electrophoresis immunoperoxidase technique (SGIP) using patients' sera. Clin. Exp. Immunol. **56** (1984) 537–544.

In this study the SDS-polyacrylamide gel electrophoresis immunoperoxidase (SGIP) assay was used for characterizing the antigenic components of *Mycobacterium leprae* using patients' sera. This technique involved the separation of mycobacterial sonicates on SDS-polyacrylamide gels, longitudinal sectioning of the gels, incubation with patients' sera and visualization of the antigen–antibody complexes by the indirect immunoperoxidase technique. A number of antigens present in *M. leprae* sonicates were recognized by leprosy patients' sera, some of which were seen in other mycobacteria as well. Antibody binding to a 33 kD antigen, present in both *M. leprae* and BCG sonicates, was reduced only in the latter after six months of multiple drug treatment of one patient. It is suggested that this is a common mycobacterial antigen with one or more *M. leprae*-specific determinants. Several antigens were identified only in *M. leprae* sonicates, only by leprosy patients: a 12, 22, 28, 36, 41 and 86 kD component. These

antigens lost their antigenicity after trypsin treatment, but were heat stable. Such *M. leprae*-specific antigens may be useful for immunodiagnosis.—Authors' Summary

Mshana, R. N., Humber, D. P., Harboe, M. and Belehu, A. Nerve damage following intraneural injection of *Mycobacterium leprae* into rabbits pre-sensitized to mycobacteria. Clin. Exp. Immunol. **52** (1984) 441–448.

Nerve damage is a common feature of leprosy although the mechanism responsible for the damage is not clearly understood. In the tuberculoid end of the leprosy spectrum where both intraneural *Mycobacterium leprae* or their antigens and cell-mediated hypersensitivity to *M. leprae* co-exist, acute neuritis affecting major nerve trunks can occur during reversal reactions. These reactions are known to be associated with increased hypersensitivity to *M. leprae* antigens. The nerve involvement is therefore thought to be a direct consequence of the patient's hypersensitivity to *M. leprae*. So far only indirect evidence based on *in vitro* studies has been produced to support such a contention. We sensitized rabbits with *M. leprae* and then injected *M. leprae* sonicate into the sciatic nerves at the peak of hypersensitivity. Seventy-two hours later, the nerves were dissected and studied histologically. Our results show that cellular infiltration and axonal degeneration can occur as a direct consequence of hypersensitivity to intraneural *M. leprae* antigens. This study, therefore, offers direct evidence for the involvement of specific cell-mediated hypersensitivity to *M. leprae* antigens in the pathogenesis of major nerve trunk damage in the tuberculoid end of the leprosy spectrum, especially during acute reversal reactions.—Authors' Summary

Ramos Zepeda, R., Gonzalez-Mendoza, A. and Morales Ortiz, R. Depressive effect of plasma on lymphocyte transformation in nodular lepromatous leprosy. Bull. Soc. Pathol. Exot. Filiales **77** (1984) 182–189.

Lymphocytes from 20 patients with nodular lepromatous leprosy (NLL) were cultured stimulated with PHA in the presence of autologous and homologous plasma; the same procedure was carried out with lymphocytes from 20 healthy people utilized as controls. A diminished capacity of transformation was noticed when lymphocytes, both from patients and controls, were cultured in plasma from NLL patients, this suggesting the presence of a plasma inhibitor factor. This effect was particularly noticeable in eight cases (40%) of the studied patients. Regarding the nature of the plasma factor, the concentration of C-reactive protein, rheumatoid factor, alpha, beta and gamma globulins, did not show any correlation with the presence of the depressive activity. It seems that, at least in some cases, the impaired lymphocyte transformation observed in NLL patients can be due to an immune complex present as a plasma factor, rather than to an intrinsic defect in lymphocytes.—Authors' Summary

Reitan, L. J. and Closs, O. *In vitro* stimulation of lymphocytes with an antigen fraction prepared from *Mycobacterium leprae* and tuberculin PPD in contacts and non-contacts of leprosy patients. Clin. Exp. Immunol. **57** (1984) 315–323.

An antigen fraction from *Mycobacterium leprae,* called MLW1, was used as stimulator in the lymphocyte stimulation test, for comparison with tuberculin PPD. The test was performed in three groups of contacts of leprosy patients with various degrees of exposure: 1) close contacts, 2) healthy occupational contacts and 3) non-close contacts and, in addition, in a group of BCG vaccinated and non-exposed controls. The MLW1 preparation induced moderate to strong responses in all three groups of contacts. Although the close contact group showed the highest median responses to all three doses tested, there were no significant differences between the contact groups. At all three dose levels the non-exposed group showed markedly and significantly lower median responses than the contact groups. The responses to tuberculin PPD was markedly and significantly lower in the close contact group than in the other groups. Both when individual responses to the two antigens MLW1 and PPD are compared and when the Δct/min' estimator is used, the results indicate that the intensity of the specific response increases with the closeness of contact with leprosy patients.—Authors' Summary

Ridley, M. J., Ridley, D. S., De Beer, F. C. and Pepys, M. D. C-reactive protein and apoB containing lipoproteins are associated with *Mycobacterium leprae* in lesions of human leprosy. Clin. Exp. Immunol. **56** (1984) 545–552.

Skin biopsies from patients with leprosy across the spectrum from tuberculoid (TT) to lepromatous (LL), including histoid lepromas and erythema nodosum leprosum (ENL) reactions, were stained immunohistochemically for the presence of C-reactive protein (CRP) and the apolipoprotein, apoB. *Mycobacterium leprae* bacillary material comprising cell walls, cytoplasmic and soluble components was present with increasing abundance towards the lepromatous end of the spectrum and always stained positively with anti-CRP.

M. leprae from armadillos did not stain with anti-human CRP, indicating that the staining of *M. leprae* in human tissues was not due to a crossreaction between anti-CRP and the organism itself. When CRP was present in large amounts apoB was also demonstrated in the same distribution. CRP was detected on bacilli and their degradation products within the cytoplasm of macrophages even in the absence of a raised serum CRP level in some ENL patients and also in two cases of advanced resolving lepromas. These findings demonstrate remarkable persistence of CRP in association with *M. leprae in vivo,* and raise intriguing questions about the possible role of CRP in relation to the handling of leprosy bacilli.—Authors' Summary

Salgame, P. R., Mahadevan, P. R. and Antia, N. H. Study of concanavalin A receptors on macrophages in leprosy. IRCS Med. Sci. **11** (1983) 991–992.

Mycobacterium leprae induces macrophage membrane alteration in lepromatous patients, as studied by macrophage ConA receptor. Other workers in our laboratory have also demonstrated lepromatous macrophage membrane alterations using the Fc receptor and *M. leprae* adherence receptor on the macrophages as membrane markers. Alteration in the ConA receptor was specific to the lepromatous group in conjunction with *M. leprae.* The requirement of an active interaction between *M. leprae* and the lepromatous macrophage in inducing membrane alteration is further substantiated by the lysate results. The study of the effect of L-lysate on ConA receptors of normal macrophages suggests the presence of a soluble suppressor factor(s) in lepromatous macrophages. This suppressor factor(s) is produced only in the lepromatous macrophages and in the presence of *M. leprae* as normal lysate does not contain any inhibitory activity.

With the present observations one could probably project an hypothesis that energy to *M. leprae* in lepromatous leprosy could be due to macrophage membrane alteration induced by a soluble suppressor factor. The membrane change in macrophages of lepromatous patients may prevent the macrophages from reacting normally with their surroundings, especially the lymphocyte. This lack of interaction could prevent the lymphocyte from being activated and participating in the cascade of events involved in a cell-mediated immune reaction.

It is hoped that the successful isolation and purification of the soluble suppressor factor(s) should make it possible to study the cellular mechanisms of immunomodulation in lepromatous leprosy without possible complication from disease processes that may affect the immune system in a nonspecific manner.—(*From* the article)

Samuel, N. M., Stanford, J. L., Rees, R. J. W., Fairbairn, T. and Adiga, R. B. Human vaccination studies in normal and contacts of leprosy patients. Indian J. Lepr. **56** (1984) 36–47.

The present communication contains the preliminary results of studies whose main aims have been to assess skin test conversion rates with the use of Leprosin A, attributable to killed *Mycobacterium leprae*; *M. vaccae*; with and without BCG in individuals who are negative to both skin tests initially, and to assess the duration of sensitivity.

The significant findings of the study are that vaccination of normals and healthy contacts with *M. leprae* with or without the addition of BCG shows significant conversion of Leprosin A and the conversion sustained until eight months. Even though the numbers of individuals in both groups who

received vaccination are small, the significance of the results is promising to observe whether vaccinated individuals are protected from developing clinical disease.—(*From* the article)

Singh, P. K., Ratna, Jain, P. K. and Mital, V. P. Immunological studies in leprosy—II: Study of lymphoblast transformation to PHA in different types of leprosy patients. Indian J. Lepr. **56** (1984) 30–35.

Ninety cases of different types of leprosy were studied for lymphoblast transformation response using PHA-M. The difference of percentage was statistically analyzed and found to be highly significant when total leprosy cases were compared with control cases and with different types of leprosy cases ($p < 0.005$), except control and TT where it was significant only ($p < 0.05$). The difference between TT and other types was also calculated and has been observed to be highly significant ($p < 0.005$). There was gradual decrease in lymphoblast transformation percentage from tuberculoid pole to lepromatous pole.—Authors' Abstract

Singh, P. K., Ratna, Jain, P. K. and Mital, V. P. Immunological studies in leprosy. III—Cutaneous response to antigens in spectrum of leprosy. Indian J. Lepr. **56** (1984) 257–263.

Delayed type of hypersensitivity response was assessed in 65 cases of leprosy of different types, and 18 controls using lepromin (Dharmendra) and candida antigens; 0.1 ml of antigen was injected intradermally and results were recorded after 48 hours. An induration of 5 mm or more was taken as positive for the early (Fernandez) reaction in the lepromin test, and also for the candida reaction. Both types of tests were positive in decreasing order from tuberculoid to borderline type while negative in borderline lepromatous and lepromatous type.—Authors' Abstract

Sinha, S., Sengupta, U., Ramu, G. and Ivanyi, J. A serological test for leprosy based on competitive inhibition of monoclonal antibody binding to the MY2a determinant of *Mycobacterium leprae*. Trans. R. Soc. Trop. Med. Hyg. **77** (1983) 869–871.

A novel serological assay for leprosy has been devised on the basis of serum inhibition of binding of ^{125}I-labeled ML04 monoclonal antibody to *Mycobacterium leprae* sonicate-coated microtiter plates. Antibodies were detected in 93% of lepromatous leprosy patients; whereas controls from the endemic area, including leprosy contacts and patients with tuberculosis, were serologically negative. The specificity and efficacy of the test may offer an advantage over previously used techniques.—(*From* Trop. Dis. Bull.)

Srivastava, D. C., Shekhawat, R. S., Saksena, H. C. and Gupta, L. N. Granulocyte adherence in leprosy. Indian J. Med. Res. **79** (1984) 487–490.

Granulocyte adherence was assessed in 45 patients suffering from three different types of leprosy (20 lepromatous, 10 borderline and 15 tuberculoid). A significant ($p < 0.001$) impairment of granulocyte adherence was found in all types of leprosy studied in comparison with equal number of matched controls. Impairment was more in the lepromatous leprosy group followed by borderline and tuberculoid groups.—Authors' Abstract

van Eden, W., de Vries, R. R. P., Stanford, J. L. and Rook, G. A. W. HLA-DR3 associated genetic control of response to multiple skin tests with new tuberculins. Clin. Exp. Immunol. **52** (1983) 287–292.

Multiple skin testing with mycobacterial antigenic preparations reveals distinct reaction patterns, which might be relevant to the development of mycobacterial disease in man. Previous work has shown that HLA-DR associated factors correlate with the position of a leprosy patient in the immunopathological spectrum of leprosy. This study was undertaken to see whether these skin test patterns in healthy persons do show any association with HLA-DR types. Out of a group of 74 healthy Caucasoid individuals [living in London] HLA-DR3 was observed to be absent from the 16 individuals who did not respond to any of the mycobacterial antigens tested. This is a striking difference from the distribution of HLA-DR3 both among the 17 individuals who responded to all mycobacterial antigens tested ($p =$

0.005) and the 41 individuals who responded to some but not all antigens ($p = 0.015$). These data show that an HLA-DR3 associated genetic factor controls, albeit indirectly, skin test responsiveness to mycobacterial antigens. It may be significant that this same HLA-DR determinant is implicated in deciding the type of disease to be developed by a leprosy patient.—A.S. (*From* Trop. Dis. Bull.)

Van Hale, H. M., Turkel, S. B. and Rea, T. H. Dermal ultrastructure in leprosy. Arch. Pathol. Lab. Med. **108** (1984) 383–386.

We studied the ultrastructure of the dermal inflammatory response in 18 patients with leprosy. Biopsy specimens from 14 lepromatous patients, including 4 with Lucio's phenomenon and 4 with erythema nodosum leprosum, were compared with biopsy specimens from 1 borderline lepromatous and 3 borderline tuberculoid patients. In all, the dermal infiltrate consisted of macrophages, lymphocytes, and mast cells. This infiltrate was predominantly perivascular, and chronic reactive changes were found in the small dermal vessels. The macrophages contained phagocytized organisms within membrane-bound vacuoles and a wide variety of lysosomal residual dense bodies. Intraendothelial organisms were occasionally seen, especially in biopsy specimens from the patients with Lucio's phenomenon. The greatest number of mast cells were also seen in the infiltrate in those cases. The frequent close association of macrophages with lymphocytes and mast cells suggests an interrelationship between these cells that appears typical of the host response to leprosy.—Authors' Abstract

Young, D. B., Dissanayake, S., Miller, R. A., Khanolkar, S. R. and Buchanan, T. M. Humans respond predominantly with IgM immunoglobulin to the species-specific glycolipid of *Mycobacterium leprae.* J. Infect. Dis. **149** (1984) 870–873.

The immunoglobulin classes of the antibody response to the species-specific phenolic glycolipid antigen of *Mycobacterium leprae* have been characterized for serum specimens from 78 patients with leprosy. These patients included the entire clinical spectrum from paucibacillary to multibacillary disease, including polar tuberculoid (TT, 11 patients), borderline tuberculoid (BT, 15), borderline (BB, 17), borderline lepromatous (BL, 13), and lepromatous (LL, 22)—clinical classifications according to Ridley-Jopling criteria. In each patient group, the levels of IgM antibody to phenolic glycolipd were significantly higher than levels of IgG or IgA. Inhibition experiments with purified antigen showed that antibodies to the phenolic glycolipid dominated the human IgM antibody response to the surface of *M. leprae.*—Authors' Abstract

Zhao Bian, *et al.* [Study of the pathologic changes of posterior tibial nerve in arrested borderline leprosy patients, with light and electron microscopy.] Chin. J. Clin. Dermatol. **13** (1984) 2–5. (in Chinese)

This article reports the pathologic changes of posterior tibial nerve in eight arrested BT leprosy patients. Observations on light microscopy showed marked thickening of the epineurium and perineurium. Endoneurium was fibrotic. The perineurium was infiltrated by inflammatory cells. The vessel walls were thickened with narrow lumen or obliterated with hyaline degeneration. Within the nerve bundles there were focal infiltrations of lymphocytes and epithelioid cells. Schwann cells showed proliferation. Nerve axons with degeneration and demyelination were demonstrated; sometimes that completely disappeared. Acid-fast bacilli were identified in infiltrated foci in all cases. Transmission electron microscopy showed marked proliferation of collagen fibrils. Schwann cells were long and thin. Mitochondria in cytoplasma were swollen and their crista disintegrated. There were vacuoles of varying sizes within the cytoplasm. Some myelin sheaths were in cracks, separated, or twisted. The lamina structure was not clear. The degenerated axon showed decrease of microfilaments with vacuoles of varying sizes. A few bacilli were found in nonmyelinated nerves. The causes that prevent *Mycobacterium leprae* from elimination in Schwann cells and axons are discussed by the authors. It is noted that the Schwann cells and the axons can be considered as a "shelter" for *M. leprae.*—Authors' English Abstract

Zhu, W. Y., *et al.* Histopathology of blood vessels and skin appendages in the skin lesions of untreated LL and BL forms of leprosy patients—a light and electron microscopy study. Chin. J. Clin. Dermatol. **12** (1983) 290–292. (in Chinese)

This paper reported the histopathological changes of blood vessels and skin appendages in skin lesions of 50 leprosy patients who were untreated or treated with DDS for only 10–40 days. In all the 50 cases many intact *Mycobacterium leprae* were observed in vascular lesions. The bacilli were particularly frequent in the capillary endothelium and were found in 49 cases. There were thrombosis and organization in medium-sized arteries and veins with destruction of arterial internal elastic lamina, fibrinoid degeneration, inflammatory infiltration and granuloma formation in vessel wall. *M. leprae* were present in some of the endothelial cells and thrombi, and were also found in hair follicles, arrector pili muscles, and sweat glands but not in sweat ducts.

Electron microscopy showed that the capillary endothelium could contain bacilli up to six in number. Lysosomes were arranged around the bacilli, but there were no bacilli in lysosomes. The capillary basal lamina became thickened and multilayered, and the collagen fibers around pericytes were markedly increased. We suggest that the relatively weak activity of endothelial cells in phagocytizing and digesting *M. leprae* may account for the extended existence of bacteremia.—Authors' English Abstract

Microbiology

Brett, S. J., Payne, S. N., Draper, P. and Gigg, R. Analysis of the major antigenic determinants of the characteristic phenolic glycolipid from *Mycobacterium leprae.* Clin. Exp. Immunol. **56** (1984) 89–96.

Antibodies to the major phenolic glycolipid purified from *Mycobacterium leprae* have been demonstrated previously in sera of leprosy but not tuberculosis patients using an ELISA. The major antigenic determinants on this molecule were investigated using antisera raised in rabbits to the purified glycolipid and with a pool of sera from human lepromatous leprosy patients. A small, but significant crossreaction was observed with the glycolipids from *M. bovis* and *M. kansasii,* which contain the phenolphthioceral dimycocerosate part of the molecule but have different sugars, and also with a semi-synthetic "attenuation indicator lipid" which shares the phenolphthiocerol but has no sugars. There was however no crossreaction with phthiocerol dimycocerosate. The disaccharide, corresponding to the two terminal sugars of the *M. leprae* glycolipid has been chemically synthesized and shown to inhibit the reaction between glycolipid and antibody in the ELISA. The crossreactivity observed with the *M. bovis* and *M. kansasii* glycolipids was not inhibited by the synthetic disaccharide. These findings suggest that the crossreactivity is associated with the phenol ring and imply the disaccharide may be a unique antigenic determinant of *M. leprae.*—Authors' Summary

Ishaque, M. Cytochrome system in cultivated *Mycobacterium lepraemurium.* Cytobios **39** (1984) 165–170.

The respiratory pigments of cell suspensions of *Mycobacterium lepraemurium* cultivated on Ogawa egg-yolk medium were investigated spectrophotometrically. The results obtained showed that whole cell suspensions of both Kumato and Hawaiian strains contained flavins, cytochromes of the a_2 and b type, as well as a CO-binding pigment similar to cytochrome o. The whole cell suspensions of *M. lepraemurium* did not show detectable quantities of c type cytochrome. However, cytochrome c was present in small amounts, and its presence became evident in the dithionite-reduced minus oxidized difference spectra of pyridine hemochromogens prepared from *in vitro*-grown cells of *M. leparemurium.*—Author's Abstract

Kale, V. P. and Bapat, C. V. Antigenic cross-reactivity between ICRC-bacilli and *M. leprae*—"*in vitro*" evaluation. Indian J. Lepr. **56** (1984) 219–231.

Leukocyte migration inhibition (LMI), in the presence of specific particulate antigen, is a good correlate of cell-mediated immunity. It can detect small differences in related antigens. In the present study, LMI was used to study the crossreactivity between ICRC bacilli and *Mycobacterium leprae* and also to examine the antigenic relationship among different ICRC isolates. The study showed a close antigenic crossreactivity in lepromin and ICRC-in. LMI has brought out strain differences in two ICRC culture isolates, C-44 and C-75. The data appear to elucidate the possible strain specific antigenic relationship of *M. leprae* with its culture isolate, e.g., ICRC strains. This may have important bearings on the development of effective antileprosy vaccine for human use.—Authors' Abstract

Kale, V. P., Bhat, A. V. and Bapat, C. V. Comparison of biochemical characterisation of ICRC bacilli with *M. leprae*: Effect of substrate alteration in the medium. Indian J. Lepr. **56** (1984) 212–218.

ICRC-bacilli strain C-44 when grown in Dubos medium or its equivalent, express *Mycobacterium avium* taxonomic biochemical characters. Assuming that difference in characters of *M. leprae* and ICRC bacilli could be due to *in vivo* and *in vitro* milieu, we altered the substrates in the medium. The bacilli grew well in the new medium containing selenium, ferric nitrate, magnesium chloride and deleting Tween 80. The ICRC strain C-44 grown in new medium expressed characters: 9/10 similarity with *M. leprae*. The 10-day Tween hydrolysis reaction is weak but positive. It is probable that "*M. leprae* culture isolate" may have acquired *in vitro* growth potential by recombination with *M. avium*, an ubiquitous mycobacterium. The *M. leprae* culture isolate thus may express some characters of both *M. leprae* and *M. avium*.—Authors' Abstract

Kale, V. P., Bhat, A. V. and Bapat, C. V. DOPA-oxidase activity on ICRC bacilli. Indian J. Lepr. **56** (1984) 58–62.

The presence of *o*-phenoloxidase is regarded as *Mycobacterium leprae*-specific character. This enzyme activity was found to be present in ICRC bacilli, strain C-44. Although this strain is cultivable *in vitro*, the expression of DOPA-oxidase activity strongly suggests that it carries *M. leprae* genome. The ICRC bacilli, therefore, may thus form a group of *M. leprae* culture isolates, distinct from other known cultivable mycobacteria which do not possess this enzyme activity.—Authors' Abstract

Kannan, K. B., Katoch, V. M., Bharadwaj, V. P., Sharma, V. D., Dutta, A. K. and Venkatesan, K. Alanine dehydrogenase in mycobacteria—a preliminary report. Indian J. Lepr. **56** (1984) 98–101.

Various mycobacterial species, namely *Mycobacterium phlei, M. vaccae, M. scrofulaceum, M. avium* and *M. tuberculosis*, have been investigated for the presence of enzyme alanine dehydrogenase which could be important for utilization of alanine by TCA cycle. It was found that alanine dehydrogenase was present in all species of mycobacteria tested irrespective of the fact that they are rapid or slow growers. Electrophoretic mobilities of alanine dehydrogenase from different species of mycobacteria were not found to be significant for taxonomical differentiation of rapid and slow growers.—Authors' Abstract

Klebanoff, S. J. and Shepard, C. C. Toxic effect of the peroxidase-hydrogen peroxide-halide antimicrobial system on *Mycobacterium leprae*. Infect. Immun. **44** (1984) 534–536.

Mycobacterium leprae are killed by myeloperoxidase (or eosinophil peroxidase), H_2O_2, and a halide, thus suggesting a mechanism for their destruction by peroxidase-containing phagocytes.—Authors' Abstract

Lee, W. Y., Kim, S. K. and Lew, J. Attempts to establish host cells for *Mycobacterium leprae in vitro* by hybridizing mouse macrophages and HeLa cells. Yonsei Med. J. **23** (1982) 8–14.

Various primary cells and an established cell line were cultured in roller tubes and in suspension to evaluate their potential roles as host cells to support the growth of *Mycobacterium leprae in vitro.* The primary cells originated from the organs of chipmunks, mice, and humans. Phagocytic ability of those cells except for macrophages was found to be low and did not vary much according to their origin. However, when macrophages from mice peritoneal exudate were exposed to the bacteria, the phagocytic efficiency was higher than 47%. In spite of those good primary results, the macrophages are not cells which can adapt well *in vitro* for long-term culture, which is essential for the growth of slow-growing *M. leprae.* Thus, somatic cell hybridization between the macrophages and HeLa cells was made by fusing them with polyethylene glycol. Those hybrids appeared to have both the characteristics of the parent cells which can provide a natural intracellular environment such as the macrophages and the infinite growth capability of the HeLa cells *in vitro.*—Authors' Abstract

Tsukiyama, F., Katoh, M. and Matsuo, Y. Modification of the fluorescent staining method for mycobacterial cells. Hiroshima J. Med. Sci. **33** (1984) 293–295.

The fluorescein diacetate–ethidium bromide (FDA/EB) staining method for determining the viability of mycobacterial cells reported by Kvach and Veras was modified for applying the method to *Mycobacterium leprae* and *M. lepraemurium.* Our method clearly differentiated green-stained cells from red-orange ones with either mycobacterial species and permitted their original fluorescence to be maintained for over four minutes.—Authors' Summary

Experimental Infections

Almeida, J. G., Joseph, P. S., Sarangapani, G. and Chacko, C. J. G. The mouse footpad test—sensitive to small proportions of drug-resistant bacilli in a sample of *M. leprae.* Indian J. Lepr. **56** (1984) 10–14.

In experiments at the Radda Barnen Research Laboratories of the SLR & TC Karigiri, the mouse foot pad test was demonstrated to detect DDS-resistant *Mycobacterium leprae* even if as few as 0.1% (1 in 1000) of the *M. leprae* tested were DDS resistant. The mouse foot pad test appears to be sensitive to minute proportions of drug-resistant bacilli in samples of *M. leprae* tested.—Authors' Abstract

Ha, D. K. K., Lawton, J. W. M. and Gardner, I. D. Experimental murine leprosy: A biochemical study emphasizing lysosomal enzyme changes *in vivo* and enzyme secretion by macrophages *in vitro.* Exp. Mol. Pathol. **40** (1984) 177–194.

This study was undertaken to identify biochemical alterations in serum, lymphoid organs, and peritoneal macrophages (PM) which reflect the histopathology of experimental *Mycobacterium lepraemurium* (MLM) infection in mice. A significant increase of acid phosphatase, β-glucuronidase, *N*-acetyl-β-D-glucosaminidase, and lysozyme was found in serum, spleen, and liver homogenates of mice infected intraperitoneally (ip) with MLM. PM from infected mice showed a substantially greater rate of secretion of β-glucuronidase, *N*-acetyl-β-D-glucosaminidase, and acid phos-

phatase than PM from normal mice. There was, however, no significant difference in the ability of PM from BALB/c and C57BL/6 mice to secrete such enzymes *in vitro*. There was also a significant increase in all these enzymes in PM in the early stage of infection but they dropped to values lower than normal in the advanced stage of infection despite the fact that such cells increased in size and protein content as the infection progressed. Infected mice were also found to have progressively elevated levels of serum lactic dehydrogenase, glutamic oxaloacetic, and glutamic pyruvic transaminases which indicated damages of hepatocytes and other tissues. Values of other blood components were also reported. Both BALB/c and C57BL/6 strains of mice, which are susceptible to the ip route of MLM infection, showed an indistinguishable pattern of biochemical alterations as reflected by their similar histopathological changes in various organs. BALB/c mice, which are still susceptible to subcutaneous (sc) route of infection showed similar characteristic changes in various serum components as before. In contrast, C57BL/6 mice, which are resistant to MLM infection sc, showed insignificant alterations in most of these biochemical parameters.—Authors' Abstract

Hoffenbach, A., Lagrange, P. H. and Bach, M.-A. Surface Lyt phenotype of suppressor cells in C57BL/6 mice infected with *Mycobacterium lepraemurium*. Clin. Exp. Immunol. **54** (1983) 151–157.

C57BL/6 mice were infected intravenously with 10^7 *Mycobacterium lepraemurium* (MLM). At increasing time intervals after infection, different isolated splenic cell subpopulations were tested for their ability to suppress the mixed lymphocyte reaction (MLR) of normal syngeneic mouse splenocytes. During the first six months after infection neither T-depleted nor plastic-adherent spleen cells from infected mice exerted a suppressive activity on the normal mouse allogeneic proliferative response. Conversely, splenic T cells from MLM-infected mice exhibited suppressive activity as early as two months after infection. Attempts to characterize the Lyt phenotype of splenic suppressor T cells from six months' infected mice showed that both Lyt 1^+2^- and Lyt 2^+ enriched cell subsets possessed the ability to suppress the MLR of the normal mouse spleen cells and Lyt 1^+2^- T cells were shown to be more efficient suppressors than Lyt 2^+ cells.—A.S. (*From* Trop. Dis. Bull.)

Løvik, M. and Closs, O. Survival of *Mycobacterium lepraemurium* in C57BL mice after acquired protective immunity. Clin. Exp. Immunol. **57** (1984) 115–122.

The protective immune response against *Mycobacterium lepraemurium* (MLM) in C57BL mice has been shown to stop the increase in bacillary numbers and the dissemination of bacilli, but the acid-fast bacilli are not cleared from the tissues. Persistence of viable bacilli was indicated by a significant increase in the number of acid-fast bacilli in the foot pad of C57BL mice that were treated with cortisone acetate several weeks after the onset of the immune response. Bacilli harvested 9 and 16 days after inoculation into immune C57BL mice showed only a marginally detectable loss of viability as determined by bacillary multiplication after transfer into susceptible C3H mice. Twenty-six weeks after being inoculated into immune C57BL mice a small proportion of the bacilli was found still to be alive. A similar finding was done 15 weeks after primary inoculation of MLM into mice that developed an apparently effective protective immune response four weeks after being inoculated. Sixty-seven weeks after inoculation of immunized C57BL mice with MLM, bacillary numbers in the foot pad were as with patent immunity, but the bacilli were found to be fully viable, suggesting incipient reactivation of the infection. When bacillary numbers were followed over a period of 52 weeks in the organs of normal C57BL mice inoculated with a low dose of bacilli, it was found that after a plateau phase bacillary numbers started to increase again. Thus, in all experiments part of the bacillary population had survived the protective immune response against MLM in C57BL mice.—Authors' Summary

Mathew, R. C., Curtis, J. and Turk, J. L. T cell proliferation in *Mycobacterium lepraemurium* infection. II. Characteriza-

tion of cells that transfer resistance in subcutaneously infected mice. Immunology **51** (1984) 703–710.

T lymphocyte proliferation. Lyt phenotypes and their role in the evolution of protective immunity were studied in BALB/c and C57BL/6 mice infected subcutaneously with *Mycobacterium lepraemurium*. Antigen-induced proliferation was not demonstrable with T-enriched cells obtained from the spleens. However, these cells were capable of spontaneously proliferating in the absence of added antigen for a limited period. This proliferation was dependent on the presence of a phagocytic and adherent accessory cell. During the period when the T cells proliferated spontaneously they consisted of a mixture of Lyt-1 and Lyt-23 and were able to transfer protection to syngeneic recipient mice. Furthermore, the multiplication of the organisms was curbed during the same period demonstrating a strong association between the ability to proliferate spontaneously Lyt-1/Lyt-23 cells and protective immunity. T cells from normal BALB/c mice showed a marked suppressive effect on protection suggesting that these cells may be responsible for the susceptibility of this strain to a moderate subcutaneous infection.—Authors' Summary

Skamene, E., Gros, P., Forget, A., Patel, P. J. and Nesbitt, M. N. Regulation of resistance to leprosy by chromosome 1 locus in the mouse. Immunogenetics **19** (1984) 117–124.

Mice of different inbred strains vary in their resistance to intravenous infection with *Mycobacterium lepraemurium* (MLM). The mean survival time of MLM-infected A/J and DBA/2 mice is significantly longer than that of similarly infected C57BL/6 and BALB/c mice. The typing of AXB/BXA recombinant inbred strains (A = A/J,B = C57BL/6) for the trait of relative resistance/susceptibility to MLM revealed a perfect match with the strain distribution pattern of resistance/susceptibility to *M. bovis* (BCG), the trait which is controlled by the *Bcg* (*Ity, Lsh*) locus on chromosome 1. The control, by this gene, of response to MLM was further confirmed by the demonstration that BALB/c-*Bcg*^{r}-congenic mice, which carry the DBA/2-derived *Bcg*^{r}-(resistant) allele on chromosome 1, are significantly more resistant to MLM infection than their BALB/c (*Bcg*^{s}, susceptible) counterparts.—Authors' Abstract

Turcotte, R., Chaput, J. and Lemieux, S. Enhancement of resistance in *Mycobacterium lepraemurium* infected C3H mice by treatment with sonicated *M. lepraemurium* or splenectomy. Clin. Exp. Immunol. **56** (1984) 97–104.

C3H mice were first infected in a hind foot pad with 10^7 freshly harvested *Mycobacterium lepraemurium* bacilli. Four weeks later, when a granulomatous reaction was detected at the inoculation site, the animals were treated with two doses of a whole sonicated preparation of *M. lepraemurium* administered two weeks apart in the contralateral foot pad. Such treatment was found to prolong the survival time of infected mice by 55–60 days. To study the involvement of the spleen in the immunomodulation of resistance to *M. lepraemurium* infection, splenectomy was performed in mice prior to infection via two different routes. Splenectomy significantly prolonged the mean survival time of mice infected in the foot pad but did not affect survival of those infected intraperitoneally. Treatment of splenectomized foot pad-infected mice with sonicated bacilli abrogated almost completely the beneficial effect of splenectomy.—Authors' Summary

Epidemiology and Prevention

Daniel, J. R., Maniar, J. K. and Ganapati, R. An approach to leprosy work in South Bombay—a preliminary communication. Indian J. Lepr. **56** (1984) 280–291.

The city of Bombay with its teeming eight million citizens is characterized by varied types of living patterns in its different parts and the approach to leprosy control work

should be flexible to suit these facets of living conditions. Earlier reports (Ganapati and Girija 1979) have indicated the possibility of the successful application of techniques based on mass surveys in North Bombay, where people belonging to low socio-economic strata live in somewhat organized slums or shanty towns. However, extreme South Bombay is marked by the paucity of such vast slums, and one is struck by the more permanent multistoried housing structures. Living in commercial establishments as well as footpath dwelling is common.

This presentation consists of an attempt to gauge the leprosy problems in this part of the city, taking advantage of 425 patients registered at a leprosy clinic run in conjunction with the dermatology outpatient department of a big general hospital over a period of 40 months; 212 cases (50%) hailing from South Bombay proper were the subject matter for analysis.

Sixty-six percent (140) belonged to progressive types of leprosy classifiable as BT through LL on the Ridley-Jopling classification and 30.7% were bacteriologically positive; 42.9% of the patients had some degree of deformity. Males formed 80% of the sample and 76% were above 15 years of age. Analysis of duration of residence revealed that 68% were living in Bombay for over six years and 53.5% were residing in the city for 11 years or more. This finding is contrary to the expectation of leprosy patients in Bombay belonging to a "floating population."

Attempts at field work revealed the following findings: Slum pockets being few (only four), patients were expected to live in residential buildings, but it was found that 25% of the population were staying in work places; 17% were footpath dwellers, and 18.9% shared their accommodation with people other than family members; 10.4% were domestic servants staying in the residences of their employees. The labor class constituted 50.5%; the unemployed housewives group formed 21.7% and beggers 0.9%; 4.2% only were slum dwellers.

Locating and examining contacts of patients was difficult since 42.9% could not be traced owing to faulty addresses or patients having changed residences or shifted to native places. Of the 111 patients (52.3%) contacted, 26.4% were living with families and 26.1% were staying alone or with others; 56 families were visited, 190 contacts representing 71.7% of the enumerated family members could be examined. Seven patients detected out of these accounted for a prevalence rate of 37 per 1000 among contacts examined.

An analysis of the attendance pattern for treatment at the clinic showed that only 36.3% of the patients had a satisfactory rate of attendance (i.e., over 75% of the expected weeks of treatment); 18.4% had dropped out after initial reporting.

This study indicates the need for intensifying field efforts to identify the patients in their places of residence in order to promote attendance at the clinic, in spite of a variety of inherent difficulties of urban work which seem to be peculiar to this part of the city. Although mass surveys may not be undertaken in populations of the type encountered in this study, contact examination is definitely possible and is rewarding as far as detection of cases is concerned.—Authors' Abstract

Ferreira, J., Bernardi, C. and Gerbase, A. Controle da Hanseníase num sistema integrado de atencão de saúde. [Control of Hansen's disease in an integrated health care system.] Bol. Of. Sanit. Panam. **95** (1983) 507–515. (in Portuguese)

The authors present the current policy adopted in the state of Rio Grande do Sul, Brazil, to control leprosy and its relation to the existing health system. They also present the results of six years of work following the establishment of a computerized nominal file for registering patients. The distribution of new cases is described by clinical type, sex, age group and incidence rates for the period from 1975 to 1980. Cases declared cured during this period, variations in the prevalence rates, and control indexes for patients and contacts are also indicated. Together with this description, classification criteria, particularly for type I, are analyzed, as are criteria for declaring a case cured, the effect of cases "statistically cured" on the number of patients registered and a policy for placing patients in colony-hospitals.—Authors' English Summary

Hunter, J. M. and Thomas, M. O. Hypothesis of leprosy, tuberculosis and urbanization in Africa. Soc. Sci. Med. **19** (1984) 27–57.

Leprosy today is a problem of global magnitude affecting possibly up to 15 million people. Its rise and fall in medieval Europe is an historically fascinating enigma. Partial cross-immunization by epidemic tuberculosis, reinforced by the growth of cities, has been proposed as a mechanism in leprosy's European disappearance, but evidence is lacking. In the case of Africa in recent decades, analysis of leprosy and tuberculosis rates, and of levels of urbanization, albeit with imperfect data, suggests a possible environmental hearth for leprosy, the existence of some cross-interference between tuberculosis and the milder, paucibacillary form of leprosy, and a negative correlation between leprosy and urbanization. It is argued that the rise of the city in Africa, acting through a combination of influences, including tuberculosis, is leading to a decline of leprosy.—Authors' Abstract

Keeler, R. Hansen's disease in children under 14 years of age; report of an eleven year programme in Trinidad and Tobago. Caribbean Med. J. **43** (1982) 15–16.

The leprosy control program in Trinidad and Tobago started in 1971. During the 11 years of the program studied, 275 cases of leprosy were diagnosed in children, of which 4% were BL or LL. In the first five years of the program, 216 of the patients were diagnosed (with a peak of 65 new cases in 1973) compared with only 59 in the last six years (3 cases in 1981). Only 13 children were less than 4 years old at diagnosis. The success of the program is attributed to the use of outpatient facilities and intensive case-finding, treatment and follow-up of all leprosy patients.—C. A. Brown (*From* Trop. Dis. Bull.)

Lerche, A., Enk, G., Jensen, H. and Black, F. T. Lepra—ogsã i Danmark. En oversigt og fire sygehistoier. [Leprosy—even in Denmark. Review and report of four cases.] Ugeskr. Laeger **145** (1983) 3885–3888. (in Danish)

Leprosy is a disease which occurs sporadically in Denmark, affecting mainly immigrants from Asiatic and African countries. During the past five years, Denmark has received 15,000 persons from areas with endemic leprosy, which is a pronounced rise in the number of immigrants compared to previous figures. In the light of this trend, a short summary of the clinical picture, histopathology, immunology and the latest principles of chemotherapeutic treatment of leprosy is given. During the past two years, four patients with leprosy have been diagnosed in Denmark. These case reports are presented.—Authors' English Summary

Mathur, N. K., Sharma, M., Bumb, R. A. and Yogi, G. Study of multiple case families. Indian J. Lepr. **56** (1984) 200–206.

1) Multiple-case families constituted only 5.76% of the families of leprosy patients; 2) the number of secondary cases was found to be apparently related to the size of the family; 3) the younger age group was found to be more susceptible to contact leprosy from a household index; 4) no constant relation was found between the type of leprosy in the index case and the secondary case; 5) an LL index case was found to be responsible for the maximum number of secondary cases; 6) conjugal leprosy was noted in 10.7% of the cases.—(*From* the Authors' Conclusions)

McGlashan, N., Ali, M. and Shepherd, S. Some health problems of the Maldives. Ecol. Dis. 1 (1982) 221–228.

This paper includes analyses of some information obtained by the Maldives Ministry of Health with the WHO. No correlation was found between birth rate and infant death rate and no firm pattern in variation in the infant death rate among the islands could be found apart from the fact that the main island with better facilities had significantly fewer deaths than some other islands. Reduction of the infant death rate of 99.4/1000 per year is a major priority.

The prevalence rate of malaria has been reduced to 0.37% (in 1975–1979) from 16% in 1965 by the use of insecticide spraying. There are signs that continuing effort is required.

Leprosy is a problem with an incidence (as derived from numbers of cases diagnosed) in 1981 of 6.7/1000 per annum. Variations among the islands, taking account of patients grouped together for treatment, are unexplained but 11 islands showed significantly more cases in 1981 than between 1976 and 1979.

[The collection of these kinds of data are a vital prerequisite to planning the development of health services.]—P.R. Gully (*From* Trop. Dis. Bull.)

Reddy, B. N. and Bansal, R. D. An epidemiological study of leprosy in a rural community of Pondicherry. Indian J. Lepr. **56** (1984) 15–23.

In a rural area endemic for leprosy, a total population survey had been undertaken in six [Indian] villages covering a population of 5667. Out of the 5281 persons examined, 191 were found to be suffering from leprosy, giving a prevalence rate of 36.16/1000. The prevalence was highest in children aged between 5 and 14 years, i.e., 41.61/1000. Among adults the highest prevalence was seen among those aged above 45 years, i.e., 45.66/1000. Both sexes were found to be equally affected in this area. Tuberculoid leprosy was the most common type found with a prevalence rate of 23.29/1000, followed by indeterminate type with a prevalence rate of 5.3/1000. The lepromatous rate was 3.69%. The disability rate was found to be 16.23%, with a mean disability index of 0.927.—Authors' Abstract

Sehgal, V. N., Ghorpade, A. and Saha, K. Urban leprosy—an appraisal from northern India. Lepr. Rev. **55** (1984) 159–166.

From an urban leprosy program in India, details were collected from 1661 new patients in order to delineate its pattern clearly. It was revealed from this study that males aged from 20 to 29 years were the largest and commonest age-at-onset group, although no age group was immune to leprosy. The patients were largely derived from unskilled workers and belonged to the low-income strata. Urban leprosy as such appears to be a negligible problem but a threatening situation is developing because of the influx of migrants from endemic belts, a pattern seen in almost all studies of this kind. This study also draws attention to the high percentage of lepromatous or borderline-lepromatous cases registered in an urban situation.—Authors' Summary

Skinsnes, O. K. Epidemiology and decline of leprosy in Asia. Int. J. Dermatol. **22** (1983) 348–367.

The article begins with the premise that effective chemotherapy has now been available long enough to evaluate the incidence of newly registered cases as a means of determining epi/endemic trends and evaluating the epidemiologic effects of the widespread use of chemotherapy in leprosy. Pertinent characteristics of untreated leprosy epi/endemics are reviewed. Epidemiologic patterns of leprosy in Norway, Hawaii, Japan, Okinawa, Taiwan, Hong Kong, the Pescadore Islands of Taiwan, mainland China, Gudiyatham Taluk in India, The Philippines, Thailand, and Spain, U.S.A., and other non-Asian areas are reviewed. The time required to achieve a reduction in the newly registered case index to 15% of its peak is presented for a variety of locales. In many cases it is possible to project the time expected to achieve an end to the epi/endemic of leprosy in these areas. In general, it is estimated that by the time 25–30% of all leprosy cases are under treatment, the decline in the newly registered case index begins. In the areas surveyed, there have been large increases in populations. Nevertheless, there has been a steady, progressive decline in the disease despite the importation of new cases by immigration. The decline in leprosy noted in the areas considered here, supported by the globally increasing numbers of registered patients and patients under treatment around the world, may justify the suggestion that *Mycobacterium leprae* can now be regarded as an endangered species, it being recognized that it usually takes decades for endangered species to disappear even when unprotected.—(*From* the article)

Thirumalaikolundusubramanian, P. and Prince, J. S. Leprosy among primary school children. Indian J. Pediat. **50** (1983) 285–288.

Of the 6371 primary school children examined at Vridhachalam Taluk (Tamil

Nadu, India), 173 (2.7%) were found to have leprosy. The sex ratio in the affected group of boys and girls was 3:2. Over 90% of the cases had tuberculoid leprosy and only 0.5% had lepromatous leprosy. History of contact with leprosy was present in 450 (7%) children. This includes the 173 who had clinical manifestations. Thirty-one parents of the 173 afflicted children were literates. Fourteen of them knew that their children were suffering from leprosy.—Authors' Abstract

van Eden, W. and de Vries, R. R. P. Occasional review—HLA and leprosy: A reevaluation. Lepr. Rev. **55** (1984) 89–104.

The discovery in experimental animals of immune response genes (Ir-genes) located in the Major Histocompatibility Complex (MHC), provided an impetus for exploring HLA—the human MHC—encoded genetic control of the immune response in man. In this area particular attention was paid to leprosy on the supposition that genetic factors were involved in this disease, in the variable immune status of the patients, and in the specific immune defect in leprosy-affected patients. In many studies on the distribution of HLA-phenotypes among groups of patients and controls and among the members of multi-case leprosy families a role for HLA-encoded factors in the susceptibility to leprosy was shown, but entirely and quite unexpectedly, to tuberculoid leprosy and not lepromatous leprosy. These studies were reviewed previously. However, more recent studies gave convincing support to a more general role for HLA in determining the type of the disease to develop following infection. At the present stage it seems justified to state that the susceptibility to both polar tuberculoid (TT) and lepromatous (BL/LL) leprosy is controlled, at least partly, by HLA-linked genes and that these genes do not influence susceptibility to leprosy per se, but rather determine the type of disease to develop, most probably by controlling the leprosy-specific immune response.

Recent findings based on population—and family studies as well as *in vitro* experiments, to investigate the role of HLA in leprosy—are discussed in the review.—(*From* the Authors' Introduction)

Yellapurkar, M. V. Health management information system in leprosy control programme. Indian J. Lepr. **56** (1984) 86–97.

Health Management Information System was introduced methodically and enforced with ruthless punctuality in Maharashtra State from April 1981. It has paid excellent dividends so far as the implementation of the National Leprosy Control Program is concerned. Key indicators have been fixed for new case detection, bacteriological examination, regularity of treatment and screening of old patients for activity status. Monitoring of these activities is done regularly and feedback is provided. Marks are assigned for each key indicator and ranking is done based on the achievement of targets by each district, municipal corporation, health circle, etc., every month. The same procedure is adopted at a primary health center and even lower level. This has introduced a spirit of competition and generated a desire to better one's own performance by identifying and removing deficiencies. Maximum assistance is being derived from the primary health care and use is being made of multi-purpose workers, community health volunteers, and other ancillary agencies in case finding and case holding programs. The improvement in performance in respect to all key indicators during 1981–1982 has been between 40–60% over the performance during 1980–1981.—Author's Abstract

Rehabilitation

Chaise, F., Sedel, L. and Witvoet, J. Résultats de la chirurgie directe du nerf sciatique poplité externe dans les névrites de la maladie de Hansen. [Treatment of neuritis of Hansen's disease by direct surgery to the common peroneal nerve.] J. Chir. (Paris) **120** (1983) 515–519. (in French)

Twenty-two patients with common peroneal neuritis from Hansen's disease were

treated surgically. Physiopathologic and semiologic features of the affection are discussed, as well as the rules for therapeutic protocols, which should involve both medical and surgical treatment, and the operative technique described. Results on motor function appear to be satisfactory, but are dependent on many factors (duration of the neuritis, importance of the compressive factor, immunopathological form of the disease, quality of medical treatment). The indications for these neurolytic procedures are defined, and are predominantly any hyperalgic deficiency neuritis. The only contraindications are chronic painless palsies where improvement is doubtful because of neural fibrosis.—Authors' English Summary

El Samed, A., El Hawala, I., Amer, S. A. and Amer, K. Clinical electrophysiologic assessment of ulnar nerve transposition in tuberculoid leprosy. Int. J. Dermatol. **22** (1983) 481–484.

Ulnar nerve transposition was accomplished in 24 tuberculoid leprosy patients, making a total of 27 operations. Results were assessed clinically and electrophysiologically, pre- and postoperatively, and compared with a control group of 30 patients. Excellent results were obtained in early cases with minimal electromyographic changes. Late cases did not improve after surgery.—Authors' Abstract

Reddy, B. N. and Bansal, R. D. An epidemiological study of leprosy disability in a leprosy endemic rural population of Pondicherry (South India). Indian J. Lepr. **56** (1984) 191–199.

The disability rate in this study was 16.23%. The highest disability rate of 30.76% was found in those aged 45 years and above. Disabilities were found to be more common among male leprosy patients, with a disability rate of 21.05% compared to that of 11.45% found among female leprosy patients. None of the indeterminate leprosy patients showed any disabilities; whereas all the neuritic and lepromatous leprosy cases showed disabilities. The disability rate among tuberculoid leprosy patients and borderline leprosy patients was found to be 3.25% and 35%, respectively. Persons whose monthly per capita income was less than Rs. 200 constituted 93.50% of the cases with disabilities. Anesthesia of the hand was seen in 67.4% of the cases. The mean disability index (DI-2 type) was 0.927.—Authors' Abstract

Other Mycobacterial Diseases and Related Entities

Bussey, H. I., Merritt, G. J. and Hill, E. G. The influence of rifampin on quinidine and digoxin. Arch. Intern. Med. **144** (1984) 1021–1023.

Serum drug concentration data from the first of the two patients described herein suggest that rifampin may directly increase the metabolism of quinidine and thereby negate the influence of quinidine on the serum digoxin concentration (SDC). Data on the second patient suggest that rifampin may directly increase the metabolism of digoxin producing lower SDC values. In both cases, the discontinuation of rifampin therapy appears to have allowed reversion toward prerifampin metabolism of both quinidine and digoxin.—Authors' Abstract

Gracheva, M. P. On the possibility of the determination of bactericidal potency of alveolar macrophages by means of the NBT test. Zh. Mikrobiol. Epidemiol. Immunobiol. (1984) pp. 87–88. (in Russian)

The NBT test on alveolar macrophages can be used for the indirect evaluation of their bactericidal potency. This test has made it possible to show that the development of the tuberculous process in the lungs is characterized by the increasing intensity of the reduction of NBT by alveolar macrophages, which indirectly indicates their considerable bactericidal potency. But 3–4 weeks after infection macrophages, although capable of considerable bactericidal action, do not react to stimulation by *My-*

cobacterium tuberculosis.—Author's English Abstract

Heironimus, J. D., Winn, R. E. and Collins, C. B. Cutaneous nonpulmonary *Mycobacterium chelonei* infection. Successful treatment with sulfonamides in an immunosuppressed patient. Arch. Dermatol. **120** (1984) 1061–1063.

A 52-year-old man, who had received immunosuppressive therapy for four years after renal transplantation, had a deep-set skin infection in his thigh caused by *Mycobacterium chelonei. In vitro* studies indicated that the organism was resistant to antimycobacterial agents but potentially sensitive to high-dose sulfonamide therapy. Repeated surgical excisions failed to eradicate the infection, as documented by histopathologic examination. The combination of a reduced dose of immunosuppressive medication and the administration of high-dose sulfonamide therapy resulted in clinical recovery.—Authors' Abstract

McMurray, D. N., Yetley, E. A. and Burch, T. Effect of malnutrition and BCG vaccination on macrophage activation in guinea pigs. Nutr. Res. **1** (1981) 373–384.

Host defense functions, particularly cell-mediated immunity, may be profoundly altered by malnutrition. Activated macrophages are required as effector cells in the final stages of a successful cell-mediated immune response against microbial pathogens. Macrophage activation was assessed by measuring the activity of superoxide dismutase (SOD) in peritoneal macrophages obtained from BCG-vaccinated and non-vaccinated guinea pigs maintained on purified diets containing 8% or 25% casein. Protein deficiency, as measured by reduced hemoglobin and serum albumin concentrations, was accompanied by significant reductions in delayed hypersensitivity to purified protein derivative (PPD) and impaired lymphocyte blastogenic responses *in vitro* to PPD and phytohemagglutinin. In contrast, macrophage SOD activity was inversely correlated with protein nutritional status, irrespective of vaccination. These results suggest that the thymus-dependent (T) lymphocyte subsets responsible for delayed hypersensitivity, blastogenesis and macrophage activation may be affected differently by protein deprivation. Alternatively, enhanced macrophage activity may not be the result of T cell function in this model.—A.S./J. Alexander (*From* Trop. Dis. Bull.)

Pappas, M. G., Hajkowski, R. and Hockmeyer, W. T. Dot enzyme-linked immunosorbent assay (Dot-ELISA): A micro technique for the rapid diagnosis of visceral leishmaniasis. J. Immunol. Methods **64** (1983) 205–214.

A micro enzyme-linked immunosorbent assay utilizing antigen dotted onto nitrocellulose filter discs (Dot-ELISA) was developed for the rapid diagnosis of visceral leishmaniasis. *Leishmania donovani* promastigotes applied to filter discs in volumes of 1 μl were placed in 96-well microtiter plates, blocked with bovine serum albumin, then incubated with fourfold dilutions of patient sera. After incubation with peroxidase-conjugated anti-human antibody, washing and addition of precipitable substrate, positive reactions appeared as blue dots on a white background which were easily read by eye. The procedure is performed at room temperature, takes about two hours, and is economical. At a reciprocal diagnostic titer of $\geq$32, 41 of 42 (98%) leishmaniasis patients [from Kenya] were positive, and positive titers ranged from 512 to 524,288. Control sera from healthy [US] individuals showed 1 of 50 (2%) false-positive reactions. Sera from patients with African trypanosomiasis, Chagas's disease, and lupus erythematosus were crossreactive in the Dot-ELISA. No crossreactivity was noted with sera from patients with amebiasis, coccidioidomycosis, cutaneous leishmaniasis, viral hepatitis, hydatidosis, malaria, schistosomiasis, syphilis, toxoplasmosis or trichinosis. In replicate experiments, 90% of 167 sera tested did not vary in titer. This rapid and inexpensive test should prove to be an important field diagnostic technique for visceral leishmaniasis.—A.S. (*From* Trop. Dis. Bull.)

Ridley, M. J., Heather, C. J., Brown, J. and Willoughby, D. A. Experimental epithelioid cell granulomas, tubercle formation and immunological competence: an ul-

trastructural analysis. J. Pathol. **141** (1983) 97–112.

An ultrastructural study of the cells comprising tubercles in experimental mycobacterial granulomas in rats is presented. Tubercle formation was compared in: 1) primary infections due to BCG at 49 days, 2) reinfection with BCG at 7 days, 8 months after primary infection and 3) lesions due to preformed BCG/anti-BCG complexes in antibody excess in unprimed animals at 10 days. The most rapid elimination of antigen with resolution of the lesion in the reinfection lesions was effected by the early recruitment of cells morphologically characteristic of activated macrophages and immature epithelioid cells. The next best performance was in the immune complex lesion which at its height was maintained by a roughly constant size due to promonocytes, monocytes, macrophages, activated macrophages, and immature epithelioid cells accumulated at the site. True epithelioid cells were rare. The slowest rate of healing in the primary 49 day granulomas was associated with the whole spectrum of mononuclear phagocyte series of cells. All granulomas were surrounded by a cuff of mixed lymphocytes, interdigitating cells, and fibroblasts.

The rapid resolution of the reinfection lesions appeared as a loosely compacted infiltration of cells which allowed intimate contact of lymphocytes and macrophages. This was distinct from the tightly compacted and compartmentalized zones of lymphocytes and macrophages which inhibited contact in the most slowly resolving lesions. An intermediate arrangement was seen in the immune complex granuloma. Another factor which predisposed to rapid resolution was the high vascularity of the central region of the granulomas. In the slow resolving group vascularity was diminished and peripherally situated.—Authors' Summary

Ridley, M. J., Heather, C. J., Ridley, D. S. and Willoughby, D. A. The long-term evolution of mycobacterial BCG and preformed immune complex BCG/anti-BCG granulomas in rats. J. Pathol. **141** (1983) 41–54.

In previous studies it was found that infections with BCG or complexed BCG/anti-BCG in rat skin produced granulomas that appeared to resolve at eight months. In this follow-up study one year later, it appeared that while lesions due to preformed complexes had resolved, those due to BCG alone had undergone a massive reactivation. Nevertheless despite the loss of CMI the infection was restricted. The bacilli, present in enormously increased numbers, were dead; the host macrophages were large and activated. Epithelioid cells and dendritic cells were common. The granuloma was confluent, with patchy necrosis and inconspicuous polymorph infiltration.

Although preformed complexes with viable bacilli formed at equivalence had produced a resolving lesion, the outcome of the natural infection was complicated by an imponderable balance of immunological responses. CMI does not appear to have been a determinant during the crucial phases of the infection.—Authors' Summary

Ridley, M. J., Ridley, D. S. and Willoughby, D. A. Extravascular immune complexes in experimental mycobacterial BCG granulomas. J. Pathol. **141** (1983) 469–582.

Quantitative results of mycobacterial BCG antigen, immunoglobulin and complement in rat skin lesions during the evolution of the granuloma reveal peak values of these factors at 49 days. The combination of antigen, Ig and complement, present extracellularly and in polymorphs at this time, indicates immune complex formation at an antigen–antibody ratio which may approximate to equivalence. This development coincides with mass lysis of host macrophages, and is followed by a sharp reduction in the antigen load.

At eight months, surviving bacilli are coated with antibody and complement, and sequestrated in activated macrophages. It is possible that this antibody is nonspecific and protective to the bacilli, leading to a second multiplication of organisms. But by one year and eight months all the bacilli are dead, and immunoglobulins and complement are at very low levels.

Although immune complex deposition and macrophage lysis was not associated with complete elimination of bacilli, it

marked a turning point in the infection when the bacterial load was high and cell-mediated immunity (CMI) was lacking. CMI may be important, especially at low antigen levels, but the crucial role here appears to have been played by complexed antibody. These experimental findings parallel those in human cutaneous leishmaniasis. They may explain some forms of necrosis in this condition and in tuberculosis.—Authors' Summary

Shelley, W. B. and Folkens, A. T. *Mycobacterium gordonae* infection of the hand. Arch. Dermatol. **120** (1984) 1064–1065.

A 70-year-old woman was seen for two chronic nodules on the dorsum of her left hand. They had a uniquely mamillated surface, but histopathologically showed nonspecific granulomatous changes with no organisms seen. Laboratory studies disclosed the lesions were due to *Mycobacterium gordonae,* an organism commonly ignored as a pathogen. The histopathologic changes were reproduced by intradermal testing with tuberculin. The lesions, unaffected by ketoconazole, as well as by a variety of antibiotics, including minocycline hydrochloride, slowly involuted during a one-year period. To our knowledge, this patient is the first documented case of cutaneous infection from this organism. *M. gordonae* must be added to the list of true mycobacterial pathogens.—Authors' Abstract

Zielinski, C. C., Savoini, E., Ciotti, M., Orani, R., Konigswieser, H. and Eibl, M. M. Dialyzable leukocyte extract (transfer factor) in the treatment of superinfected fistulating tuberculosis of the bone. Cell. Immunol. **84** (1984) 200–205.

The effect of the addition of dialyzable leukocyte extract (DLE) (transfer factor) to tuberculostatic drugs in the treatment of superinfected fistulating tuberculosis of bones and joints was evaluated in a controlled study. Eleven patients whose disease had persisted for a mean of 20 ± 4.8 years and had proved to be resistant to antibiotics and tuberculostatic drugs were treated with an additional combined tuberculostatic drug regimen consisting of isoniazide, ethambutol, and rifampin for a control period of two years; after this therapy had failed as judged by the persistence of the superinfected fistulae and of the symptoms, DLE was added to the regimen. The result of this therapeutic approach was evaluated after another two years. Through this therapy, a closure of the fistulae was achieved in 9 out of the 11 patients ($p < 0.001$) with a concomitant decrease of symptoms. DLE may prove beneficial in the treatment of patients with superinfected fistulating tuberculous osteomyelitis.—Authors' Abstract