CURRENT LITERATURE

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

General and Historical

Bloom, B. R. and Godal, T. Selective primary health care: Strategies for control of disease in the developing world. V. Leprosy. Rev. Infect. Dis. **5** (1983) 765–780.

Leprosy afflicts 10–15 million people in the world, primarily in tropical and subtropical developing countries. In areas endemic for leprosy, the incidence may reach 4–6 cases per 1000 population, and the prevalence of the disease frequently exceeds 10 per 1000 population in parts of Africa and Asia. While these figures are not high in relation to those for other tropical diseases, many developing countries consider leprosy a major health problem because a significant proportion of cases result in deformity and subsequent social stigmatization. Leprosy comprises a wide spectrum of clinical and pathologic stages that have been classified histopathologically. In polar lepromatous disease there is specific immunologic unresponsiveness of cell-mediated immunity to *Mycobacterium leprae* antigens, while, in the tuberculoid form of the disease, strong cell-mediated immunity is present but tissue damage seems to be a consequence. This review discusses the detailed immunologic analyses of the histopathology and pathogenesis of the various stages of leprosy. It will be argued that lepromatous leprosy presents an extraordinary model for understanding the mechanisms of immunologic unresponsiveness in humans. The present effectiveness and limitations of chemotherapy in the face of emerging resistance to dapsone are briefly discussed. Recent advances in the development of vaccines are discussed in terms of their immunologic potential and epidemiologic necessity. The implications of an effective prophylactic or immunotherapeutic vaccine used in combination with chemotherapy are also presented.—Authors' Abstract

Chemotherapy

Almeida, J. G., Christian, M., Chacko, C. J. G., Taylor, P. M. and Fritschi, E. P. Studies on dapsone-resistant *Mycobacterium leprae* in leprosy patients of Gudiyatham Taluk, the leprosy control area of the Schieffelin Leprosy Research and Training Centre, Karigiri. 2. A progress report. Lepr. Rev. **54** (1983) 185–191.

The 1580 LL and BL leprosy patients in a community of 480,000 persons in South India were studied for the occurrence of dapsone-resistant *Mycobacterium leprae* between March 1978 and February 1981. Patients with a BI $\geq$ 2+ were biopsied for mouse inoculation, even if they were improving on dapsone monotherapy. Between 89 and 116 patients per 1000 patients screened were estimated to harbor dapsone-resistant *M. leprae.*—Authors' Summary

Balakrishnan, S., Kumar, A., Rozario, J. A., Thiagarajan, M. and Sirumban, P. Paper spot test and DDS/creatinine ratios in relation to treatment taken by leprosy patients. Lepr. India **55** (1983) 231–236.

The findings on the positivity of the paper spot test and the mean dapsone/creatinine (DDS/Cr) ratios in relation to the percentage of treatment taken by 316 leprosy outpatients on 100, 50, or 25 mg DDS daily are presented. Thirty-three percent of the subjects on 25 mg were found to give neg-

ative spot test as against 11–12% in the patient groups on 50 and 100 mg dose schedules. The mean DDS/Cr ratios in the spot test negative urine specimens were consistent for all dosage groups and ranged from 7.1–9.6 μg/mg. The ratios in the spot test positive urine specimens showed, in general, a direct proportion to the percentage of treatment taken, particularly in the 75–100% and 50–75% groups. The significance and implications of the findings are discussed.—Authors' Abstract

Barnhill, R. L. and McDougall, A. C. Thalidomide: Use and possible mode of action in reactional lepromatous leprosy and in various other conditions. J. Am. Acad. Dermatol. **7** (1982) 317–323.

The literature concerning the use and possible mode of action of thalidomide in reactional lepromatous leprosy and in various other conditions is reviewed. Although it has no action against the leprosy bacillus, its value in the treatment of the adverse reactions in this type of leprosy is well established, many leprologists considering it to be superior to any other drug for this purpose. Its efficacy in actinic prurigo is also impressive, and there are reports suggesting benefit in discoid lupus erythematosus. By contrast, its reported action in a number of other conditions, including severe aphthous stomatitis, Behçet's syndrome, pyoderma gangrenosum, nodular prurigo, and postherpetic neuralgia, needs confirmation in a larger number of cases, backed in some instances by clinical trial. The mechanism of action of this drug may be related to 1) antiinflammatory effects, particularly an inhibition of neutrophil chemotaxis, 2) immunosuppressive effects, or 3) effects on neural tissue. Furthermore, structure-activity studies may allow separation of these and other possible effects. This review is in no way intended to lend support to the indiscriminate use of a potentially hazardous drug in various diseases of unknown cause, but rather to draw attention to a number of conditions in which the drug has been found effective. The further judicious use of thalidomide or a nonteratogenic analogue, with careful observation of results, may contribute to knowledge of the underlying pathology in some of these conditions, and possibly also to the mechanism of action of the drug itself.—Authors' Abstract

Boddingius, J., de Bruijn, W. C. and Verdaasdonk, M. A. M. Microanalytical (TEM) investigations on the presence of anti-leprosy drugs (DDS and clofazimine) in araldite-embedded liver and peripheral nerves. Beitr. Electronenmikroskop. Direktabb. Oberfl. **16** (1983) 489–496.

The drug dapsone (DDS, diamino-diphenyl sulfone) for many years has been of great importance and has been applied as monotherapy in the treatment of leprosy. During the last few years, multiple drug therapy has been introduced, including also clofazimine. Determination of intracellular levels and of location, in the cells, of the drug(s) might throw light on still controversial issues such as which (bacillated) tissues are reached readily by sufficient quantities of the drug(s) and which are not.

In the study presented, micro-analytical TEM methods were applied both to research samples of DDS and of clofazimine and to ultrathin sections of glutaraldehyde-fixed and araldite-embedded tissues of mice fed for four months with 0.1% DDS in their diet and of their controls. Tissues of control mice were negative for both S and Cl, i.e., no signals were obtained. In contrast, organelles in Kupffer cells and in liver parenchyma cells of DDS-fed mice gave a distinct S-signal. All tissue components screened of peripheral nerves of DDS-fed mice, however, failed to give a signal for S. This supports a previous hypothesis that antileprosy drug(s) might not sufficiently penetrate and/or be stored in sufficient quantities in peripheral nerves in which, generally, *Mycobacterium leprae* is "hiding" in Schwann cells.—Authors' Abstract

Bourland, J., Van Loo, L. and Pattyn, S. R. Dapsone-resistant leprosy in Burundi. Lepr. Rev. **54** (1983) 239–242.

Between 1978 and 1981 a dapsone-resistance survey was performed in four out of five regions of Burundi. Among 1791 leprosy patients, 925 were multibacillary (51%) and prevalence of dapsone resistance was 3.7%, with variations in regions between 1.2–6.1%. Since the selection of patients was

on a clinical rather than a bacteriologic basis, this should be a minimum figure. Incubation time of dapsone resistance was from eight to more than 20 years of monotherapy. Two cases of primary dapsone resistance were also diagnosed.—Authors' Summary

Bullock, W. E. Rifampin in the treatment of leprosy. Rev. Infect. Dis. **5** Suppl. (1983) S606–S613.

The minimal inhibitory concentration of rifampin for *Mycobacterium leprae* is <1 μg/ml. Therapy with rifampin has proved efficacious both in mice experimentally infected with *M. leprae* and in humans with leprosy. Rifampin kills *M. leprae* more rapidly than do other antileprosy drugs currently available. Consequently, *M. leprae* bacilli from patients with lepromatous disease are rendered noninfectious within three weeks after the institution of rifampin therapy, as determined in the mouse foot pad test system. Administration of this antibiotic substantially reduces the quantities of *M. leprae* discharged in the nasal secretions of lepromatous patients within three weeks, thus rapidly decreasing the potential infectivity of these individuals. Intermittent rifampin therapy for leprosy has been successful, with a low incidence of adverse reactions to the drug. Worldwide, the prevalence of primary and secondary resistance of *M. leprae* to dapsone has increased markedly. Therefore, the World Health Organization recommends a multidrug regimen that includes intermittent administration of rifampin for the treatment of leprosy.—Author's Abstract

Burte, N. P., Chandorkar, A. G., Muley, M. P., Balsara, J. J. and Bulakh, P. M. Clofazimine in lepra (ENL) reaction, one year clinical trial. Lepr. India **55** (1983) 265–277.

Twenty lepromatous leprosy patients with lepra reaction and suspected dapsone resistance were treated with tapering doses of clofazimine. Clinical assessment was carried out every week. Bacteriological examination was carried out every six months. Fifteen patients became reaction free at the end of three months and the severity and frequency of reactions was reduced in other patients. Nerve tenderness, arthralgia, nodular eruptions, and all other signs and symptoms except anesthesia showed complete recovery in 15 patients and severity of the reactions was reduced in others. Gynecomastia regressed in two out of three patients within nine months. In a majority of patients, the BI and MI was reduced at the end of three months, and further reduced after six months, and in one case both the BI and MI became negative. Clinical and bacteriological improvement is attributed to the antibacterial effect of clofazimine, while reduction in incidence of (ENL) reactions was attributed to the anti-inflammatory effect of clofazimine. Regression of gynecomastia may be due to either improvement of involvement of testes or liver or both. Apart from dyschromia, clofazimine did not produce any severe side effects or toxicity.—Authors' Abstract

Burte, N. P., Chandorkar, A. G., Muley, M. P., Balsara, J. J. and Bulakh, P. M. Effect of one year clofazimine therapy on autonomic functions in lepromatous leprosy with lepra (ENL) reaction. Lepr. India **55** (1983) 278–285.

Twenty patients of either sex with lepromatous leprosy with frequent type II (ENL) reactions were selected for the study after exclusion of autonomic disorders. ANS functions were evaluated before and after clofazimine therapy, at an interval of two months, for one year. Sweat function test, Valsalva maneuver, histamine triple response, cold pressor test, and homatropine instillation were carried out in 20 normal healthy volunteers (controls) and the (ENL) patients. Clofazimine was administered initially 100 mg three times daily for one month and then gradually reduced to a dose of 100 mg biweekly for the last three months. Before the clofazimine therapy, 18 patients had abnormal sweat functions, 5 patients had abnormal Valsalva scores, 5 patients had abnormal cold pressor responses, and all 18 patients had abnormal histamine triple response tests. The homatropine instillation test was normal in all the patients. ANS functions did not improve significantly with clofazimine therapy, except in one patient with abnormal cold pressor response who showed slight improvement in pressor re-

sponse which, however, did not reach the normal value. ANS function tests indicate complete involvement of local axon reflex and hyporeactivity of sympathetic system and cardiac regulatory mechanisms in these patients. The parasympathetic system seems to be normal as seen from the homatropine instillation test.—Authors' Abstract

Cynamon, M. H. and Palmer, G. S. *In vitro* susceptibility of *Mycobacterium fortuitum* to amoxicillin or cephalothin in combination with clavulanic acid. Antimicrob. Agents Chemother. **23** (1983) 935–937.

The comparative *in vitro* activity of cefoxitin, cephalothin, amoxicillin, and clavulanic acid in combination with the latter two agents against 13 isolates of *Mycobacterium fortuitum* was evaluated by agar dilution susceptibility testing. Amoxicillin was more active than cephalothin but less active than cefoxitin against the strains tested. Clavulanic acid in combination with these β-lactams usually improved the activity by one or two dilutions compared with the β-lactams alone.—Authors' Abstract

Gelfand, M. and Froese, E. H. Red cell hypoplasia following dapsone and pyrimethamine. Cent. Afr. J. Med. **29** (1983) 181–183.

An elderly gentleman, who was taking dapsone and pyrimethamine (Deltaprim) as a malarial prophylaxis, fell ill. He was found to have a red cell aplasia. The drug was stopped and he made a full recovery. He was treated with prednisolone and the vitamin B complex.—Authors' Summary

Ghosh, S., McDougall, A. C., Hazra, S. K. and Yawalkar, S. J. controlled comparison of therapeutic effects of DDS in combination with daily or once-monthly rifampicin in patients with lepromatous leprosy. Indian J. Dermatol. **26** (1981) 1–6.

This controlled trial in 32 previously untreated patients with lepromatous leprosy was undertaken to compare the therapeutic effects of adding rifampin 450 mg daily (Regimen A) or 1200 mg once-monthly in a single oral dose given under supervision (Regimen B) to DDS 50 mg daily for six months. Clinical and histopathologic improvements and bacteriologic regression, indicated by the decreases in the Bacterial Index and Morphological Index of the skin and nose-blow smears, were quite satisfactory and practically identical after six months' treatment. The once-monthly rifampin schedule was better tolerated than the daily one. Rifampin 1200 mg once-monthly in a single oral dose for six months could, therefore, be therapeutically and economically an ideal and easily supervisable component of combination regimens for the initial treatment of multibacillary (LLp, LLs, and BL) types of leprosy.—Authors' Summary

Hastings, R. C. and Jacobson, R. R. Activity of ansamycin against *Mycobacterium leprae* in mice. (Letter) Lancet **2** (1983) 1079–1080.

Ansamycin (LM-427), a semisynthetic derivative of rifamycin S, reportedly shows activity *in vitro* against rifampin-resistant *Mycobacterium avium*. The drug was tested for anti-*M. leprae* activity in mouse foot pad infections by the continuous feeding method and found to be effective with a minimal effective dose of about 0.3 parts per million (0.00003% w/w) in the diets. The same strain of *M. leprae* was sensitive to rifampin with a minimal effective dose of 1 to 10 parts per million (0.0001% to 0.001% w/w) in the diets. A rifampin-resistant strain of *M. leprae* is being tested for crossresistance to ansamycin.—(*From* the Letter)

Ji Baohong, Chen Jiakun, Zhang Jialin, Hou Yuhong, Ni Guoxing and Zhang Renbao. Secondary dapsone-resistant leprosy in Shanghai Municipality. Lepr. Rev. **54** (1983) 197–202.

A formal survey of the prevalence of secondary dapsone-resistant leprosy, conducted in Shanghai Municipality according to the THELEP protocol, has revealed an estimated prevalence of from 5.66 to 8.62 per 100 patients at risk.—Authors' Summary

Levy, L. Primary resistance to dapsone among untreated lepromatous patients in Bamako and Chingleput. Lepr. Rev. **54** (1983) 177–183.

More than one-third of the patients with lepromatous leprosy, presumed previously untreated, who have thus far been admitted into the THELEP controlled clinical trials in Bamako and Chingleput, have been found to harbor dapsone-resistant *Mycobacterium leprae*.—Author's Summary

Levy, L. THELEP controlled clinical trials in lepromatous leprosy. Lepr. Rev. **54** (1983) 167–176.

The events leading to the development of the THELEP Standard Protocol for controlled clinical trials in lepromatous leprosy are recounted, and the structure of the Standard Protocol is described. Trials of multidrug regimens including dapsone, rifampin and clofazimine or prothionamide have been undertaken in Bamako and Chingleput.—Author's Summary

Li Wen-Zhong, *et al.* Observations on recent therapeutic effects of DDS resistant leprosy. Chin. J. Dermatol. **12** (1983) 126–129. (in Chinese)

Two groups (11 cases each) of secondary dapsone (DDS) resistant leprosy were treated with R761 (150 mg daily) and rifampin (150 mg daily) for half a year with rather remarkable clinical improvement. The Morphological Index (MI) was decreased to less than 5% within one month, and to almost 0 in six months; but the Bacteriologic Index (BI) decrease was not marked in comparison with that caused by DDS. Histopathological examination revealed that the decrease of bacterial density and the percentage of solid-stained bacilli coincided fundamentally with the results of the skin smear examination. BI decreased to 32% and 30%, respectively. In both groups, the lepra reaction was increased in the period of treatment. Both showed rather marked effects. There was no marked difference in clinical, bacterial and histopathological changes between the two groups. The determination of activity of *Mycobacterium leprae* showed that the loss of infection activity on mouse foot pads was quicker in the rifampin group in comparison with the R761 group.—Authors' English Abstract

Neelan, P. N., Noordeen, S. K., Balakrishnan, S. and Pandian, P. R. Prevalence survey of secondary dapsone resistance in leprosy in Kancheepuram and Tiruvannamalai Control Units of Tamil Nadu. Lepr. India **55** (1983) 222–230.

A field survey was designed and carried out in parts of Kancheepuram and Tiruvannamalai Leprosy Control Units in Tamil Nadu (population 418,000) with the objective of finding out the prevalence of secondary dapsone resistance among 790 lepromatous (LL and BL) cases who formed the patient population at risk based on certain treatment criteria. Using the mouse foot pad experiment, three resistant cases were identified in the Kancheepuram Unit (prevalence rate of 1.0%) and 11 cases in the Tiruvannamalai Unit (prevalence rate of 2.2%). The metabolic status of dapsone was found to be normal in more than 90% of the patients, showing no relationship to occurrence of resistance.—Authors' Abstract

Polasa, K. and Krishnaswamy, K. Effect of food on bioavailability of rifampicin. J. Clin. Pharmacol. **23** (1983) 433–437.

The area under the plasma concentration-time curve of rifampin was determined with and without food administration in six healthy male volunteers. Rifampin (10 mg/kg) was administered orally in the fasting state on one occasion and following a wheat-based breakfast on another. Administration of rifampin with food reduced mean peak plasma concentration and prolonged the time to reach peak concentration (2 hr vs 4 hr). Total area under the concentration-time curve from 0–8 hr and the rate of absorption were also significantly reduced when rifampin was administered with food.—Authors' Abstract

Ramu, G. and Sreevatsa. Evaluation of drug regimen in lepromatous leprosy—II. Lepr. India **55** (1983) 200–208.

A two-year follow-up study of four drug regimens in 45 cases is reported; whereas the combination of rifampin and dapsone had been found to effect clearance of bacteremia within a week and effect negativity of nasal smears in a shorter period of time, at two years the clinical and bacteriological results in the DDS, DDS + rifampin, DDS + thiacetazone + INH, and DDS + clofazimine regimen were similar.

However, on inoculating bacilli obtained from the dartos muscle into the foot pads of mice, multiplication was found in 1 out of 11 cases on rifampin and DDS; whereas 2 out of 9 cases on DDS + thiacetazone + INH; 2 out of 10 cases on DDS + clofazimine, and 4 out of 8 cases on DDS alone showed multiplication. Therefore at the end of two years there was no significant difference in the results of treatment with any of the drug combinations used in the trial. However, the drug combinations have been found to be better than monotherapy with dapsone alone.—Authors' Abstract

Reyes-Janvier, P. D. and Tantiongco, P. R. Chemotherapy trial with a triple-drug regimen, including once-monthly Rimactane® (rifampicin), in patients with multibacillary types of leprosy. Acta Leprol. (Genève) **1** (1983) 133–141.

Twenty-five previously untreated patients with multibacillary types of leprosy (22 LL and 3 BL) were treated for six months with a triple-drug regimen comprising 1200 mg Rimactane® in a single dose once monthly, 100 mg Lamprene three times a week, and 50 mg dapsone daily. Moderate to marked clinical improvement was observed in 96% of the patients treated. The Morphological Index averages of the skin smears either reached or came near to 0% in all patients following six months' treatment.

Average decreases in the Bacteriologic Indices of the skin smears and skin sections were 0.8 and 1, respectively. Moderate to marked histological improvement was observed in 48% of the 25 patients treated. The triple-drug regimen, including 1200 mg once-monthly Rimactane® (rifampin) administration, was tolerated well by all patients. This triple-drug regimen was effective, well tolerated and fairly economical in the treatment of patients with multibacillary types of leprosy.—Authors' Summary

Terencio de las Aguas, J. Terapéutica combinada en la lepra. [Therapeutic combinations in leprosy.] Acta Leprol. (Genève) **1** (1983) 143–150. (in Spanish)

The importance of polychemotherapy in multibacillary leprosy (LL and BL) in patients without any previous therapy is presented and patients who have already been diagnosed and are under monotherapy and most of all in resistant patients.

Sulfones, clofazimine, and rifampin are considered primary drugs and prothionamide-ethionamide are considered secondary drugs. The therapeutic plan consists of treatment with two or three drugs initially and continuing indefinitely with at least one of the drugs. The advantages of clofazimine-sulfones and rifampin-sulfones are pointed out. The necessity of immunotherapy for the recovery of cellular immunity against the bacillus is pointed out as the only form of therapy which prevents relapses and drug resistance.—(*Adapted from* English Summary)

Utji, R., Kosasih, A. and Santoso, A. U. S. Dapsone-resistant leprosy in Jakarta: A preliminary report. Lepr. Rev. **54** (1983) 193–195.

In a first effort to demonstrate the emergence of dapsone-resistant *Mycobacterium leprae* in Indonesia, one case of secondary resistance and one of primary resistance were demonstrated by inoculation of the mouse foot pad.—Authors' Summary

Clinical Sciences

Girdhar, B. K., Girdhar, A., Ramu, G. and Desikan, K. V. Borderline leprosy (BL) in an infant—report of a case and a brief review. Lepr. India **55** (1983) 333–337.

A case of borderline leprosy in a 19-month-old infant, beginning at the age of 9–10 months, is reported, along with a brief review of the literature on childhood leprosy.—Authors' Abstract

Grover, S., Bobhate, S. K. and Chaubey, B. S. Renal abnormality in leprosy. Lepr. India **55** (1983) 286–291.

Adequate kidney biopsy was studied in

54 cases of leprosy, of which 45 were lepromatous leprosy, 4 were of the tuberculoid type and 5 belonged to the borderline type of leprosy. Membranous glomerulonephritis (31.5%) was the commonest type of glomerular lesion, followed by mesangioproliferative glomerulonephritis (11.1%). It is concluded that renal lesions can occur in any type of leprosy. Reaction of renal tissues to *Mycobacterium leprae* could be due to various local immunologic or physiological factors.—Authors' Abstract

Hussain, S., Malaviya, G. N. and Girdhar, B. K. Nerve abscess in a deep seated branch of medial plantar nerve in the foot. Lepr. India **55** (1983) 371.

Nerve abscesses are usually seen in the main nerve trunks at the location where the nerves are relatively superficial. We report here a case of nerve abscess in a deep-seated branch of medial plantar nerve presenting as swelling in the foot.—(*From* the article)

Katoch, V. M., Katoch, K., Dutta, A. K., Sharma, V. D. and Ramu, G. Hepatitis-B virus infection in patients with leprosy—a brief communication. Lepr. India **55** (1983) 193–196.

The prevalence rate of hepatitis-B surface antigen (HBsAg) were determined in 413 patients with different types of leprosy and 133 healthy controls from the same population, in a study undertaken over a period of more than three years. The average frequency of Australia antigen (HBsAg) was 7.7% in leprosy cases as compared to 6.0% in their healthy counterparts. Across the spectrum, 7.2% of lepromatous patients (LL), 8.5% of borderline lepromatous (BL), 9.1% of borderline borderline (BB), 8.6% of borderline tuberculoid (BT), and 8.8% of tuberculoid (TT) cases were positive for HBsAg. Although the prevalence of Australia antigen was slightly higher in borderline tuberculoid, borderline borderline, and tuberculoid cases, it was not statistically significant. No association between carriership of HBsAg and lepromatous leprosy could be found in the present study.—Authors' Abstract

Lamba, P. A. and Srinivasan, R. Central serous retinopathy in leprosy. Lepr. India **55** (1983) 209–211.

The involvement of fundus is rare in leprosy. Even more so, fundus lesions, if any, are not seen very well because of anterior segment lesions and pupillary adhesions. A case of central serous retinopathy is recorded in association with progressive lepra reaction (type II) in a case of leprosy.—Authors' Abstract

Mathur, N. K., Bumb, R. A. and Mangal, H. N. Zinc restores hair growth in lepromatous leprosy. (Letter) Br. J. Dermatol. **109** (1983) 240.

This interesting Letter to the Editor reports a controlled study of supplemental oral zinc sulfate in lepromatous leprosy patients. Regrowth of eyebrows began in all eight cases lacking eyebrows receiving zinc sulfate 220 mg daily plus dapsone 100 mg daily after about six months' therapy and full growth had occurred within 18 months. In four cases lacking eyebrows who received dapsone 100 mg daily alone, none showed regrowth during the same period of observation.—RCH

Mhasawade, B. C. Leprosy—a case for mental health care. Lepr. India **55** (1983) 310–313.

One hundred twenty institutionalized cases of leprosy were tested for anxiety and depression on standard scales before and after psychiatric treatment. The latter seems to be effective in reducing both anxiety and depression after a course of treatment of three months. This appears to be a sound justification to advocate mental health care in institutions of leprosy in conjunction with physical care.

Leprosy is a chronic and disabling disease entity. With the social stigma associated to the disease the psychiatric hazards of the disease are as bad as its physical manifestations. However, usually, only the latter attract attention. Ignorance about the disease and social values about the disease can at once land a person in depression on utterance of the diagnosis. Further, anxiety about the outcome of the disease in particular and the future in general are known to

exist in sufferers of leprosy.—Author's Abstract

Pal, R. Level of serum sodium in leprosy. Indian J. Dermatol. **27** (1982) 135–137.

Serum sodium concentrations were found to be within normal ranges both in tuberculoid and lepromatous leprosy. There was no alteration of serum sodium levels with specific treatment with dapsone 50 mg daily.—(*From* the article)

Pannikar, V. K., Arunthathi, S., Chacko, C. J. G. and Fritschi, E. P. A clinico-pathological study of primary neuritic leprosy. Lepr. India **55** (1983) 212–221.

Normally neural involvement in leprosy is an ascending neuritis from the nerve involvement in the dermal lesions. However, in some cases neural involvement is seen in the absence of any dermal lesions. In some of these pure neuritic cases, dermal lesions appear sometime later. It is, therefore, more appropriate to designate such cases as "primary neuritic" cases.

This study is aimed at diagnosing primary neuritic leprosy among patients presenting with only neuritic symptoms. An attempt is also made to classify primary neuritic leprosy on a clinical and histopathological basis.

During the period 1979–1980, 30 patients reported to the outpatient department of Schieffelin Leprosy Research and Training Centre, Karigiri, India, with complaints of neuritic origin. In addition to clinical examination and routine skin smears, investigations such as skin, nerve and nasal biopsies, nerve conduction velocity and lepromin testing were carried out where feasible. Seventeen of these patients were diagnosed as primary neuritic leprosy and in seven patients other neurological conditions were diagnosed. The remaining six patients were kept under observation and have not shown evidence of leprosy during a two-year period of following-up. It is interesting that four of the 17 primary neuritic cases developed patches during a follow-up period of two years.

In the final analysis seven patients (41.2%) were classified into the lepromatous group and ten patients (58.8%) in the nonlepromatous group. These classifications will have a bearing on duration of treatment and for their subsequent release from control.—Authors' Abstract

Piepkorn, M., Brown, C. and Zone, J. Auricular chondritis as a rheumatologic manifestation of Lucio's phenomenon: Clinical improvement after plasmapheresis. Ann. Intern. Med. **98** (1983) 49–51.

We report a patient with the Lucio phenomenon in whom elevated circulating immune complexes shown by Raji cell assay declined after immunosuppressive therapy and plasmapheresis, concurrent with clinical improvement. Of additional interest was the transient appearance of auricular chondritis during therapy, a feature that to our knowledge has not been previously reported.—(*From* the article)

Saúl, A. and Novales, J. La lèpre de Lucio-Latapi et le phénomène de Lucio. [Lucio-Latapi leprosy and the Lucio phenomenon.] Acta Leprol. (Genève) **1** (1983) 115–132. (in French)

The Lucio-Latapi leprosy or diffuse lepromatous leprosy is a clinical variety of lepromatous leprosy first described by Lucio and Alvarado in 1852 and reidentified by Latapi in 1936. It is frequent in Mexico (23%) and in Costa Rica, and very rare in other countries. It is characterized by a diffuse infiltration of all the skin which never is transformed into nodules, by a complete alopecia of eyebrows and eyelashes and body hair, by anhydrotic and dysesthesic zones of the skin and by a peculiar type of lepra reaction named Lucio's phenomenon or necrotic erythema which is a vasculitis of vessels especially of the dermo-hypodermic union and of the hypodermis. Clinically this vasculitis is represented by well-shaped erythematous spots and later becomes necrotic with scabs, ulcerations and scars. Three points of confusion are stressed: the differences between nodules and nudosities, Lucio's leprosy and Lucio's phenomenon, and necrotic erythema and necrotic erythema nodosum leprosum. The differences between the pure and primitive form of Lucio's leprosy and the secondary one is also discussed, such as the laboratory findings, histopathological data, pronostic and treatment. Lucio's leprosy is considered the most

anergic of the entire immunological spectrum of leprosy.—Authors' English Summary

Sengupta, S. R., Dhole, T. N., Jahagirdar, V. L., Yemul, V. L. and Chawhan, R. N. Study of alpha one antitrypsin activity in lepra reaction. Lepr. India **55** (1983) 242–246.

In our earlier study, we reported elevation of serum alpha one antitrypsin levels in patients with lepromatous leprosy and lepra reaction. In this study estimation of serum alpha one antitrypsin levels in 50 lepra reaction patients (8 of type I and 42 of type II) and 50 age and sex matched healthy controls is described.

Alpha one antitrypsin levels were elevated in lepra reaction patients (type I—mean value of 332 mg% and S.D. ± 118.8 and type II—mean value of 450 mg% and S.D. ± 73.7) when compared with the healthy controls (mean value of 285 mg% and S.D. ± 66.05). The increase in levels in type II lepra reaction patients was statistically significant.

The results are discussed to correlate the increased levels of alpha one antitrypsin and the high bacterial load leading to the release of various proteases in type II lepra reaction.—Authors' Abstract

Singh, K., Iyenger, B. and Singh, R. Dermatomic distributions of hypopigmented macular lesions of leprosy: neural dependence of melanocytic functions. Experientia **39** (1983) 723–725.

Dermatomic analysis of the distribution of the hypopigmented patches of leprosy has revealed a pattern wherein patches are most frequent in dermatomes of the brachial plexus, decrease gradually in frequency in succeeding spinal segments, and increase again in dermatomes of the lumbar plexus. The predilection of hypopigmented patches for certain dermatomes may be a reflection of easy vulnerability of the neural pigmentary mechanism and/or a reflection of selective multiplication of *Mycobacterium leprae* in nerves of certain dermatomes, even though the organisms might have been seeded all over the body by hematogenous spread. These preliminary observations are discussed.—Authors' Summary

Zawar, P. B., Chawhan, R. N. and Swami, R. M. Electrocardiographic changes in lepra reaction. Lepr. India **55** (1983) 197–199.

The electrocardiographic (EKG) changes were evaluated in 54 patients with lepra reaction. Abnormalities of the EKG observed were in the form of prolongation of QTc in 24 (44.44%), ST-T changes in 9 (16.66%), and bundle branch block and ventricular extrasystoles in 2 each (3.70%). The mean QTc interval in 64 normal adults was 0.42 seconds (S.D. ± 0.03, range 0.36–0.44 seconds). It was 0.44 seconds (S.D. ± 0.05, range 0.38–0.52 seconds) in patients with lepra reaction. The difference in the QTc values in the two groups was statistically significant ($p < 0.01$). The EKG abnormalities in patients with lepra reaction appear to be due to myocardial involvement.—Authors' Abstract

Immuno-Pathology

Boddingius, J., Imkamp, F. M. J. H., Hendriksen, E. G. J. and de Bruin, M. Electron and light microscope studies of motor nerve damage in leprosy patients. Beitr. Eleltronenmikroskop. Direktabb. Oberfl. **16** (1983) 475–481.

Electron and light microscopical investigations presented here on the tibial nerve obtained from amputated extremities show that, histopathologically, motor nerve damage in leprosy patients in many respects is comparable to sensory nerve damage. An exception perhaps forms the presence, in endoneurial plasma cells, of colloidal inclusions of varying sizes which, by confluence, ultimately give rise to one large inclusion within the extended RER-cisternae. Further histopathological features comprised: extensive endoneurial fibrosis, loss of large myelinated fibers and occasionally, "onion-

skin appearance" of the perineurium. The finding of solid *Mycobacterium leprae* inside the motor nerve of a patient treated, in total, for 25 years with antileprosy drugs [20 yr dapsone (DDS); 5 yr rifampin], once more stresses the importance of long-term antileprosy drug therapy and, particularly, of continuation of such therapy long after skin smears have become bacteriologically negative.—Authors' Abstract

Brett, S. J., Draper, P., Payne, S. N. and Rees, R. J. W. Serological activity of a characteristic phenolic glycolipid from *Mycobacterium leprae* in sera from patients with leprosy and tuberculosis. Clin. Exp. Med. **52** (1983) 271–279.

Serological activity against a purified phenolic glycolipid from *Mycobacterium leprae,* which may be obtained in large amounts from *M. leprae*-infected armadillo liver, was investigated using immunodiffusion and an enzyme linked immunosorbent assay (ELISA). Generally a good correlation was obtained between these techniques, but the ELISA was more sensitive and convenient. Relatively high IgG and IgM anti-glycolipid antibody levels were found in lepromatous leprosy patients. The antibody titers to the glycolipid were, however, low when compared with antibody titers to crude sonicates. Since the glycolipid is present in large quantities, this suggests that it is not very immunogenic. Antibody against the glycolipid, especially of the IgM class, was demonstrable in some tuberculoid leprosy patients, although at much lower titers than in the lepromatous leprosy sera. In lepromatous leprosy patients that were skin-smear negative after more than five years of treatment the IgG anti-*M. leprae*-derived glycolipid activity had decreased markedly. The anti-IgG and IgM glycolipid antibody levels in tuberculosis patients did not differ significantly from the levels in appropriate normal healthy subjects. The glycolipid antibody levels in patients infected with *M. kansasii, M. avium* or *M. intracellulare* also fell within the range of normal healthy individuals.—Authors' Summary

Bullock, W. E., Watson, S., Nelson, K. E., Schauf, V., Makonkawkeyoon, S. and Jacobson, R. R. Aberrant immunoregulatory control of B lymphocyte function in lepromatous leprosy. Clin. Exp. Immunol. **49** (1982) 105–114.

The capacity of peripheral blood mononuclear (PBM) cells from patients with leprosy to generate immunoglobulin-secreting cells in response to pokeweed mitogen (PWM) was evaluated by a reverse hemolytic plaque forming cell (PFC) assay. The PFC responses of PBM cells from patients with lepromatous (LL) leprosy were significantly higher ($p < 0.01$) than those of PBM cells from normal controls and patients with tuberculoid leprosy. Co-culture of T lymphocytes from normal donors with PBM cells from LL patients reduced the PFC response of these cells to the normal range. $T4^+$-helper lymphocytes from LL donors did not induce supranormal responses to PWM by normal PBM cells enriched for B lymphocytes. $T8^+$-suppressor lymphocytes from normal donors greatly reduced the response of cultures containing normal allogeneic B cells plus $T4^+$ cells. Conversely, when $T8^+$ cells from LL donors were cocultured with normal B cells plus $T4^+$ cells, they failed to suppress the response to PWM. In summary, these studies have demonstrated abnormally high PWM-stimulated PFC responses by B lymphocytes from patients with LL. This aberration, in turn, is associated with a loss of regulatory function by $T8^+$-suppressor cells in LL patients.—Authors' Summary

Furukawa, F., Sekita, K., Hamashima, Y., Ozaki, M. and Imamura, S. Evaluation of circulating immune complexes and antinuclear antibodies in Japanese patients with leprosy. Arch. Dermatol. Res. **275** (1983) 144–146.

In 79 patients with leprosy a significant increase of anti-extractable nuclear antigen (ENA) antibodies and circulating immune complexes (CIC) was found. No correlation between CIC and anti-ENA antibodies was demonstrable. Since such a correlation is known from antinuclear antibodies and CIC in patients with systemic lupus erythematosus, it appears likely that anti-ENA antibodies do not play a causative role in CIC-mediated pathogenesis of leprosy.—Authors' Summary

Kaplan, G., Van Voorhis, W. C., Sarno, E. N., Nogueira, N. and Cohn, Z. A. The cutaneous infiltrates of leprosy. A transmission electron miscropscopy study. J. Exp. Med. **158** (1983) 1145–1159.

The dermal lesions of 18 patients with leprosy have been examined by transmission electron microscopy. The patients exhibited a spectrum of disease from polar lepromatous to polar tuberculoid with intermediate stages in various states of therapy and relapse. The nature and quantities of inflammatory cells and bacteria have been determined by electron microscopy to supplement previous light and fluorescence microscopy studies.

Lepromatous leprosy was characterized by many parasitized foam cells containing large, multibacillary vacuoles with intact, osmiophilic *Mycobacterium leprae*. Bacteria were embedded in an electron-lucent matrix. No extracellular bacteria were evident. Only small numbers of scattered lymphocytes were found. As one approached the borderline state, smaller numbers of bacilli were present as singlets and doublets in small vacuoles of macrophages. The more reactive forms showed increasing bacillary fragmentation, larger numbers of lymphoid cells, and an occasional epithelioid cell.

At the tuberculoid end of the spectrum, clear evidence of an exuberant lymphocyte response was evident. Large numbers of T cells with extremely long and complex filipodia were closely associated with epithelioid and multinucleated giant cells. Many of the mononuclear phagocytes appeared nonviable, and areas of necrosis were evident. Bacillary remnants were scarce and the cytoplasm of the epithelioid cells contained occasional dense bodies and many stacks of endoplasmic reticulum and mitochondria. These results suggest that Leu 3a/OKT4 helper cells may be capable of driving the effector function of mononuclear phagocytes. This would lead to a significant microbicidal effect on *M. leprae*, perhaps through the production of toxic oxygen intermediates.—Authors' Summary

Malhotra, B., Das, K. D., Tutakne, M. A. and Aggarwal, S. K. Precipitation of type I (upgrading) reaction in leprosy by skin testing with antigen and irritants. Lepr. India **55** (1983) 305–309.

Twenty leprosy patients (18 BT; 2 BB) were skin tested with lepromin, PPD, and DNCB to assess their immunologic status. Two of the patients (both BT) developed signs of acute neuritis with a sudden onset about four weeks after the test with DNCB, lepromin, and PPD. The patients had been on DDS therapy for the last 3–4 months. Presumably DNCB, PPD, or lepromin testing precipitated the reaction. The suggestion is made that a lower concentration of lepromin should be used initially and if it gives a negative reaction, then a higher concentration may be used. This is similar to PPD testing. This may be particularly important in TT and BT cases already on treatment.—(*From* the Authors' Abstract)

Mshana, R. N., Humber, D. P., Harboe, M. and Belehu, A. Immune responses to bovine neural antigens in leprosy patients. II. Absence of *in vitro* lymphocyte stimulation to peripheral nerve myelin proteins. Lepr. Rev. **54** (1983) 217–227.

Nerve damage is common in leprosy although the mechanisms involved are poorly understood. We have isolated myelin proteins from bovine sciatic nerves and used them to detect sensitization to these antigens as a possible mechanism for nerve damage in leprosy patients. These proteins as well as *Mycobacterium leprae* sonicate were used in an *in vitro* lymphocyte stimulation assay and data from leprosy patients compared to healthy contacts who served as controls. Furthermore, for each patient a correlation between the lymphoproliferative response to the myelin proteins and clinical parameters of nerve damage was looked for.

Our results do not show any differences between the patients and control subjects in their responses to myelin proteins. There was also no correlation between these responses and any clinical parameter of nerve damage or classification of the patient. Myelin basic protein, P_1, stimulated lymphocytes from all individuals studied and behaved like a mitogen. A significant positive correlation was found between lymphocyte stimulation to *M. leprae* and the number of enlarged peripheral nerves.

It is felt that unlike experimental allergic neuritis or encephalomyelitis, leprosy neuropathy is most likely not mediated via an autoimmune sensitization to myelin proteins. Our negative findings could, however, be due to lymphocyte trapping in nerve lesions. Furthermore, the possibility that autosensitization to other nerve components, e.g., non-myelin, may be involved in the pathogenesis of some nerve lesions in leprosy cannot be ruled out. Our studies, however, offer further support to the concept that hypersensitivity to intraneurally located *M. leprae* antigens is the main mechanism whereby nerve damage is produced in leprosy.—Authors' Summary

Olcén, P., Harboe, M., Warndorff, T. and Belehu, A. Antigens of *Mycobacterium leprae* and anti-*M. leprae* antibodies in the urine of leprosy patients. Lepr. Rev. **54** (1983) 203–216.

Forty-six newly diagnosed untreated leprosy patients and 11 control persons were examined for acid-fast bacilli, *Mycobacterium leprae* antigen(s) and anti-*M. leprae* antibody-like activity in concentrated urine samples. No acid-fast bacilli were found. Two of 23 paucibacillary and 11 of 23 multibacillary patients had detectable antigen(s) in the urine. The antigen(s) was/were absorbed by anti-BCG in seven out of eight examined samples. A significant correlation between the maximal Bacteriological Index and antigen concentration was found. Extensive differences in the anti-*M. leprae* antibody-like activity were seen within the group of control persons and the different groups of patients throughout the spectrum of leprosy. The results of examinations of the antibody-like activity after absorptions with Cowan I staphylococci, Sepharose anti-human IgG, heat treatment and assays for total IgG, IgA and IgM gave good evidence that most of the activity was due to anti-*M. leprae* antibodies of the IgG class.—Authors' Summary

Sakuntala, R., Pratap, V. K., Sharma, N. K. and Dayal, S. S. Acid mucopolysaccharides in leprosy lesions. Lepr. India **55** (1983) 252–260.

Uniform accumulation of acid mucopolysaccharides in all types of leprosy lesions was seen, except late tuberculoid lesions which showed the accumulation only at the periphery. Absence of acid mucopolysaccharides was significant in well-formed epithelioid granulomas and in giant cells of late tuberculoid cases. Generally a progressive decrease with advancing chronicity of the disease was noted. The dermal zone without any cellular infiltrate showed abundant acid mucopolysaccharides in comparison to those areas having inflammatory cell infiltrate in 70.83% of LL, 42.86% of BL, 33.3% of BB, 40.0% of BT, and 13.51% of TT cases. In indeterminate cases the distribution was the same as that of control cases. Testicular hyaluronidase digestion established that hyaluronic acid constituted the main bulk of acid mucopolysaccharides. The possible source of hyaluronic acid is discussed.—Authors' Abstract

Sengupta, S. R., Yemul, V. L. and Dhole, T. N. Lymphocyte transformation test in lepromatous leprosy patients and their healthy siblings. Lepr. India **55** (1983) 261–264.

Lymphoproliferative response to *Mycobacterium leprae,* PHA, PPD, and mixed leukocyte culture (MLC) were measured in 20 cases of lepromatous leprosy, 17 of their normal healthy siblings, and 15 healthy controls. Seven siblings of LL patients were HLA-D identical, which was identified by doing a MLC reaction.

All healthy siblings including HLA-D identical responded normal to all stimulating agents including *M. leprae* antigen. In contrast 20 cases of LL responded very poorly to *M. leprae* antigen and almost near normal to other stimulating agents. The specific unresponsiveness of LL patients to *M. leprae* antigen does not result from an HLA linked genetic defect and the defective CMI response to *M. leprae* antigen seems to be acquired and not genetically determined.—Authors' Abstract

Microbiology

Bhatia, V. N., Balakrishnan, S., Venkataramaniah, H. N. and Harikrishnan, S. Mouse foot pad growth of *M. leprae* in relation to bacteriological index. Lepr. India **55** (1983) 247–251.

A retrospective analysis was made of the mouse foot pad growth of *Mycobacterium leprae* from 35 cases of lepromatous leprosy with Bacteriologic Indexes (BI) ranging from 1.33 to 4.0 (Dharmendra scale). Of these 35 cases, 6 were found to be harboring dapsone-resistant bacilli and 18 cases, sensitive bacilli. In 11 cases there was no growth in the control group of animals. The analysis showed that there was no difference in the mean BI between those showing no growth and those showing growth in the first, second, or third harvest. A minimum BI of around 1.5 is considered adequate for positive foot pad takes. Another interesting observation made in the study was that the growth rate in the control group foot pads was consistently higher in mice receiving dapsone-resistant bacilli as compared to those inoculated with bacilli sensitive to the drug.—Authors' Abstract

Cocito, C. and Delville, J. Properties of microorganisms isolated from human leprosy lesions. Rev. Infect. Dis. **5** (1983) 649–656.

Diphtheroids, which in addition to *Mycobacterium leprae* are present in human leprosy lesions, were identified as true corynebacteria by DNA and cell wall analysis. Peptidoglycan (adjuvant) of these leprosy-derived corynebacteria (LDC) consists of N-acetyl-glycosaminyl-N-acetyl (glycolyl)-muramic acid and L-Ala-D-Glu (NH_2)-(L)-meso-A_2pm-(L)-D-Ala(A_2pm = diaminopimelic acid). (The amino group of the tetrapeptide is attached to the carboxyl group of the muramate.) Peripheral polysaccharide (antigen) is arabinogalactomannan with lateral chains of mannofuranose and arabinofuranose. To the latter are linked mycolic acids containing groups of isomers with 24–36 carbon atoms and containing between zero and four double bonds. DNAs of LDC isolates have a guanine + cytosine content of 56% and demonstrate a high degree of homology. LDC ribosomes crossreact with antisera against mycobacteria and with sera from patients with leprosy. Thermostable antigen M of LDC crossreacts with the main antigens of tuberculin and lepromin. LDC thus represents a homogeneous and unique group of corynebacteria immunologically related to *M. leprae*. Leprosy might be the result of a pathogenic cooperation between both organisms, as suggested by the enhancement of *M. leprae* growth rate promoted in mice by living LDC.—Authors' Abstract

Dutta, A. K., Katoch, V. M. and Sharma, V. D. Effect of pyridine extraction on the acid fastness of mycobacteria. Lepr. India **55** (1983) 299–304.

The effect of pyridine extraction on mycobacterial acid fastness has been studied using *Mycobacterium leprae* and some cultivable mycobacteria. The results revealed that not only *M. leprae* but some other mycobacteria, notably *M. vaccae* and *M. phlei*, also lose their acid fastness when extracted with fresh pyridine for two hours at room temperature. The implication of these findings is discussed.—Authors' Abstract

Katoch, V. M. and Desikan, K. V. Observations on the cultivation of *M. leprae* in medium "V" (Veeraraghavan). Lepr. India **55** (1983) 292–298.

The medium "V" has been evaluated for the *in vitro* growth of *Mycobacterium leprae*. *M. leprae* were obtained from five untreated cases of multibacillary type of leprosy. The medium was prepared and inoculated by the method described by Veeraraghavan. Killed (autoclaved) *M. leprae* from the same biopsies were kept as controls. Growth was monitored in a double-blind manner at 60 hours, 120 hours of incubation at 8–10°C of both primary and subcultures. Counting was done by both standard Shepard and McRae method as well as by Veeraraghavan's method. There was no evidence of any multiplication in any of the cases at 60 and 120 hours of incubation.—Authors' Abstract

Khanolkar, S. R. and Wheeler, P. R. Purine metabolism in *Mycobacterium leprae* grown in armadillo liver. FEMS Microbiol. Lett. **20** (1983) 273–278.

Mycobacterium leprae organisms generally incorporated purines more rapidly than pyrimidines into nucleic acids from the incubation medium. Purine synthesis *de novo* took place at a very slow rate suggesting a preference of the organism for preformed purines. In cell-free extracts of leprosy bacilli, enzymes for scavenging and interconversion of purines were detected. The results are discussed in the light of the failure to cultivate *M. leprae in vitro,* and the use of labelled substrates to determine the viability of suspensions of leprosy bacilli and their sensitivity to antileprosy drugs.—Authors' Summary

Mittal, A., Seshadri, P. S., Prasad, H. K., Sathish, M. and Nath, I. Radiometric macrophage culture assay for rapid evaluation of antileprosy activity of rifampin. Antimicrob. Agents Chemother. **24** (1983) 579–585.

The antileprosy effect of rifampin was evaluated by a newly developed rapid *in vitro* assay wherein 31 human-derived strains and one armadillo-derived strain of *Mycobacterium leprae* were maintained for two and three weeks, respectively, in murine and human macrophages in the presence of ^{3}H-thymidine. Of these strains, 27 showed significant incorporation of the radiolabel in cultures of live bacilli as compared with control cultures of heat-killed bacilli of the same strain. Consistent and significant inhibition of ^{3}H-thymidine uptake was observed in *M. leprae* resident cultures with 3 ng–200 ng of rifampin per ml as compared with similar cultures without the drug. In general, an increase in percent inhibition was seen from 3 ng–20 ng/ml, with marginal increases at 40, 50, and 100 ng/ml. *M. leprae* strains appear to be remarkably susceptible to this drug in the *in vitro* assay.—Authors' Abstract

Wheeler, P. R. and Bharadwaj, V. P. Enzymes of malate oxidation in *Mycobacterium leprae* grown in armadillo livers. J. Gen. Microbiol. **129** (1983) 2321–2325.

A NAD-dependent malate dehydrogenase is the principal enzyme for malate oxidation by *Mycobacterium leprae.* FAD-dependent malate-vitamin K reductase was detected at about 1% the level of the NAD-dependent activity. Both enzyme activities were detected in extracts from *M. leprae* treated with NaOH to abolish host-derived activities which might be adsorbed to the bacteria and the NAD-dependent enzyme was shown to be electrophoretically distinct from the host-tissue enzyme, thus establishing that these were both authentic bacterial enzymes. *M. leprae* does not possess malic enzyme.—Authors' Abstract

Experimental Infections

Closs, O., Lovik, M., Wigzell, H. and Taylor, B. S. *H*-2-linked gene(s) influence the granulomatous reaction to viable *Mycobacterium lepraemurium* in the mouse. Scand. J. Immunol. **18** (1983) 59–63.

The genetic control of the granulomatous response to viable *Mycobacterium lepraemurium* (Mlm) was studied in C3H and C57BL/6 inbred strains, BXH recombinant inbred strains, (C3H × C57BL) F_1 hybrids, and backcross mice. The results indicate that an autosomal dominant gene, or linked complex of genes, has a marked influence on the foot pad reaction to viable Mlm. The distribution of responders and non-responders among 12 BXH recombinant inbred strains and linkage analysis in C3H × (C3H × C57BL)F_1 backcross mice indicated that the response gene(s) are linked to the *H*-2 complex and chromosome 17. The same gene(s) also influence host restriction of Mlm multiplication and thus appear to be the first *H*-2-linked gene(s) influencing resistance to a bacterial infection.—Authors' Abstract

Pandya, S. S., Naik, S. S. and Gurnani, S. An attempt to influence nerve degeneration and regeneration by using macrophage cell homogenate. Lepr. India **55** (1983) 237–241.

The effect of the contents of activated macrophages on the degenerative/regenerative process in the mouse sciatic nerve was investigated as a possible model for leprosy. The whole cellular homogenate or saline was injected every week around physically impaired (to bypass the perineurial barrier) and normal nerves. Recovery of the nerve function was monitored clinically and electromyographically. After 14 weeks animals were sacrificed and nerves were processed for histology. The data obtained from 134 experimental and control nerves were rated and analyzed statistically. The course of the nerve regeneration in the physically impaired nerve with and without homogenate was found to be similar. One of the reasons for this could be insufficient concentration of the homogenate in the endoneurial space.—Authors' Abstract

Rayyan, W. and Delville, J. Influence du β-1,3 glucane et d'autres immunomodulateurs d'origine microbienne sur l'infection lépreuse expérimentale chez la souris. [The influence of β-1,3 glucan and other immunomodulators of microbial origin on the experimental leprosy infection in mice.] Acta Leprol. **1** (1983) 93–100. (in French)

The effect of β-1,3 glucan and cell walls of *S. cerevisiae* on one hand and of peptidoglycans from strain LDC 15 and *C. renale* and cell walls of *C. hofmannii* on the other hand have been investigated in the experimental leprosy infection in mice. β-1,3 Glucan, by enhancing the function of the reticulo-endothelial system, is the most active inhibitor of the multiplication of Hansen's bacilli. Peptidoglycan of strain LDC 15 is less active and seems nonspecific.—Authors' English Summary

Satoh, M. Izaki, S., Kon, S. and Izaki, M. Fibrin and collagen deposition and fibroblasts proliferation in granuloma of murine leprosy. Comparison of two mouse strains with different immune reactions. Experientia **39** (1983) 7–10.

Comparative immunofluorescence study with murine lepromas induced in C57BL/6NJcl (immunologically high responder) and CBA/N (low responder) mouse strains revealed that fibrin formation was associated with cell-mediated immune resistance against invasive bacilli. Histochemistry on paraffin sections further elucidated fibroblast proliferation and formation of collagen fibers following fibrin deposition only in murine lepromas with positive host reactions.—Authors' Summary

Epidemiology and Prevention

Antola, M., Liturri, M. and Mercadante, F. F. Programa nacional de control de lepra. Registrado de casos nuevos de lepra (ano 1982) en la capital federal y en la provincia de Buenos Aires. [National program of control of leprosy. Registry of new cases of leprosy (1982) in the federal capital and in the province of Buenos Aires.] Lepra Bol. Epid. Bibliografico **2** (1982) 16–23. (in Spanish)

A total of 226 new leprosy patients were registered in 1982 from the federal capital and the province of Buenos Aires in Argentina. Most cases were between 45–54 years of age. Lepromatous cases made up 57.5% of the total. Only 22 of the cases were from the federal capital and the province of Buenos Aires, 42 cases were from outside the country and the rest were from other parts of Argentina, particularly Chaco (34 cases) and Corrientes (25 cases). Approximately half of the lepromatous patients had received previous treatment. For the country as a whole, there were 946 new cases diagnosed in 1982, mainly in the federal capital and the province of Buenos Aires (226 cases), Chaco (194 cases), Sante Fe (126

cases), and Misiones (102 cases).—(*From* the article)

Husser, J. A. Bilan de la lutte contre la lèpre, menée par le secteur des Grandes Endémies du Cap-Vert dans l'agglomération dakaroise de 1975 à 1979. [Summary of the fight against leprosy in Dakar by the Center for Grandes Endémies of Cap-Vert from 1975 to 1979.] Acta Leprol. **1** (1983) 63–92. (in French)

Study of Hansen's disease registered cases during five years is realized under OMSLEP rules. This population of 1428 patients is observed under "entrance" and "outlet" parameters from the patients' register. The author notices the high prevalence rate, 35.5% and the disability rate which induces a late-track. Looking for the follow-up, the out-ratio is too high and a difference exists between the paucibacillary or multibacillary defaulters.

Dakar area is characterized on Hansen's disease by: a) a low prevalence rate, under 0.5‰; b) a high lepromatous ratio, about 35.5%; c) a low child rate observed between the domiciliary contacts; and d) a constant course of the incidence of Dakar patients, while Senegal presents a decrease of Hansen's population.—Author's English Summary

Kumar, A., Sivaprasad, V., Anbalagan, M., Thangavel, N. and Durgambal, K. Utilization of medical agencies and treatment compliance by urban (Madras) leprosy patients. Lepr. India **55** (1983) 322–332.

The utilization of medical agencies and treatment compliance by 3880 leprosy patients registered with the Government Leprosy Control Unit, Saidapet, Madras, India, were studied. It was observed that 30% of the patients waited for 1.32 (±1.75) years before medical consultation because of their negligence and unawareness of the disease. About 16% and 4% of the patients consulted general hospitals and private practitioners, respectively. The leprosy clinics were most popular; 35% of the patients changed medical agencies. On the average, one patient had consulted 1.47 (±0.51) medical agencies and 1.23 (±0.52) leprosy clinics for treatment of leprosy. Only 45% of the patients attended clinic regularly; others attended irregularly (22.5%) or discontinued (32.4%). The unsuitable clinic timing (morning) was an important factor for defaulting from the clinics. Of the 2625 (67.66%) patients who attended the last clinic, each patient had missed an average of 5.5 (±8.3) DDS tablets in a month.

The implications of these findings and suggestions to improve service utilization with good compliance by patients are discussed.—Authors' Abstract

Nebout, M. Difficultés actuelles de la lutte contre la lèpre et propositions de relance des campagnes dans les pays d'Afrique francophone. [Actual difficulties of the struggle against leprosy and proposals for the countries in the French speaking regions of Africa.] Acta Leprol. **1** (1983) 159–170. (in French)

In a great number of francophone African countries, leprosy control is failing. Early case finding and contact detection have become deficient. On the other hand, some countries which have maintained multifunction mobile sanitary structures, issued from the French Service of Grandes Endémies Organization, record good results in leprosy control. Early case finding is particularly important since 80% of new leprosy cases are discovered in systematic and periodic screening in nonleprosy contact populations. The causes of failure of leprosy control are reviewed and resolutions are proposed for the improvement of existing health services. Priority should be given to strengthening existing mobile services: either highly multifunctional teams under Grandes Endémies Service supervision or traveling medical workers based in dispensaries integrated into primary health care structures. These measures must co-exist with increasing contributions from general or private clinics, increased awareness of sanitary and administrative authorities, and good public education. It is necessary that each African country chose a national leprosy medical officer for leprosy control. It might be advisable to follow the example of some countries which have achieved positive results in leprosy control by an operational strategy, adapted to African conditions, and sustained by aid from ILEP organizations.—(*Adapted from* English summary)

Rehabilitation

Hamilton, J. Deformity prevention in the field: A systematic approach. Lepr. Rev. **54** (1983) 229–237.

The importance of preventing deformity among our patients by detecting and treating neuritis is stated. The process of "silent neuritis" which leads insidiously to deformity in a number of leprosy patients is defined, and the importance of its recognition and early treatment in the field situation is stressed. An approach adopted primarily for this purpose, consisting of simple motor, sensory and nerve palpation tests repeated at varying intervals, whose results are recorded briefly and acted upon appropriately, is described. The benefits observed and problems encountered in implementing this approach are described, and areas of training and management on which its success depends are discussed.—Author's Summary

Kulkarni, V. N. and Mehta, J. M. Tarsal disintegration (T.D.) in leprosy. Lepr. India **55** (1983) 338–357.

Tarsal disintegration (TD) in leprosy has been a challenge as far as its prevention is concerned. It is, no doubt, a complex and little understood phenomenon influenced by many factors. In this study made at Dr. Bandorawalla Leprosy Hospital, Kondhawa, India, factors such as insensitivity, loss of protective reflex, infection, lepromatous infiltration of bones, etc., have been taken into consideration, but more emphasis is laid on the biomechanical factors (i.e., altered muscle pulls due to muscular paralysis resulting in imbalance) and the resulting change in weight bearing areas and weight transmission lines.

Sixteen cases of neuropathic feet were examined clinically and radiologically. All were burnt out cases of tuberculoid and borderline tuberculoid leprosy excepting one that was active and of the lepromatous type. Tracings made from actual radiographs of the patients were studied. It was found that apart from insensitivity, biomechanical factors play a lot of importance in accentuating the process of TD. The changes are predominantly seen in the tuberculoid type of leprosy. Attempts have been made to understand this process more clearly by drawing conclusions based on the kinetic and kinematic analysis of the normal human foot and comparing it with neuropathic feet.—Authors' Abstract

Kumar, A. and Anbalgan, M. Socio-economic experiences of leprosy patients. Lepr. India **55** (1983) 314–321.

Two hundred twenty-five adult leprosy patients were interviewed to study their socio-economic experiences, and various aspects of their lives. It was observed that 17.34%, 14.33% and 45.78% of patients experienced negative reactions from their families, spouses and society members, respectively. Out of 79 unmarried patients, 53 (67.1%) attributed leprosy as the only reason for not getting a partner for marriage. Out of 146 married patients, 34 (23.3%) were not living with their spouses; this also included 9 (6.2%) patients deserted by their partners. Leprosy uprooted 44 (13.55%) patients from their residences, of whom 27 settled in a leprosy village/settlement. The occupational status of 104 (46.22%) patients was adversely affected due to leprosy, of whom 43 became dependents and 17 beggars. Monthly income of 115 (51.1%) patients reduced to the extent of 84%, after getting leprosy. The social prejudice and deformities due to leprosy have played key roles in socio-economic deterioration of patients. The leprosy control program (LCP) needs to be implemented more efficiently and effectively, with active involvement of communities. The socio-medical units, if included in LCP, may be utilized more effectively to prevent the socio-economic dehabilitation of patients, as well to tackle the abnormal psychological behavior of patients.—Authors' Abstract

Other Mycobacterial Diseases and Related Entities

Ahmed, A. R. and Blose, D. A. Delayed-type hypersensitivity skin testing. A review. Arch. Dermatol. **119** (1983) 934–945. (242 references)

Delayed hypersensitivity skin testing is based on the reaction that occurs in response to the intradermal injection of an antigen. The technique, interpretation, and pitfalls of interpretation of delayed hypersensitivity skin testing are presented. The histologic findings and immunologic mechanisms characterizing this form of immunologic response are discussed. The diagnostic and clinical importance of reactivity to recall skin test batteries, common microbial antigens, dinitrochlorobenzene, and tumor-associated antigens is also discussed.—Authors' Abstract

Cheers, C. and Ho, M. Resistance and susceptibility of mice to bacterial infection. IV. Functional specificity in natural resistance to facultative intracellular bacteria. J. Reticuloendothel. Soc. **34** (1983) 299–309.

The effect of opsonic antibody on resistance or susceptibility of three strains of mice, C57Bl/10, BALB/c, and CBA to the intracellular bacteria *Listeria monocytogenes, Salmonella typhimurium,* and *Brucella abortus* was tested. Bacteria were opsonized by serum treatment before their injection into mice, or the mice were preimmunized by injection with alcohol-killed bacteria which induces antibody without macrophage activation. Antibody did not increase the rate of clearance of *Listeria* from the bloodstream, nor did it affect the subsequent growth of that organism in the spleen and liver. Blood clearance of *S. typhimurium* and of *B. abortus* was increased by preopsonization with specific antibody, indicating that opsonins were a limiting factor in resistance to these two bacteria. However, neither opsonization before infection nor immunization with alcohol-killed vaccines had any effect on the strain distribution of resistance/susceptibility, which differs for each of the three intracellular pathogens. Thus, even in the presence of adequate opsonization the three strains of mice showed different patterns of resistance/susceptibility to *Listeria, S. typhimurium,* and *B. abortus.* This implies that each has a unique cellular mechanism of early nonspecific resistance.—Authors' Abstract

Handman, E. and Hocking, R. E. Stage-specific, strain-specific, and cross-reactive antigens of Leishmania species identified by monoclonal antibodies. Infect. Immun. **37** (1982) 28–33.

BALB/c mice were infected with *Leishmania tropica* (strain LRC-L137) promastigotes. Forty days later the mice, which were now showing large ulcers at the site of infection, were injected intraperitoneally with 5×10^7 heat-killed *L. tropica* promastigotes. Three days after this the spleen cells from these mice were fused with NS-1 myeloma cells and hybridomas producing monoclonal antibodies were subsequently isolated. The anti-*Leishmania* antibodies were detected in a solid-phase radioimmunoassay with promastigotes as antigen.

Nine monoclonals were isolated which bound to promastigotes. They belonged to the IgG isotypes IgG2a, IgG2b or IgG3. By the indirect fluorescent antibody test, all 9 were shown to bind to the membrane of living promastigotes, 8 also bound to amastigotes, and 4 detected parasite antigen on the surface of infected macrophages as well as reacting with amastigotes and promastigotes. Treatment of promastigotes with two of the monoclonals before the promastigotes were added to monolayers of macrophages resulted in significantly fewer parasites in the macrophages 24 hr later: the inhibitory activity of these two monoclonals might result from some interference with the transformation of promastigotes to amastigotes. The inhibitory monoclonals were also distinguished from the other seven by the fact that they would only bind to promastigotes from cases of simple cutaneous leishmaniasis and not to parasites from cases of leishmaniasis recidiva or diffuse cutaneous leishmaniasis or other species of *Leishmania.* Some of the monoclonals recognized antigens common to *L. tropica, L. donovani* and *L. mexicana* and one monoclonal reacted with antigens common to most *Leishmania* spp. and *Crithidia fasciculata.* Some preliminary attempts were

made to identify the nature of the target antigens by treating promastigotes with sodium periodate, pronase, subtilisin or sodium metaperiodate before they were allowed to react with the monoclonal antibodies. The results suggested that the surface antigens were proteins and that carbohydrate may play a part in the structure of the antigen molecules.

The use of monoclonal antibodies in the study of various aspects of *Leishmania* spp. is discussed.—R. S. Phillips (*From* Trop. Dis. Bull.)

Hasper, M. F. Chronic cutaneous lupus erythematosus. Thalidomide treatment of 11 patients. Arch. Dermatol. **119** (1983) 812–815.

Eleven patients with severe, chloroquine-resistant chronic cutaneous lupus erythematosus were treated with oral thalidomide. Seven patients responded with a complete remission, and two patients' conditions improved significantly. One patient did not respond well to therapy and another patient had to be withdrawn from the treatment trial because of side effects. Six patients, who relapsed after discontinuing thalidomide treatment, were re-treated with maintenance drug dosages and achieved good results with no further relapses or exacerbations. In all subjects the side effects from the thalidomide were minor and reversible.—Author's Abstract

Jagannath, C. and Sengupta, D. N. Serology of tuberculosis. I. Standardization of passive haemagglutination test for the measurement of antibodies to *Mycobacterium tuberculosis*. Tubercle **64** (1983) 193–200.

A passive hemagglutination (PHA) test has been described for the measurement of antibodies to *Mycobacterium tuberculosis* (H37Rv). Red cells stabilized successively with pyruvic aldehyde and glutaraldehyde were sensitized with soluble antigens from *M. tuberculosis* and used as reagents in the PHA test. In mice and rabbits immunized with *M. tuberculosis* antigens, the PHA test could reliably measure antibody response, following both primary and secondary immune stimuli. The sensitized red cells used for the PHA test were found to retain their hemagglutinating potency for eight weeks and four months when stored appropriately at 4°C and −20°C, respectively. The test was found to be satisfactory in terms of sensitivity, simplicity, and reproducibility.—Authors' Summary

Jagannath, C. and Sengupta, D. N. Serology of tuberculosis. II. Measurement of antibodies to *Mycobacterium tuberculosis* by a passive haemagglutination test in human tuberculosis. Tubercle **64** (1983) 201–210.

A simple and sensitive passive hemagglutination (PHA) test has been evaluated in the serology of human tuberculosis. Double aldehyde stabilized red cells were sensitized with cell extracts and PPD antigens from *Mycobacterium tuberculosis* (H37Rv) and used as reagents in the test. The study was conducted on sera from 71 bacteriologically confirmed cases of tuberculosis and their controls, inclusive of 59 healthy blood donors and 28 nontuberculous chest disease patients. In addition, 318 random samples of sera and 107 finger-prick blood samples collected on filter papers from apparently healthy people were examined. For comparative evaluation, tuberculous patients' sera were examined by enzyme-linked immunosorbent assay (ELISA) and crossed immunoelectrophoresis (CIE). The distribution of IgG and IgM type antimycobacterial antibodies (AMA) in tuberculous patients' sera was evaluated by a modified PHA test.

The results of the study indicated that the PHA test was a sensitive method for the quantitation of antibodies, which could be demonstrated in all groups of sera studied. The PHA test and ELISA with the antigens used were not found to be specific enough for the serodiagnosis of tuberculosis; the results indicated the need to investigate several immunological approaches for this purpose. Both tests did differentiate between the mean AMA levels of tuberculous patients and their controls and both showed treated and relapsed cases of tuberculosis to contain higher serum levels of antibodies than did new cases. Both tests were found to be more sensitive than CIE with the intermediate gel technique. The PHA test was found to be sensitive enough for the measurement of antibodies in finger-prick blood samples, indicating its potential for field studies.—Authors' Summary

Primary resistance to antituberculosis drugs—United States. Morbidity Mortality Weekly Rep. **32** (1983) 521–522.

From 20 March 1975 through 30 September 1982, 20 city and state laboratories throughout the United States submitted 12,157 mycobacterial cultures to the Centers for Disease Control (CDC) for drug susceptibility testing as part of a survey of primary drug resistance (PDR). PDR is defined as drug resistance among persons with tuberculosis (TB) who are not known to have had prior treatment with antituberculosis (anti-TB) drugs. *Mycobacterium tuberculosis* organisms resistant to one or more anti-TB drugs were isolated from 6.9% of cases surveyed.

A marked decline occurred in the percentage of PDR over the period of the survey, and large differences were noted by race/ethnicity. There is a generally declining trend and the markedly higher percentages of PDR among Asian and Hispanic cases (overall percentages were 14.8% Asians; 11.5% Hispanics; 6.1% blacks; 4.9% whites; and 4.1% American Indians). Too few cultures were submitted from American Indians for a meaningful display of the secular trend for this group.

A highly significant ($p = 0.005$) inverse relationship was noted between age and percentage of PDR. The PDR percentages ranged from 14.0% for ages 0–10 years to 3.6% for ages 11–99 years. PDR percentages were highest for isoniazid (4.0%), streptomycin (3.8%), and ethionamide (1.1%). Percentages for other drugs tested [*p*-aminosalicylic acid (PAS)], rifampin, ethambutol, kanamycin, capreomycin, and cycloserine) were less than 1%.

There are variations in percentages of PDR by geographic area. Even after adjustment by logistic regression modeling for differences between areas in race/ethnic and age distributions, there were substantial and statistically significant differences among area-specific percentages, ranging from 3.9% for Washington state to 11.3% for the border region of south Texas surrounding Harlingen.—(*From* the article)

Ridell, M. Cross-reactivity between *Mycobacterium tuberculosis* H37Rv and various *Actinomycetes* and related organisms. Tubercle **64** (1983) 211–216.

One hundred forty-one strains of *Actinomycetales* and related organisms were investigated by immunodiffusion for the presence of antigens which crossreact with the antigens of *M. tuberculosis* H37Rv. The test strains comprised 86 different species names and 20 different genus names; they were mainly environmental organisms isolated from soil, plants, animals and such like. More than 90% of these strains were shown to have one or more antigens in common with the tubercle bacillus, and 77% had two or more antigens in common with this organism. Certain strains, of *Nocardia* and *Rhodococcus,* demonstrated abundant crossreactivity with the tubercle bacilli, sharing up to five and six precipitinogens, respectively.—Author's Summary

Tuberculosis—United States, 1982. Morbidity Mortality Weekly Rep. **32** (1983) 478–480.

In 1982, 25,520 cases of tuberculosis (TB) were reported to the Centers for Disease Control (CDC), Atlanta, Georgia, U.S.A. for a case rate of 11.0 per 100,000 population. Compared with 1981, this represents a 6.8% decrease in the number of cases reported and a decline of 7.6% in the case rate.

Rates for the 50 states ranged from 25.4/100,000 in Hawaii to 2.0/100,000 in Wyoming. The rate increased in 13 states, remained unchanged in 2, and decreased in 35 states and the District of Columbia. The rate among persons living in 56 cities of more than 250,000 population was 22.1/100,000—twice the national rate and 5.6% less than the rate for the same cities in 1981. Urban rates ranged from 61.4/100,000 in Miami, Florida, to 3.8/100,000 in Omaha, Nebraska. The rate increased in 21 of the country's 56 largest cities. Eight cities had rates at least three times the national rate: Miami, Florida; Newark, New Jersey; San Francisco, California; Houston, Texas; Atlanta-Fulton County, Georgia; Washington D.C.; Chicago, Illinois; and Honolulu, Hawaii.

Of the 25,520 TB cases reported in 1982, *Mycobacterium tuberculosis* was isolated in 19,050. The proportion of culture-positive cases increased from 70.5% of total cases in 1981 to 74.6% in 1982.—(*From* the article)